Case Report

*Nocardia neocaledoniensis* as a cause of human skin and soft tissue infection

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Running Title: *Nocardia neocaledoniensis* infection
Abstract

*Nocardia neocaledoniensis* was introduced as a new environmental species of Nocardia in 2004. We present the first case of human skin and soft tissue infection caused by this species in a patient with rheumatoid arthritis on prednisone and methotrexate.

Case Report

A 68-year-old man with a history significant for rheumatoid arthritis on methotrexate and prednisone for at least 10 years, presented for evaluation of a persistent right facial abscess. The patient lived in a house in a residential area in Central Texas, was a retired telephone employee, and volunteered as a firefighter with moderate exposure to dirt. His hobbies included hunting, fishing, and mowing the lawn. He had no recent travel outside his hometown, and no history of opportunistic infections.

Approximately 1 month prior to presentation, he noticed right facial discomfort and abscess formation in his right jaw. His primary care physician prescribed cephalexin but the patient had minimal relief of symptoms. The patient was referred to an otolaryngologist and a specimen was obtained by fine needle aspiration. The Gram stain of the specimen revealed many polymorphonuclear leukocytes but no organisms were observed. The corresponding culture recovered an organism suggestive of *Nocardia* species. The patient was started on oral trimethoprim-sulfamethoxazole and his methotrexate was discontinued. The patient underwent incision and drainage 9 days later due to increased drainage and that specimen once again revealed a *Nocardia* species with similar susceptibilities to the first, as well as coagulase negative staphylococci. The patient reported that he was compliant with trimethoprim-
sulfamethoxazole, however, 22 days after the initial drainage, additional masses were noted in
the same region. An MRI of the brain was negative for acute intracranial abnormalities.

On the basis of continued infection despite oral outpatient antibiotic therapy, the patient
was admitted to the hospital. On admission, the patient denied cardiac, pulmonary and
gastrointestinal symptoms. On physical exam, his left submandibular gland was normal but the
right submandibular triangle had a large mass (10.5 cm) adjacent to the inferior border of the
mandible. The area was erythematous and tender to palpation. Further examination of the right
angle of the jaw submaxillary triangle area revealed two additional masses, one to the anterior
and one to the posterior of the previous incision area. Both were firm and extremely tender to
touch. Imaging of the neck and lungs did not reveal any sinus tract or acute pulmonary
abnormalities. The patient was placed on intravenous imipenem and oral trimethoprim-
sulfamethoxazole. He underwent subsequent incision and drainage of the multiple skin
abscesses. The patient’s hospital course was complicated by acute renal insufficiency and
hyponatremia, and his antibiotics were later switched to oral doxycycline with the addition of
oral moxifloxacin. The patient remained clinically stable with improvement in his signs and
symptoms.

Operative cultures were obtained from each abscess and all grew *Nocardia* with the
same phenotypic characteristics (lysozyme (+), urease (+), negative hydrolysis of casein,
tyrosine and xanthine; a pattern typical of several species within the former *Nocardia asteroides*
complex). In each instance, the organism was recovered on sheep blood agar at 48 hours after
incubation at 35°C. The colonies were chalky white with a pinkish tinge (Figure 1) and the
organisms were modified acid-fast stain positive. Each culture also exhibited the same
susceptibility pattern (Table 1) when tested with the Sensititre Rapid Growing Mycobacterial
susceptibility panel (TREK Diagnostic Systems, Cleveland, OH) by using Clinical Laboratory Standards Institute (CLSI) guidelines (2) incubated at 30°C for 3 days. Pathology was negative for malignancy and fungal organisms.

Sequence-based identification was performed by sequencing of the complete 16S rRNA gene and amino acid sequencing of the secA1 gene (5,6) according to standard methods (3). A sequence comparison using RipSeq Single (Isentio, A.S., Bergen, N.O.; www.ripseq.com) GI bacterial database, which contains all published references from valid species) indicated that the isolate was a member of an unusual species of *Nocardia* (*N. neocaledoniensis*). The isolate shared 1390/1397 bp identity with no gaps (99.5% identity) by complete 16S rRNA gene sequence with the *Nocardia neocaledoniensis* type strain DSM 4417T (GenBank accession no. JF797311 and GQ85380) (4). An identity of ≥99.5% of the 16S r-RNA gene is considered adequate for a species identity for *Nocardia* (3). By secA1 the isolate showed 99% amino acid identity (one a.a. mismatch) which meets the species definition using the gene (3). The nearest other validated species type strain by complete 16S rRNA gene sequencing and secA1 was *N. thailandica*. The 16S rRNA and secA1 gene sequences have been submitted to GenBank.

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*Nocardia* species are gram-positive, variably acid-fast, strictly aerobic bacteria that form branched filaments (7). Transmission is mainly from inhalation or direct contact, and it has been reported to cause cutaneous, subcutaneous, lymphocutaneous, central nervous system, pulmonary, and systemic infections (1). Immunocompromise has been noted in numerous reports as a risk factor for nocardiosis. These characteristics correlate with our patient who was a recipient of both steroids and methotrexate for at least 10 years to treat rheumatoid arthritis.
In 2004, Saintpierre-Bonaccio, et al. (9) reported the phenotypic and genotypic characteristics that distinguished *N. neocaledoniensis* from other strains of *Nocardia*. This organism was isolated from soil in New Caledonia. *N. neocaledoniensis* has been isolated from clinical specimens obtained from three patients with conjunctivitis although its role as a pathogen was questioned (10). The organism also has been implicated in mastitis outbreaks among Italian dairy herds (8). Our patient was found to have *N. neocaledoniensis* skin and soft tissue infection, identified through phenotypic and genotypic characteristics, which he may have contracted through occupational or recreational exposure. The initial unsatisfactory response of this patient to oral trimethoprim-sulfamethoxazole as an outpatient may have been secondary to the abscess formation requiring surgical drainage. The susceptibility of this isolate is documented in Table 1. He improved with oral trimethoprim-sulfamethoxazole plus intravenous imipenem in conjunction with surgical debridement and later with oral doxycycline and moxifloxacin. To the best of our knowledge, this is the first report of human skin and soft tissue infection caused by *N. neocaledoniensis* and provides evidence of this species as a human pathogen. It is likely that newer pathogenic species of *Nocardia* will continue to emerge with the use of sequencing for organism identification.
Acknowledgment:

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References


Table 1: Susceptibility results of the clinical isolate of *N. neocaledoniensis* by broth microdilution.

<table>
<thead>
<tr>
<th>ANTIBIOTIC</th>
<th>MIC (µg/ml)</th>
<th>Interpretation</th>
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<tr>
<td>Amikacin</td>
<td>≤ 1</td>
<td>S</td>
</tr>
<tr>
<td>Amoxicillin/clavulanate</td>
<td>≥ 64/32</td>
<td>R</td>
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<td>Cefepime</td>
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<td>S</td>
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<tr>
<td>Ceftriaxone</td>
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<tr>
<td>Ciprofloxacin</td>
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<td>I</td>
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<td>Clarithromycin</td>
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<tr>
<td>Doxycycline</td>
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<td>S</td>
</tr>
<tr>
<td>Imipenem</td>
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<td>S</td>
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</tr>
<tr>
<td>Trimethoprim/sulfamethoxazole</td>
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<td>S</td>
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Figure 1: Colony morphology of *N. neocaledoniensis*. Note pinkish hue to the colonies. Smooth colonies are coagulase negative Staphylococcus.
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_Nocardia neocaledoniensis_ as a Cause of Skin and Soft Tissue Infection


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