

Successful treatment of pulmonary nocardiosis with fluoroquinolone in bronchial asthma and bronchiectasis

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Abstract

A 72-year-old Japanese woman was admitted at Saga University Hospital for fever, malaise, and productive cough. Six years ago, she had been diagnosed with bronchial asthma and was treated with inhaled corticosteroids. Chest radiograph and computed tomography on admission showed infiltrates in the right middle lobe, a mass lesion in the left lower lobe, and bronchiectasis in both lower lobes. Sputum examination showed Gram-positive rods with phagocytosis by neutrophils. These bacilli were identified as *Nocardia otitidiscaviarum* by 16S ribosomal RNA sequencing. Therefore, she was diagnosed with pulmonary nocardiosis and was treated with trimethoprim/sulfamethoxazole (TMP-SMX) and minocycline (MINO). However, she had to discontinue these antibiotics because of severe nausea and anorexia and instead was treated with fluoroquinolone for 6 months. There was resolution of the disease thereafter. Pulmonary nocardiosis with bronchial asthma and bronchiectasis can be successfully treated with fluoroquinolone, an alternative to TMP-SMX or MINO.

Introduction

Nocardia is a family of aerobic Gram-positive bacteria that comes from the order Actinomycetales. Nocardiosis mainly occurs as an opportunistic infection, but it can also affect immunocompetent hosts. Pulmonary nocardiosis is an infrequent but clinically severe disease. The risk factors for nocardiosis were reported to be intake of immunosuppressive therapy, including systemic corticosteroids and underlying pulmonary disease, such as chronic obstructive pulmonary disease (COPD) and bronchiectasis [1].

Case Report

A 72-year-old Japanese woman was admitted to our hospital for fever, malaise, and productive cough. Two weeks before admission, she had been infected with influenza A and had been treated with oseltamivir 150 mg/day for 5 days. She had recovered from influenza, but had productive cough and low-grade fever. She had a history of bronchial asthma at the age of 66 years and had been on combination of inhaled corticosteroid (ICS) and

long-acting β_2 agonist (fluticasone propionate 1000 $\mu\text{g}/\text{day}$ and salmeterol 100 $\mu\text{g}/\text{day}$) for 2 years. The status of her asthma was partly controlled, with a few exacerbations requiring systemic corticosteroid treatment. She had never smoked and had no history of dust exposure.

On admission, her body temperature was 38.0°C and coarse crackles were heard at the left lower lung field. Other physical examination findings including consciousness and skin were normal. Her laboratory findings on admission showed a white blood cell count of 13,900/ μL with 83.7% neutrophils, haemoglobin of 11.8 g/dL, and C-reactive protein of 12.08 mg/dL. Other blood examinations and arterial blood gas were within normal range. Chest radiograph showed segmental infiltration in the bilateral lower lung fields (Fig. 1A). Chest computed tomography (CT) showed irregularly shaped solid opacity in the right middle lobe, a cavitary mass in the left lower lobe, and bronchiectasis in both lower lobes (Fig. 1B,C). Sputum examination showed numerous radial-shaped Gram-positive rods with phagocytosis by neutrophils; these bacilli were weakly acidic on Kinyoun stain (Fig. 2). After 16S

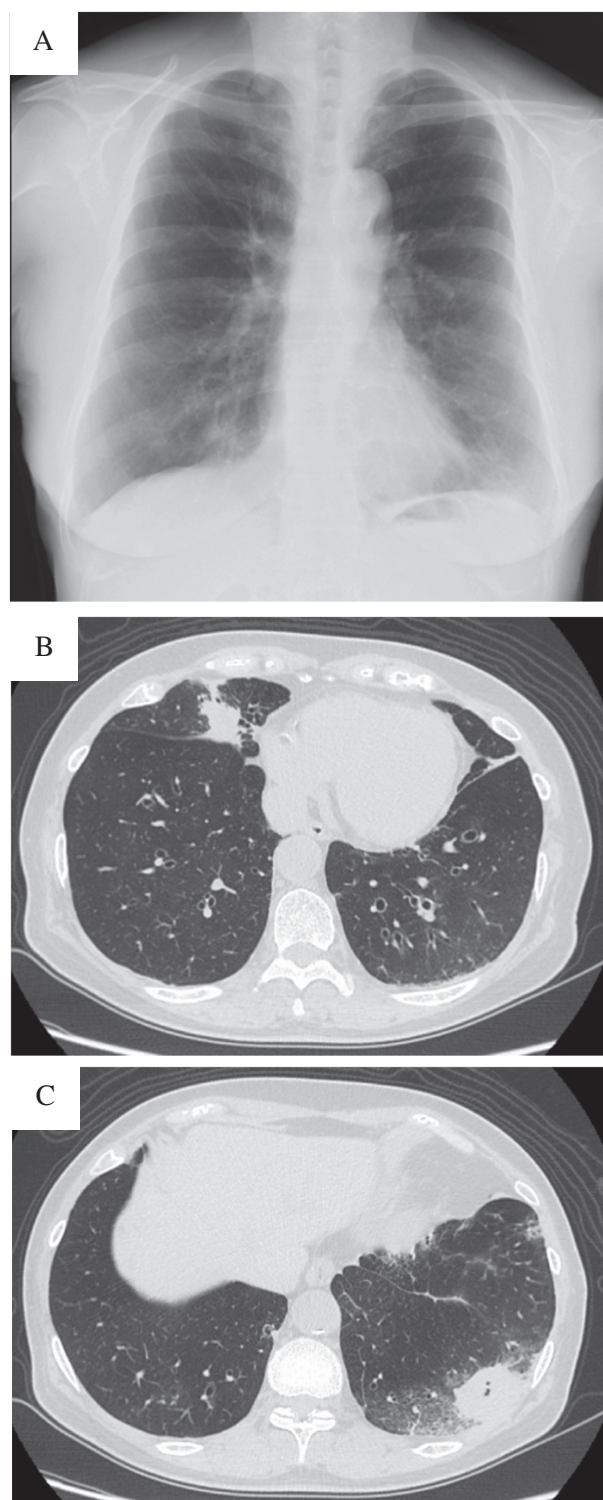


Figure 1. Chest radiograph and computed tomography (CT) findings of a 72-year-old woman with pulmonary nocardiosis. (A) Chest radiograph shows pulmonary infiltrates in the bilateral lower lung fields. (B) Chest CT shows an irregularly shaped solid opacity in the right middle lobe, a cavitary mass in the left lower lobe and bronchiectasis in both lower lobes.

ribosomal RNA gene sequencing, these bacilli were identified as *Nocardia otitidiscaviarum*. Culture of sputum collected for three consecutive days identified the identical bacteria. She was diagnosed with pulmonary nocardiosis because there was no involvement of other organs, such as the central nervous system.

She was started on trimethoprim/sulfamethoxazole (TMP-SMX) (2400 mg/480 mg per day) and ceftriaxone (2 g/day) for the first 5 days. Results of drug susceptibility showed an insufficient minimum inhibitory concentration (MIC) of 16 µg/mL for ceftriaxone; the MICs (µg/mL) for the other antibiotics were 2.0 µg/mL for TMP-SMX, 1.0 µg/mL for minocycline (MINO), 0.25 µg/mL for imipenem/cilastatin (IPM/CS), and 1.0 µg/mL for levofloxacin (LVFX). Ceftriaxone was then shifted to MINO 200 mg/day. However, after 2 weeks of treatment, she had severe nausea and anorexia, which were attributed to TMP-SMX. Treatment was changed to MINO monotherapy, but there was persistence of nausea and anorexia for 2 more weeks. Intravenous IPM/CS was offered as the next option, but the patient did not consent to this treatment because of her unwillingness to be hospitalized. Therefore, treatment was shifted to LVFX 500 mg once daily. After 1 month of treatment, her symptoms and abnormal chest radiological findings improved. She was advised to continue treatment with LVFX for 6 months. One year after treatment, she had no recurrence of pulmonary nocardiosis.

Discussion

Pulmonary nocardiosis may be caused by bacterial species, including *Nocardia asteroides*, *Nocardia brasiliensis*, *Nocardia farcinica*, *Nocardia nova*, and *N. otitidiscaviarum* [2]; the present case was due to *N. otitidiscaviarum*, which is rare. Jiang et al. reported a review of 23 cases with nocardiosis by *N. otitidiscaviarum*. Among these 23 cases, there were 11 cases of lymphocutaneous (48%), five cases of pulmonary (22%), two cases of brain (9%), one case of pyothorax (4%) infection, and four cases of disseminated infections (17%) [3]. Other previous study on the clinical and microbiological characteristics of 113 patients with nocardiosis in Taiwan showed that only three cases (2.7%) were caused by *N. otitidiscaviarum*; these included two pulmonary infections and one cutaneous infection without dissemination [4]. Similar to the present case, these three patients had high MIC for TMP-SMX, which indicated resistance. The radiological manifestations of pulmonary nocardiosis are infiltration, ground-glass shadow, cavity, and pleural effusion [5]. Pulmonary nocardiosis affects immunocompromised hosts or individuals with underlying chronic pulmonary disease. The risk factors have been reported to be malignancy, organ transplantation, AIDS,

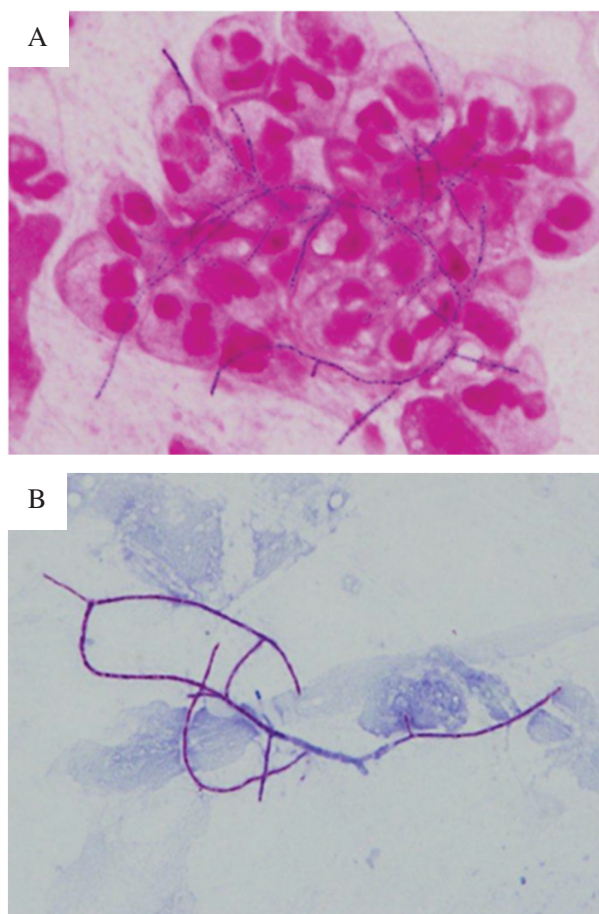


Figure 2. Microscopic findings of sputum in a 72-year-old woman with pulmonary nocardiosis. (A) Gram's stain shows radial Gram-positive rods with phagocytosis by polymorphonuclear leukocytes ($\times 400$). (B) These bacilli were weakly acidic on Kinyoun stain ($\times 400$).

and systemic corticosteroid treatment [1]. Chronic pulmonary diseases, including COPD, bronchiectasis, pneumoconiosis, alveolar proteinosis and bronchial asthma, were also reported as risk factors for pulmonary nocardiosis. In particular, COPD and bronchiectasis were associated with a high incidence of pulmonary nocardiosis, whereas only a few cases of bronchial asthma have been reported. Although nocardia is not part of the normal flora in humans, it can colonize the respiratory tract of patients with malignant tumours, pulmonary tuberculosis, cystic fibrosis, and bronchial asthma. It has been reported that use of high-dose ICS in COPD and bronchial asthma increased the risk for developing pneumonia [6]. In that study, a relationship was found between the ICS dose and risk of pneumonia or lower respiratory tract infection (LRTI). Patients with asthma receiving the highest strength of ICS ($\geq 1000 \mu\text{g}/\text{day}$) had a 2.04 increased risk of pneumonia or LRTI compared with those with asthma

who did not receive ICS [6]. This case had a preceding influenza virus infection, which could have damaged the airway epithelium and predisposed the patients to acquire pulmonary nocardiosis [7]. We considered that the combination of preceding influenza infection, bronchiectasis, and bronchial asthma and use of high-dose ICS in this patient probably aggravated the immunologically deteriorated airway, making its normal defences against nocardia weak.

TMP-SMX is the first-line treatment for pulmonary nocardiosis. Ceftriaxone, IPM, amikacin, and MINO are also used as alternative treatment [8]. In this case, TMP-SMX and MINO were not continued because of adverse effects. Fortunately, treatment with fluoroquinolone for 6 months was successful without relapse. As demonstrated by few previously reported cases, fluoroquinolones can be used in pulmonary nocardiosis, depending on drug susceptibility results and oral bioavailability [9,10]. It also has the advantage in terms of medical economics because it may be given on a prolonged outpatient basis.

In conclusion, fluoroquinolone might be an effective alternative treatment for pulmonary nocardiosis patients who cannot tolerate the adverse effects of TMP-SMX or MINO.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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