Pulmonary Nocardiosis with Bilateral Diffuse Granular Lung Shadows in a Patient with Subcutaneous Panniculitic T-cell Lymphoma

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Abstract

A 40-year-old woman undergoing prednisolone and cyclosporine therapy for subcutaneous panniculitic T-cell lymphoma complained of a cough for a few weeks. A chest X-ray revealed bilateral diffuse granular shadows. Additionally, the patient was discovered to have multiple subcutaneous abscesses. Gram-stained smears of sputum and pus from the abscess showing branched gram-positive rods led to a diagnosis of pulmonary nocardiosis with dissemination to the lungs and subcutaneous tissues. Combination therapy consisting of sulfamethoxazole/trimethoprim and panipenem/betamipron produced rapid improvement of radiographic abnormalities. It is suggested that pulmonary nocardiosis should be considered in the differential diagnosis of diffuse granular shadows on chest X-rays, especially in immunocompromised patients.

Key words: Nocardia farcinica, gram stain, hematogenous dissemination, immunocompromised host

Introduction

Nocardiosis is a disease caused by a species of the family Nocardiaceae, which are aerobic, weakly acid-fast and gram-positive rods showing delicate branching filamentous hyphae. Nocardial infection may be localized to the skin or may involve the lungs, and frequently disseminates to other sites. It’s prevalence has increased as an opportunistic infection in immunocompromised hosts with recent increases in immunosuppressive therapy (1–3). Pulmonary nocardiosis can produce a variety of radiographic abnormalities, however, a case with bilateral diffuse granular shadows on chest X-ray, mimicking miliary tuberculosis, is rare. In this report, we describe a case of pulmonary nocardiosis presenting with bilateral diffuse granular lung shadows on the chest X-ray in a patient with subcutaneous panniculitic T-cell lymphoma.

Case Report

In December 25, 2000, a 40-year-old woman was referred to our division for investigation of a consolidation in the right upper lung field on her chest X-ray. She had a few weeks’ history of a mild productive cough.

In 1992, she suffered reddish and painful subcutaneous nodules on both legs. She was diagnosed as having cytophagic histiocytic panniculitis (CHP) at the dermatology department in our hospital, and prednisolone therapy (60 mg per day) was initiated. Her symptoms gradually improved, and by 1996 the dose of prednisolone was tapered to 15 mg per day. In February 2000, her symptoms recurred and the subcutaneous panniculitic T-cell lymphoma was identified via detailed histological examination of the biopsied subcutaneous nodule. CHOP (cyclophosphamide, doxorubicin, vincristin, and prednisolone) therapy was initiated, alleviating her symptoms. Prednisolone (30 mg per day) and cyclosporine (200 mg per day) were used to maintain her stable condition. The patient also had a history of diabetes mellitus since 1999. Her hemoglobin A1c was kept between 5.9 and 6.2% by diet therapy during the previous 6 months.

Because the consolidation on her chest X-ray was initially suspected of representing a bacterial pneumonia, the patient was treated with faropenem beginning on December 25, 2000. After noting neither subjective symptomatic improvement nor improvement of chest X-ray findings, the antibiotic was changed to levofloxacin on January 8, 2001. On January 10, 2001, fiberoptic bronchoscopy was performed. Routine culture of bronchoalveolar lavage fluid (BALF) obtained from the
right bronchus (B) was negative and its smear was negative for acid-fast bacilli. Gram stain of BALF was not performed at that time. Specimens obtained from transbronchial lung biopsy revealed nonspecific inflammatory findings. In the end of January 2001, multiple subcutaneous masses appeared on her back and right lower thigh, enlarging rapidly. Bilateral diffuse small granular shadows also appeared in her chest X-ray. She was admitted to our division for further examination and therapy on February 2, 2001.

On physical examination, her temperature was 37.1°C, pulse rate was 102 beats/min, and respiration 23 breaths/min. Blood pressure was 150/90 mmHg. Mild inspiratory crackles were audible, predominantly in the right lower lung field. Two soft, subcutaneous masses measuring 30×15 cm and 15×15 cm were noted on her back, and another on her right lower thigh measured 10×15 cm. Neurological findings were normal. Laboratory tests on admission showed elevation of the white blood cell count (15,600/μl, with 97% neutrophils, 1% lymphocytes, and 2% monocytes), increased C-reactive protein (10.5 mg/dl), and accelerated erythrocyte sedimentation rate (59 mm/h), suggesting moderate inflammation. Mild anemia (RBC: 332×10⁶/μl), and a modest decrease in the levels of total protein (5.6 g/dl) and albumin (2.8 g/dl) were seen. The level of lactate dehydrogenase (LDH) was markedly increased (1,182 mU/ml). Impairment of lymphocyte blastogenic responses to concanavalin A and phytohemagglutinin, indicating dysfunction of cell-mediated immunity, was noted. A PPD test yielded negative results.

A chest X-ray taken on admission revealed a wedge-shaped area of consolidation with irregular hyperlucent regions in the right upper lung field and bilateral diffuse granular shadows (Fig. 1). A CT showed diffuse granular pulmonary nodules bilaterally, and destructive cavitory changes in the right segment (S2) (Fig. 2). Hilar and mediastinal lymph nodes were not swollen. CT scan of her back also revealed multiple masses exhibiting homogeneously low internal density, indicative of subcutaneous abscesses (Fig. 3). Drainage of one of the subcutaneous abscesses yielded a large quantity of grayish-white pus. A smear of sputum was negative for acid-fast bacilli. However, a gram-stained smear of sputum revealed a few gram-positive rods showing delicate branching filamentous hyphae, a characteristic unique to Nocardia species (Fig. 4). Similar findings were also seen in the gram-stained smear of pus from the abscess.

Based on the unique appearance of the gram stains, the pa-
Patient was diagnosed as having pulmonary nocardiosis with dissemination to the lungs and subcutaneous tissues. Oral administration of sulfamethoxazole/trimethoprim (3,200 mg/640 mg per day) and intravenous administration of panipenem/betamipron (1 g per day) were immediately initiated. Clinical symptoms and laboratory findings showed rapid improvement. Two weeks into the therapeutic regimen, the patient’s C-reactive protein level decreased to negative, after which panipenem/betamipron was stopped and the dose of sulfamethoxazole/trimethoprim was reduced (1,600 mg/320 mg per day). The diffuse granular shadows were nearly absent 3 weeks later.

Pathogens isolated from sputum and abscess were ultimately identified as Nocardia farcinica (N. farcinica) on the basis of its biochemical nature. In addition, the same pathogens were isolated from blood obtained on admission. Furthermore, colonies of acid-fast bacteria unlike tubercle bacilli were noted on the 4-week reading of the BALF culture, obtained prior to admission. Pathogens from these colonies were also identified as N. farcinica. The patient was discharged on the 22nd day of hospitalization. She continues on sulfamethoxazole/trimethoprim therapy, and remains in good condition.

Discussion

Pulmonary nocardiosis is a subacute or chronic pneumonia caused by a species of the family Nocardiaceae. N. asteroides is the most predominant and N. brasiliensis the next most common species to be isolated. N. farcinica, which previously could not be distinguished from N. asteroides has also been reported to cause pulmonary diseases (4). Although about half of all reported cases of nocardiosis are in healthy people, it is more frequently recognized as an opportunistic infection in immunocompromised patients with underlying disease, organ transplants, lupus erythematosus or lymphoma or in those receiving long-term steroid therapy (5-9).

Table 1. Antimicrobial Susceptibilities of an Isolated Strain of N. farcinica

<table>
<thead>
<tr>
<th>Agents</th>
<th>MIC (µg/ml)</th>
</tr>
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<tbody>
<tr>
<td>PIPC</td>
<td>&gt;128</td>
</tr>
<tr>
<td>CAZ</td>
<td>&gt;128</td>
</tr>
<tr>
<td>CPR</td>
<td>4</td>
</tr>
<tr>
<td>CPZ</td>
<td>32</td>
</tr>
<tr>
<td>AZT</td>
<td>&gt;64</td>
</tr>
<tr>
<td>IPM/CS</td>
<td>0.5</td>
</tr>
<tr>
<td>PAPM/BP</td>
<td>0.5</td>
</tr>
<tr>
<td>GM</td>
<td>32</td>
</tr>
<tr>
<td>AMK</td>
<td>1</td>
</tr>
<tr>
<td>MINO</td>
<td>0.5</td>
</tr>
<tr>
<td>ST</td>
<td>0.5</td>
</tr>
<tr>
<td>CPFX</td>
<td>4</td>
</tr>
<tr>
<td>LVFX</td>
<td>8</td>
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</tbody>
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Pulmonary nocardiosis is usually contracted when organisms are inhaled from contaminated soil. About half of all cases of pulmonary nocardiosis have disseminated diseases outside the lungs (10). Central nervous system involvement is the most common manifestation of disseminated disease. In the present case, Nocardia was ultimately isolated from BALF obtained from the right B2. Therefore, it was proposed that the pulmonary lesion in the right S2 represented a primary lesion from which hematogenous dissemination to the lung, skin and subcutaneous tissues originated. This case demonstrated no neurological phenomena.

Pulmonary nocardiosis can produce a variety of radiographic abnormalities (11, 12). The most common findings are air-space consolidations and large irregular nodules, often cavitary. Few cases similar to this one have been reported regarding the findings of diffuse granular shadows mimicking miliary tuberculosis (11, 13).

Nocardia species grow more slowly than most bacterial pathogens on nonselective culture media; their colonies may not be apparent for days or weeks (10, 14). This explains why we initially failed to isolate the pathogen from routine BALF culture. Therefore, it is crucial to be on alert for the suspicion of nocardiae, and run cultures longer than usual to maximize the likelihood of isolating this organism. Nocardia species can be isolated on nonselective mycobacterial media because of their weak acid fastness; however, this requires one or two months for detection. For prompt diagnosis, a microscopic examination of specimen smears is useful. In this case, the morphology of organisms in the gram stain was characteristic enough to allow them to be distinguished from other bacteria,
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mycobacteria and fungi, thus enabling us to select appropriate antibiotics for the treatment.

Nocardiosis is often fatal with inappropriate treatment. The prognosis of pulmonary nocardiosis is poor and is worse for patients with the following findings: symptoms of fewer than 3 weeks' duration; disseminated infection, especially brain abscess; history of prior corticosteroid therapy; status-post antineoplastic therapy (9, 15, 16). Sulfamethoxazole/trimethoprim is the drug of choice. Several other drugs, including minocycline, amikacin, imipenem and new quinolones, have been shown to be efficacious in the treatment of nocardiosis (6, 17, 18). In the present case, the combination of sulfamethoxazole/trimethoprim and panipenem/betamipron was highly effective. Later, we confirmed that an isolated strain of *N. farcinica* had high susceptibility to both drugs *in vitro* (Table 1). Because the present patient must continue immunosuppressive therapy for treatment of her underlying disease, antibiotic therapy should be continued at least for 1 year (19).

Pulmonary nocardiosis is expected to be a more frequently encountered disease due to the increasing use of immunosuppressive therapies. The disease should be considered in the differential diagnosis of diffuse granular shadows on chest X-ray, especially in immunocompromised patients. Microscopic examination of specimen smears is an important tool for prompt diagnosis.

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References