Disseminated Nocardiosis Caused by *Nocardia concava* with Acute Respiratory Failure and Central Nervous System Involvement Treated with Linezolid

Naomi Kobayashi¹, Naoko Sueoka-Aragane¹, Natsuko Naganobu¹, Hitomi Umeguchi¹, Koji Kusaba², Zenzo Nagasawa³, Katsukiyo Yazawa³, Tohru Gono³, Shinya Kimura¹ and Shinichiro Hayashi¹

**Abstract**

*Nocardia concava* was identified as a new species in 2005; however, the clinical manifestations of *Nocardia concava* infection have yet to be clarified. We herein present the case of an immunosuppressed patient who developed disseminated nocardiosis caused by *N. concava* with multiple abscesses in the lungs, cutis, subcutaneous tissue, skeletal muscles and kidneys accompanied by central nervous system involvement, including meningitis and ventriculitis. The patient was cured with appropriate treatment including linezolid after testing for susceptibility. Linezolid should be considered as an alternative agent for treating disseminated nocardiosis because of its effective distribution to multiple sites.

**Key words:** *Nocardia concava*, disseminated nocardiosis, linezolid, 16S rRNA

(Intern Med 51: 3281-3285, 2012)

(DOI: 10.2169/internalmedicine.51.7733)

**Introduction**

*Nocardia concava* was first isolated in two cases of cutaneous infection in Japan and was identified as a new species in 2005 (1). A case of systemic nocardiosis caused by *N. concava* in which multiple abscesses were observed in the lungs and liver was first reported in China (2). In spite of improvements achieved with combination antibiotic therapy, that patient died due to deterioration as a result of infection and multiple organ failure. Since that case is the only reported case of nocardiosis caused by *N. concava*, the clinical manifestations of *N. concava* infection have not been clarified. In addition, the antimicrobial susceptibility patterns of *Nocardia* vary depending on the species (3-5). Resistance to β-lactam agents varies between 20% and 50%, although β-lactamase activity is observed in all *Nocardia* isolates. Therefore, identifying *Nocardia* species is indispensable for selecting appropriate antibiotics.

Disseminated nocardiosis is defined as two noncontiguous sites of involvement that are disseminated from a pulmonary or cutaneous focus (3, 6). Because *Nocardia* spreads to various organs, including the central nervous system (CNS), bones, muscles, joints, kidneys and heart valves, nocardiosis patients present with a wide range of nonspecific clinical features, making it difficult to distinguish the disease from other severe infections and malignancies. Detection of *Nocardia* species has been reported to be rare in spite of hematogenous spread because several weeks of culture is required for identification (7). In general, blood cultures are performed for only one week, thus resulting in less frequent identification of *Nocardia* species.

We herein present a case of an immunosuppressed patient who developed disseminated nocardiosis caused by *N. concava* with multiple abscesses and CNS involvement, including meningitis and ventriculitis. Although a diagnosis of metastatic carcinoma was initially suspected based on the clinical manifestations and radiological findings, *N. concava* was
identified in the clinical samples using a sequence analysis of 16S rRNA as well as biochemical and chemotaxonomic examinations. The patient was cured with appropriate treatment with linezolid after testing for susceptibility.

## Case Report

The patient was a 73-year-old man with a 12-year history of multiple myeloma. Two months after receiving high-dose dexamethasone for multiple myeloma exacerbation, the patient noticed multiple red nodules and erythemas with pain, swelling and warmth on his precordia and bilateral extremities. Fever, anorexia and general fatigue subsequently occurred, and he was admitted to the hospital. Prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX) was not administered. The patient’s body weight was 66 kg and his height was 161 cm. A physical examination revealed a temperature of 39.2°C. Neither crackles nor heart murmurs were heard. Red nodules with pustules in the center were observed on the left superior eyelid, precordia, left arm, both thighs and precordial region. An alert cognitive state of consciousness was observed, and other neurological evaluations revealed no remarkable findings. A laboratory examination revealed a white cell count of 10.4×10³/μL with neutrophil predominance (87%). The remaining laboratory data were as follows: hemoglobin: 10.5 g/dL, serum creatinine: 0.93 mg/dL, albumin: 1.3 g/dL, lactate dehydrogenase: 190 U/L, sodium: 122 mEq/L and C-reactive protein: 15.06 mg/dL. The serum levels of IgG and β-2 microglobulin were 2,310 mg/dL and 4.8 μg/mL, respectively, which had remained unchanged over the previous six months. In spite of positive test results for serum human T lymphotrophic virus type I (HTLV-I) antibodies, no abnormal lymphocytes were noticed in the bone marrow or peripheral blood. An arterial blood
Table. Antibiotic Susceptibility Test

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>MIC (μg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
<td>32</td>
</tr>
<tr>
<td>Cefepime</td>
<td>&gt;32</td>
</tr>
<tr>
<td>Imipenem</td>
<td>&gt;16</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>≤1</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>1</td>
</tr>
<tr>
<td>Amikacin</td>
<td>≤2</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>1</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>2/38</td>
</tr>
<tr>
<td>Linezolid</td>
<td>4</td>
</tr>
<tr>
<td>Minocycline</td>
<td>≤1</td>
</tr>
</tbody>
</table>

The antimicrobial breakpoints are as follows. Ceftriaxone, 8 μg/mL; Cefepime, 8 μg/mL; Imipenem, 4 μg/mL; Gentamicin, 4 μg/mL; Tobramycin, 4 μg/mL; Amikacin, 8 μg/mL; Ciprofloxacin, 1 μg/mL; Trimethoprim-sulfamethoxazole, 2 μg/mL/38 μg/mL; Linezolid, 8 μg/ mL; Minocycline, 1 μg/mL.

Discussion

Identifying pathogenic species using biochemical and molecular analyses is necessary in order to select appropriate antibiotics, especially in cases of nocardiosis. The antimicrobial susceptibility patterns of Nocardia differ geographically and vary depending on the species (3-5). Among 15 Nocardia strains, the frequency of cases resistant to β-lactam agents is 33%, 20-52% and 20-30% for amoxicillin, ceftriaxone and imipenem, respectively (4, 5). In addition, the microbiological and clinical spectrum of nocardiosis has been altered due to improved identification of the isolates. The application of molecular techniques such as the se-
Quencing of 16S rRNA has led to an increase in the number of distinct clinically significant species of this genus (11, 12). A phylogenetic analysis based on a sequence analysis of 16S rRNA led to the identification of a novel species of Nocardia, N. concava (1).

The N. concava isolated in our case evidenced resistance to imipenem as two reference strains, IFM0354 and IFM 0576 (1). Although the MIC values for TMP-SMX, ciprofloxacin and amikacin evidenced susceptibility, these antibiotics did not improve the patient’s condition until linezolid was added. There are two possible explanations for this: the immunity of the host, who had multiple myeloma and was an HTLV-I carrier; and the different bioavailability of linezolid compared with other antibiotics. Multiple myeloma is accompanied by serious abnormalities in humoral immunity. HTLV-I-infected carriers have been reported to have immune deficiencies associated with an increased risk of certain infectious disease complications (13). Linezolid, the first oxazolidinone, can be used for treating infections with most Gram-positive bacteria. The characteristics of this drug include a unique mechanism of action that involves the inhibition of the formation of a functional 70S initiation complex in the 50S bacterial ribosomal subunit and good distribution to multiple sites including the CNS, lungs and skin (14). These characteristics might have contributed to the rapid improvement observed in our case. According to a recent review, linezolid is associated with cure or improvement in all reviewed cases of nocardiosis (15). However, its use was discontinued in the majority of cases due to the development of serious complications, including myelosuppression and peripheral neuropathy. Fortunately, our patient did not suffer from such adverse effects, and effective treatment was accomplished.

In conclusion, N. concava can cause disseminated infection in immunocompromised patients. When the response to β-lactam is poor, linezolid should be considered as an alternative agent for treating disseminated nocardiosis due to its effective distribution to multiple sites. Because Nocardia evidences a species-specific drug susceptibility profile, appropriate antibiotics should be selected based on antibiotic susceptibility tests.
The authors state that they have no Conflict of Interest (COI).

Funding

This work was supported by research grant #21406003 from the Cooperative Research Grant of NEKKEN and by the National BioResource Projects sponsored by the Ministry of Education, Culture, Sports, Science & Technology of Japan.

References

10. Susceptibility Testing of Mycobacteria, Nocardiae, and Aerobic Actinomycetes; Approved Standard. NCCLS document M24-A.

© 2012 The Japanese Society of Internal Medicine
http://www.naika.or.jp/imonline/index.html