MINI-REVIEW

Nocardia veterana infections: case report and systematic review

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Abstract

Members of the genus *Nocardia* are filamentous, Gram-positive, aerobic bacteria and exist ubiquitously in most environments. In 2001, the species *Nocardia veterana* was first isolated, and it predominantly causes pulmonary infections in immunocompromised hosts. We present the first report of a soft-tissue abscess caused by *N. veterana* in a 59-year-old woman being treated for chronic cutaneous graft-versus-host disease. After failing to improve with empirical treatment, two incision and drainage procedures were required. She subsequently completed a 1-year course of oral antibiotic therapy consisting of trimethoprim-sulfamethoxazole then azithromycin. No relapse occurred over the next 5 years of follow up. To better characterize *N. veterana* infections, we performed a systematic literature review and summarized all previously reported cases. Overall, the rising prevalence of immunocompromising conditions warrants increased vigilance for infections caused by atypical or opportunistic pathogens.

Keywords: Abscess, graft-versus-host disease, *Nocardia veterana*, nocardiosis, trimethoprim-sulfamethoxazole
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Introduction

Members of the genus *Nocardia* are filamentous, Gram-positive, aerobic bacteria and exist ubiquitously in most environments [1,2]. They classically lead to infections in immunocompromised hosts [1], but 15% of patients in a large series had no predisposing conditions [3]. In 2001, the species *Nocardia veterana* was first isolated at a veterans' hospital in Australia, from which its name is derived [4]. It has been demonstrated to predominantly cause pulmonary infections in immunocompromised hosts [5–7], and only two reports have identified *N. veterana* as the cause of abscesses [8,9].

Materials and methods

We present the first report of a soft-tissue abscess caused by *N. veterana* in a 59-year-old woman being treated for chronic cutaneous graft-versus-host disease (GVHD). Review of medical records was approved by our institution's institutional review board. To better characterize *N. veterana* infections, we performed a systematic literature review and summarized all previously reported cases.

Case presentation

A 59-year-old woman with a history of acute lymphoblastic leukaemia—status post-haematopoietic stem cell transplantation—presented to the emergency department for evaluation of a right shoulder cutaneous abscess. Her post-transplant course had been complicated by multiple episodes of gastrointestinal and cutaneous GVHD. At this time, she was receiving phototherapy for chronic cutaneous GVHD and had

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started taking prednisone (30 mg daily) 6 months before presentation. Her medications included tacrolimus, acyclovir, fluconazole and monthly pentamidine. Two weeks before presentation, she had been evaluated by her oncologist for a 5 × 7 cm erythematous, indurated region on her right shoulder, and empiric treatment with oral minocycline (100 mg twice a day) was initiated. Continued pain prompted an outpatient ultrasound, which demonstrated a fluid collection. Her referring provider then sent her to the emergency department for further evaluation.

Incision and drainage were performed in the emergency department and yielded copious, purulent drainage that was sent for culture. Antibiotic therapy was empirically switched to oral clindamycin (600 mg three times a day). She was afebrile and discharged shortly thereafter. Two days later, she was admitted after a wound check showed increasing erythema around the incision and drainage site. Laboratory studies were notable for leucocytosis (15 200/μL; reference range 4000–10 000/μL), but she remained afebrile. Magnetic resonance imaging of her right upper extremity demonstrated a 2-cm soft-tissue abscess involving superficial fascia of the lateral deltoid and focal myositis (Fig. 1). Antibiotic therapy was broadened to intravenous vancomycin and piperacillin-tazobactam.

On day 2 of hospitalization, the abscess was incised and drained by general surgery. The following day, the culture from her initial presentation to the emergency department grew 4+ Gram-positive rods, prompting *Nocardia* spp. to be suspected. Antibiotic therapy was switched to oral trimethoprim-sulfamethoxazole (800 mg-160–mg twice a day). Magnetic resonance imaging of the brain and a CT scan of the chest showed no evidence of involvement, and she was discharged on day 4.

Four days after discharge, the isolate from her initial presentation was identified as *N. veterana*. The MicroSEQ® 500bp 16S rRNA Sequencing Kit (Applied Biosystems, Foster City, CA, USA) was used. Samples were processed and analysed consistent with the manufacturer's instructions. Data were assembled with MicroSEQ software, and amplicons were compared against the MicroSEQ database. Clinical and Laboratory Standards Institute MM18 criteria were used for making an identification. The aligned sequence was 409 bp, with no mixed bases. The isolate was 100% match to *N. veterana* in the MicroSEQ database; however, the National Center for Biotechnology Information BLAST database has been updated since the time of the isolate's processing, and a *Nocardia elegans* strain was retrospectively identified as a 100% match during the preparation of this report. Notably, three strains of *N. veterana* were 100% matches.

Susceptibility testing was sent out to the University of Texas Health Center's Department of Microbiology Research in Tyler, Texas. The isolate's susceptibility profile is summarized in Table 1. Two weeks later, the woman was seen as an outpatient and had been tolerating trimethoprim-sulfamethoxazole therapy. Seventy-three days after discharge, elevated creatinine (3.1 mg/dL, baseline 1.9 mg/dL; reference range 0.6–1.2 mg/dL) was attributed to the use of trimethoprim-sulfamethoxazole in combination with tacrolimus, and antibiotic therapy was switched to oral azithromycin (500 mg daily). This decision was informed by the isolate's susceptibility profile and discussion with the reference laboratory.

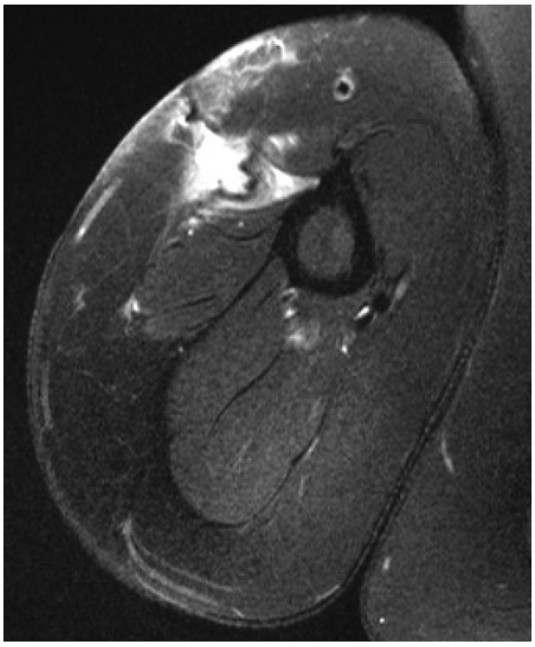

FIG. 1. *Nocardia veterana* abscess: T2-weighted magnetic resonance imaging demonstrates 2-cm abscess involving the superficial fascia of the right lateral deltoid muscle.

Roughly 1.5 months later, her creatinine had returned to baseline (1.7 mg/dL), and she had been tolerating azithromycin without adverse events. In the absence of symptoms attributable to her *N. veterana* infection, azithromycin therapy was discontinued 289 days after its initiation. She continued to receive phototherapy for GVHD and remained on prednisone (20 mg daily), acyclovir, fluconazole and monthly pentamidine. She was seen 6 months after completing her 1-year course of therapy and displayed no signs of relapse. More than 5 years since completing therapy, no relapse has occurred.

Literature review and discussion

Our case concerned an *N. veterana* infection in a 59-year-old woman who had been receiving immunosuppressive therapy for chronic cutaneous GVHD. She failed to respond to empiric

TABLE 1. ***Nocardia veterana*** **isolate susceptibility profile**[a]

Susceptible	Intermediate	Resistant	No standardized breakpoint for *Nocardia* spp.
Amikacin (MIC ≤1 μg/mL)	Ceftriaxone (MIC 16 μg/mL)	Amoxicillin-clavulanate (MIC 32–16 μg/mL)	Ertapenem (MIC unavailable; susceptible by bacterial breakpoint)
Clarithromycin (MIC ≤0.06 μg/mL)	Kanamycin (MIC unavailable)	Ciprofloxacin (MIC >4 μg/mL)	Meropenem (MIC unavailable; susceptible by rapidly growing mycobacteria breakpoint)
Imipenem (MIC ≤2 μg/mL) Linezolid (MIC 2 μg/mL) Trimethoprim-sulfamethoxazole (MIC 1–19 μg/mL)	Minocycline (MIC 2 μg/mL)	Doxycycline (MIC 16 μg/mL) Moxifloxacin (MIC 4 μg/mL) Tobramycin (MIC >16 μg/mL)	Tigecycline (MIC 4 μg/mL)

[a]Susceptibility results are reported with reference to their MICs and respective, standardized breakpoints.

minocycline, and an abscess was incised and drained twice before resolving. Fortunately, oral antibiotic therapy was capable of treating the infection then serving as prophylaxis against relapse. Acute kidney injury complicated her course, but azithromycin therapy ultimately proved tolerable and successful. The isolate was resistant to several antibiotic choices, and susceptibility testing was integral to her management.

To better characterize *N. veterana* infections, we searched PubMed with the following operators: ('*Nocardia veterana*' OR '*N. veterana*') AND (infection OR infections). Articles' citation lists were also reviewed to identify cases. We excluded one abridged report of a mycetoma [10] whose full details were published in a later manuscript [11]. Table 2 summarizes our case and all reported cases of *N. veterana* infections.

TABLE 2. ***Nocardia veterana*** **infections**

Age/sex	Clinical syndrome	Immunocompromising co-morbidities	Initial anti-nocardial regimen	Length of treatment	Outcome	Ref.
83/F	bowel abscess	malignancy	TMP-SMX	>3 months	success	[8]
73/M	brain abscess	diabetes mellitus	meropenem	1 year	success	[9]
66/M	endophthalmitis	heart transplant, diabetes mellitus	meropenem, linezolid	planned length of 12 months	success	[12]
42/F	mycetoma	SLE	amoxicillin	>6 years	success	[11]
72/M	nodular lymphangitis	immunosuppressive therapy for interstitial pneumonitis	TMP-SMX	planned length of 3 months	stable at time of report	[13]
40/M	peritoneal infection	AIDS, chronic hepatitis B, malignancy	died before treatment initiation	not applicable	died before treatment initiation	[14]
24/M	pulmonary infection	chronic granulomatous disease	amikacin, ceftriaxone, trimethoprim	>3 months	stable at time of report	[15]
40/F	pulmonary infection	HIV	TMP-SMX	6 months	success	[16]
43/F	pulmonary infection	immunosuppressive therapy for SLE	TMP-SMX	6 months	success	[17]
47/M	pulmonary infection	liver transplant	TMP-SMX	6 months	success	[17]
52/M	pulmonary infection	not specified	not reported	not reported	not reported	[18]
52/M	pulmonary infection	HSCT recipient treated for GVHD	TMP-SMX	397 days	success	[19]
52/F	pulmonary infection	HSCT recipient treated for GVHD	TMP-SMX	154 days	success	[19]
54/M	pulmonary infection	heart transplant	TMP-SMX	15 days	success	[16]
59/M	pulmonary infection	liver transplant	imipenem	>6 months	success	[16]
63/M	pulmonary infection	lung transplant, immunosuppressive therapy for bronchiolitis obliterans	TMP-SMX	16 weeks	died after discontinuing immunosuppression	[15]
65/M	pulmonary infection	HSCT recipient treated for GVHD	imipenem/cilastatin, amikacin	722 days	died from encephalitis of unknown aetiology	[6]
67/F	pulmonary infection	recurrent pneumonias and bronchiectasis	minocycline	>7 weeks	symptomatic improvement at time of report	[17]
78/M	pulmonary infection	history of tuberculosis	not reported	not reported	not reported	[4]
not reported	pulmonary infection	lung transplant	TMP-SMX	30 days	success	[7]
58/M	pulmonary infection with bacteraemia	malignancy, recent prednisone course for autoimmune haemolytic anaemia	TMP-SMX, azithromycin, piperacillin-tazobactam	3 weeks	success	[20]
30/M	pulmonary infection with bacteraemia	HIV, chronic hepatitis B, history of tuberculosis	TMP-SMX	<1 month	died from multi-organ failure	[5]
51/M	pulmonary and urinary tract infections with bacteraemia	malignancy, peritoneal dialysis	TMP-SMX	<2 months	died from underlying malignancy	[21]
59/F	soft-tissue abscess	HSCT recipient treated for GVHD	TMP-SMX	1 year	success	our case

Abbreviations: AIDS, acquired immunodeficiency syndrome; GVHD, graft-versus-host disease; HIV, human immunodeficiency virus; HSCT, haematopoietic stem cell transplantation; SLE, systemic lupus erythematosus; TMP-SMX, trimethoprim-sulfamethoxazole.

Mean age was 55 years, and 29% were women. Pulmonary infections accounted for 17 of 24 infections, with abscesses being the second most common (3 of 24). In total, 25% had previous solid organ transplantations, 17% of patients had undergone haematopoietic stem cell transplantation and were undergoing treatment for GVHD, and 13% were people living with human immunodeficiency virus. The duration of treatment ranged from 3 weeks to >6 years. Trimethoprim-sulfamethoxazole monotherapy was used as initial anti-nocardial therapy for 13 of 24 individuals and led to treatment success in 9 of 13 (69%) of them. Combination therapy or other monotherapy (e.g. amoxicillin) was successful for six of eight (75%) individuals. The number of patients was too small to determine whether the difference in outcome is statistically significant.

Overall, *N. veterana* has a predilection for causing pulmonary infections in individuals with immunocompromising conditions [4–7,15–20], and trimethoprim-sulfamethoxazole is commonly used to treat infections caused by *Nocardia* spp. [1]. When planning management for an immunocompromised host, a prolonged treatment duration is recommended. For our patient, the concurrent use of immunosuppressive therapy to manage GVHD heightened her susceptibility to *N. veterana* infection, and disseminated disease was fortunately averted by extended antibiotic therapy. The rising prevalence of immunocompromising conditions warrants increased vigilance for infections caused by atypical or opportunistic pathogens.

Conflict of interest

The authors declare no conflicts of interest.

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