First Report of *Nocardia beijingensis* Infection in an Immunocompetent Host in the United States

Jennifer A. Crozier, Swati Andhavarapu, Lisa M. Brumble, Taimur Sher
Department of Medicine, Mayo Clinic Florida, Jacksonville, Florida, USA

Here we describe the first reported case of *Nocardia beijingensis* infection in the United States, made rarer by its presence in an immunocompetent patient.

CASE REPORT

**A** 48-year-old Caucasian male presented to an outside facility with a 1-month history of nonproductive hacking cough, low-grade fevers, drenching night sweats, and weight loss, which prompted further investigation. His medical history was unremarkable. His social history was remarkable for his work as a cotton farmer and no tobacco or alcohol use. He had traveled to Eastern Europe 1 year earlier. Computed tomography (CT) of the chest, abdomen, and pelvis showed a 5-cm ill-defined mass in the right hilum, causing narrowing of the branches of the upper-lobe bronchus and peripheral lung collapse. Also noted was lymphadenopathy in the hilar, periaortic, and aortcopulmonary window. Findings on the CT scan were concerning for possible carcinoma, lymphoma, or thymoma. A mediastinoscopy with lymph node biopsy was performed, but it was nondiagnostic.

The patient was referred to the Mayo Clinic Florida for further evaluation. Physical examination revealed decreased breath sounds in the left apical lung. There was no lymphadenopathy noted in the cervical, supraclavicular, or axillary region. A complete blood count demonstrated mild anemia, neutrophil-predominant leukocytosis of 20,000 cells/µl, and thrombocytosis of 935,000/µl. The lactate dehydrogenase level was normal at 219 U/liter. C-reactive protein was elevated at 209 mg/liter. Testing for human immunodeficiency virus (HIV) and hepatitis B and C viruses was negative. A positron emission tomography (PET) scan revealed a 9.9- by 5.1- by 6.9-cm left paramediastinal mass extending to the left superhilar region with a maximum standardized uptake value (SUV) of 29.6 (Fig. 1 and Fig. 2). Compared to the results of the CT scans done previously, a new hypermetabolic 1.4-cm suprasternal notch nodule that was suspicious for an abnormal lymph node was found. A PET scan also revealed a diffusely hyperstimulated bone marrow. A bone marrow biopsy specimen showed myeloid and megakaryocytic hyperplasia, and the findings were consistent with reactive marrow changes.

The patient subsequently underwent a Chamberlain-McNeil left thoracotomy, during which a solid lung that was extremely vascular was encountered and biopsy specimens of the left lung and thymus were obtained. Further surgical dissection revealed a round hard lymph node that was noted on imaging and that was palpated and excised. Pathology showed lung tissue with acute and chronic changes of granulomatous inflammation and organizing pneumonia. Thymic tissue had an atrophic appearance and was negative for any neoplasm. Flow cytometry was negative for abnormal T- or B-cell populations. Gram staining and Grocott’s methenamine silver staining of the thymic tissue were negative.

Mediastinal lymph nodes showed reactive hyperplasia. Interestingly, on the Gram stain, Gram-positive bacilli with a beaded filamentous appearance were identified. The sputum, lung, and lymph node biopsy specimens were cultured, and all revealed *Nocardia beijingensis*. Results were confirmed by DNA sequencing. Sequencing was completed with the first ~ 500 bp of the 16S rRNA gene for bacterial identification. The sample met all quality parameters, and the isolate had a 100% match to *N. beijingensis* in our Mayo Clinic custom library. The sequence was also compared to the National Center for Biotechnology Information (NCBI) GenBank database and the commercial bacterial library from Applied Biosystems, with a 100% match. Empirical treatment with imipenem, doxycycline, and trimethoprim-sulfamethoxazole was initiated during the hospitalization, with marked improvement in the patient’s symptoms. Cultures for sensitivity were completed using commercially available Sensititre plates from Trek Diagnostics, which utilizes a microtiter broth dilution method. The drugs contained in the sensitivity panel and all MIC breakpoint interpretations, when available, are based on Clinical and Laboratory Standards Institute (CLSI) recommendations.

Upon availability of the susceptibility results (Table 1), the antibiotics were changed to ceftazidime (treatment for 6 weeks) and trimethoprim-sulfamethoxazole for a total of 6 months. With 6 weeks of treatment, the patient’s blood counts normalized (hemoglobin of 14 g/dl, leukocyte count of 5,800 cells/µl, and platelet count of 324,000/µl). Inflammatory markers, including C-reactive protein, improved to 0.3 mg/liter.

Clinically, nocardiosis is a rare and potentially life-threatening Gram-positive bacterial infection. The genus *Nocardia*, the causative organism, comprises a group of phylogenetically diverse but morphologically similar organisms. They are aerobic, nonmotile, and non-spore forming and exhibit characteristic filamentous branching with fragmentation into bacillary or coccoid forms (1). *Nocardia* is an opportunistic pathogen most commonly affecting...
immunocompromised patients, although approximately one-third of patients are immunocompetent (2). The patients at highest risk are those with hematopoietic stem cell transplantation, solid organ transplantation, HIV infection, malignancy, and chronic glucocorticoid therapy (3).

*Nocardia beijingensis* was first isolated by Wang et al. from soil in a sewage ditch in China in 2001 (4). In 2004, the first human infections were reported in Thailand and Japan (5). In 2008, a case of cutaneous *N. beijingensis* in an immunocompetent host was reported in France (6). In 2011, the first pulmonary case outside Asia was reported (7). This case is the first report, to our knowledge, of *N. beijingensis* infection in the Western Hemisphere.

Clinically, nocardiosis presents in three patterns: pulmonary, primary cutaneous, and disseminated disease. The lungs are the most common primary site of infection (8). The clinical presentation of pulmonary nocardiosis can be acute, subacute, or chronic. In one study by Martinez et al., the most common symptoms included fever, productive cough, dyspnea, chest pain, and constitutional symptoms (9). These nonspecific symptoms make diagnosis difficult, with studies showing that the time from development of symptoms to diagnosis can range from 42 days to 12 months (9,10). The differential diagnosis of pulmonary nocardiosis includes fungal infections, actinomycosis, mycobacterial infections, and malignancy. Radiographic data can be variable. Chest radiographs can display focal or multifocal disease with nodular and/or consolidation infiltrate as well as cavitary lesions (2,9). *Nocardia* can disseminate to virtually any organ, including most commonly the central nervous system (CNS). Neurologic symptoms typically develop with gradual presentation as headache, nausea, vomiting, seizures, or alterations in consciousness. CNS imaging should be considered for any patient with neurologic symptoms in the setting of pulmonary nocardiosis and for any patient with significant immunosuppression regardless of the presence of CNS symptoms (3).

The diagnosis of *Nocardia* infection requires the isolation and identification of organisms from a clinical specimen. Staining with modified acid-fast stain and Gram stain are particularly important to provide a rapid, presumptive diagnosis while awaiting culture results (11). *Nocardia* is slow growing and may take 48 h to 3 weeks to appear; it can grow on most nonselective media (12). Molecular techniques, such as PCR, restriction enzyme analysis, and 16S rRNA gene sequencing, have revolutionized the identification of specific *Nocardia* species (9). The species identification is important since different species have different antibiotic resistance profiles (13).

No prospective controlled trials are available to guide nocardiosis treatment, and most recommendations are based on clinical expert opinions. Sulfonamides have been the agent of choice for the treatment of nocardiosis for more than 50 years (3). For patients who are allergic to sulfonamides, desensitization should be performed when possible. For initial treatment, a combination of two or three intravenous agents, depending on the infection se-

### TABLE 1: *N. beijingensis* isolate antimicrobial susceptibility results

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC</th>
</tr>
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<tbody>
<tr>
<td>Amikacin</td>
<td>≤1</td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
<td>≥64</td>
</tr>
<tr>
<td>Cefepime</td>
<td>16</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>≤4</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>4</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>8</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>8</td>
</tr>
<tr>
<td>Imipenem</td>
<td>≤2</td>
</tr>
<tr>
<td>Linezolid</td>
<td>2</td>
</tr>
<tr>
<td>Minocycline</td>
<td>≤1</td>
</tr>
<tr>
<td>Mexilitoxacin</td>
<td>1</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>≤1</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>≤0.25/0.1</td>
</tr>
</tbody>
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*The second value is for sulfamethoxazole.*
verity, is recommended until susceptibility results are available (13). Oral therapy is an option for patients who improve clinically (14). Ogawa and colleagues reported a case of pulmonary N. beijingensis infection in an immunocompromised renal transplant patient who was successfully treated with imipenem-cilastatin and transitioned to ceftriaxone and oral minocycline (15). The duration of antimicrobial therapy has not been established, but a prolonged course is typically pursued, with at least 6 months of treatment for pulmonary and disseminated nocardiosis, due to the relapsing nature of Nocardia infections.

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REFERENCES