

A NOCARDIA BRASILIENSIS INFECTION SECONDARY TO A LOXOSCELES RECLUSA BITE: A SPINAL CORD STIMULATION CASE REPORT

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Background: *Nocardia brasiliensis*, an uncommon human pathogen, is rarely seen in infections secondary to insect bites or stings. However, *Nocardia brasiliensis* can infect an individual through an ulcerative wound, such as one mediated by the phospholipase D toxin immune response following a *Loxosceles reclusa* (i.e., brown recluse spider) bite.

Case Report: This report presents the case of a patient who underwent a spinal cord stimulator (SCS) trial with an unknown brown recluse spider bite on her left foot. We describe the *Nocardia brasiliensis* cutaneous infection following a brown recluse bite and the effective management of the infection through long-term antibiotic use, which allowed for the eventual successful implantation of the SCS.

Conclusion: The present case urges health care providers to conduct thorough, full-body examinations prior to any surgical procedure to identify and treat all remote infections prior to SCS implantations, as advised by the Neurostimulation Appropriateness Consensus Committee's recommendations for infection prevention.

Key words: Nocardiosis, *Loxosceles reclusa*, *Nocardia brasiliensis*, spinal cord stimulation, case report

BACKGROUND

Nocardia is an aerobic genus of actinomycetes with a distinct filamentous, hyphae-like branching appearance (1). One of the most common clinical manifestations of *Nocardia* infections, otherwise known as nocardiosis, is primary cutaneous nocardiosis. Cutaneous nocardiosis is more common in immunocompromised individuals and is caused by an open wound being exposed to soil or a contagion harboring the bacteria (2). Cutaneous nocardiosis often manifests as pustules, nodules, granules, ulcerative wounds, or necrosis (3). In rare instances, cutaneous involvement originates from a bug bite as the initial wound. The present case describes a patient who underwent a spinal cord stimulator (SCS) trial with an unknown *Loxosceles reclusa* (i.e., brown recluse) spider

bite on her left foot, resulting in a 28-month-long delay in the final implantation of the device secondary to the patient's long-term reliance on oral antibiotics due a *Nocardia brasiliensis* infection.

CASE PRESENTATION

Written patient permission and informed consent were obtained for this case report. A patient in their 70s, with a history of diabetes, presented for a SCS trial procedure with a minor wound on her left foot that appeared to be healing. The patient advised the providers that the wound was associated with an insect bite and had drastically improved over the previous 7 days. She was given specific instructions on how to monitor the insect bite and when to seek medical treatment if neces-

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sary. Three days later, she presented for her lead pull after a successful trial with a new rapidly progressing left lower extremity erythematous wound with edema and drainage. She noted the wound was initially itchy, but she now complained of pain and severe tenderness with palpation. The patient reported at her lead pull appointment that she went to an urgent care during the trial and was placed on doxycycline and cefalexin. Despite appropriate antibiotic use, the appearance of the bite was worsening. She was advised to immediately seek emergency care. The patient presented to the emergency department with a normal body temperature (97.5°F). The purulent blister spontaneously drained while the patient was in the emergency room. The patient's bloodwork was normal and the erythema was demarcated with a skin marker. She was instructed to continue the cefalexin and doxycycline and to return if her symptoms progressed. Within 48 hours, the erythema and pain extended into the medial thigh.

She presented back to the emergency department with malaise, nausea, and hot and cold flashes. Images taken at the emergency room demonstrated an ulcerative lesion that quickly spread across the dorsal aspect of her foot (Fig. 1A). Doppler studies were negative for deep vein thrombosis. A left lower extremity x-ray and magnetic resonance image (Fig. 2A, 2C, 2E) were negative for osteomyelitis, but demonstrated soft tissue swelling and skin thickening, suggestive of cellulitis. Secondary to tracking redness in the medial proximal



Fig. 1. The patient presented to the emergency room with erythema and an ulcerated, granular wound and purulent blister-like eruption 4 days after the trial and approximately 2 weeks since the bite (A). After 48 hours of appropriate antibiotic use, the patient continued to experience tracking redness into the proximal medial thigh (B) and was placed on intravenous ampicillin/sulbactam and vancomycin. Following discharge on oral minocycline for 3 months, the patient's pustules began to decrease in size (C), and the patient temporarily was able to cease oral antibiotics. The wound did not completely close (D) until patient was placed on amoxicillin and clavulanate for 6 weeks and then Cefalexin for an additional 8 months secondary to a return of pruritis, erythema, and edema in the left lower extremity.

thigh despite 96 hours of antibiotic use (Fig. 1B), the patient was admitted. There were also concerns about a purulent blister-like eruption in the dorsal aspect of the left foot, elevated body temperature (101.4°F), mild tachycardia at 103 beats per minute, an elevated C-reactive protein of 4.50 mg/dL, and an elevated erythrocyte sedimentation rate of 103 mm/hr. The pustular area was originally identified as a spider bite by the consulting podiatrist in the hospital who debrided and drained the superficial abscess on the patient's foot. Seeing that there are currently no existing diagnostic tools for a brown recluse spider bite, the infectious disease specialist that managed the patient's long-term antibiotic use identified the bite based on the pruritis, erythema, pain, granular nature of the wound, and formation of pustular blisters. Six days after the initial hospitalization, a bacterial wound culture grew *Nocardia brasiliensis*. A consulting infectious disease physician placed the patient on minocycline prior to discharge. She initially remained on the minocycline for 2 months. At that time, the patient's wound pustules began to decrease in size (Fig. 1C). However, 8 months after initially ceasing antibiotic use, the patient presented back to the infectious disease specialist secondary to a return of pruritis, erythema, and edema in the left lower extremity. She received an additional round of intravenous ampicillin/sulbactam before being placed on amoxicillin-clavulanate potassium for 6 weeks, followed by cefalexin for an additional 8 months until the wound had completely healed (Fig. 1D). The decision was made to not proceed with implantation until after completion of antibiotics, infectious disease clearance, and updated labs demonstrated normal erythrocyte sedimentation rate, C reactive protein level, and white blood cell count. Ultimately, the patient was able to proceed with her SCS implantation 28 months after her trial procedure.

DISCUSSION

The present case urges health care providers to conduct thorough examinations prior to any surgical procedure to identify and treat all remote infections prior to SCS implantations, as advised by the Neurostimulation Appropriateness Consensus Committee's recommendations for infection prevention (4). Late SCS infections may result from blood-borne bacterial dissemination. Brown recluse spider bites are challenging to diagnose and *Nocardia brasiliensis* infections are rare especially following insect bites with limited existing publications

Fig. 2. Diagnostic imaging before and after long-term minocycline use. When the patient presented to the emergency room, a T2 MRI demonstrated skin thickening (A, Arrow #1) and significant soft tissue swelling (A, Arrow #2), suggestive of cellulitis along the dorsal aspect of the left foot. Reactive marrow edema is also visible, but there are no cortical bone changes to suggest osteomyelitis (A, Arrow #3). A T2 MRI also demonstrated significant soft tissue edema extending up the lower extremity (C, Arrow #1). An x-ray taken upon the patient's admittance to the hospital (E) showed no evidence of osteomyelitis. Following three months of minocycline use, an updated MRI (B) suggested continued skin thickening (B, Arrow #1) and doors subcutaneous edema (B, Arrow #2) without evidence of marrow edema. The soft tissue edema no longer extended into the talocrural region (D, Arrow #1) and there continued to be no evidence of osteomyelitis in the x-ray (F).



(Table 1) (5-13). The ability to diagnose a brown recluse bite is limited, as there are no existing diagnostic tests. The tools utilized by providers described in the present case, clinical presentation, geography, and seasonality, are the only current tools for diagnosis of a brown recluse spider bite. Common presentations of a brown recluse spider bite include early itching that develops into a stinging pain, erythema, and progression from a puncture wound to ulcerative lesion formation mediated by the phospholipase D toxin in the spider's venom (14). The severity of the wound ranges from a red plaque surrounding a shallow ulcer, to cutaneous necrosis (7). Brown recluse spider bites also demonstrate seasonality, with over 95% of cases occurring between April and October (15). Historically, brown recluse have been isolated to the southern and central regions of the United States. However, secondary to climate change, there have been increased incidences of brown recluse found in northeastern territories of the United States (16). *Nocardia brasiliensis* infections are uncommon and typically affect immunocompromised individuals (2). A

literature review suggests many patients with *Nocardia brasiliensis* infections require long-term antibiotic treatment (Table 1). The patient presented here was unable to proceed with the implantation procedure for over 2 years due to her long-term reliance on antibiotics.

CONCLUSIONS

The presented case urges health care providers to be cognizant of a patient's infection status and perform thorough pre-operative examinations prior to any device implantation procedure to ensure there are no minor wounds that could potentially be concealing a developing bacterial infection. Furthermore, although rare, physician knowledge on identification of brown recluse spider bites and the appropriate treatment of *Nocardia brasiliensis* infections is helpful.

Authorship Statement

David Provenzano MD, and Cecilia Maclae were involved with manuscript preparation. Leonard DeRiggi, MD was involved with image interpretation.

Table 1. Previously documented cases of *Nocardia brasiliensis* infections following insect bites or stings. Most patients presented with erythema, ulcerated skin lesions, and pustular eruptions. Successful treatment required continuous, and often long-term, antibiotic use.

Author	Causation	Symptoms	Diagnostic Tool	Diagnosis	Treatment
Leggiadro et al. 1987 (5).	Tick bite	Fever, skin lesion, and lymph-adenopathy	Culture of with subsequent hematoxylin and eosin staining	Primary cutaneous nocardiosis with regional lymph-adenopathy	Cephalexin for 9 days followed by 10 days of sulfisoxazole
O'Connor et al. 1992 (6).	Unknown insect bite	Fever, multiple small insect bites with pustules, lymphangitis, and left inguinal adenopathy	Wound and blood cultures	Cutaneous nocardiosis	Intravenous amoxicillin/clavulanate/doxycycline for 7 days, intravenous linezolid and sulfamethoxazole/trimethoprim for 10 days, oral amoxicillin/clavulanate and linezolid for 3 weeks and oral amoxicillin/clavulanate for 5 months
Paredes et al. 1999 (7).	Unknown insect bite	Purulent nodule formation and erythema	Genome analysis of purulent exudate obtained from nodule	Primary cutaneous nocardiosis	Trimethoprim-sulfamethoxazole followed by 5 weeks of minocycline
Slevogt et al. 2001 (8).	Unknown insect bite	Purulent nodular lesion with central necrosis	Gram stain of purulent exudate with subsequent 16S rRNA gene sequencing	Primary cutaneous nocardiosis	Trimethoprim-sulfamethoxazole for 12 weeks
Chu et al. 2017 (9).	Wasp sting	Elevation of white blood cell counts, and a skin ulcer	Culture of necrotic drainage	Primary cutaneous nocardiosis	Trimethoprim-sulfamethoxazole orally for 3 weeks
Secchin et al. 2017 (10).	Unknown insect bite	Ulcerated lesion and ascending lymphangitis	Genome analysis of a culture grown from ulcer exudate	Cutaneous nocardiosis stimulating cutaneous lymphatic sporotrichosis	Trimethoprim-sulfamethoxazole intravenously for 9 days and trimethoprim-sulfamethoxazole orally for 14 days
Mu et al. 2019 (11).	Unknown insect sting	Painful erythema, formation of subcutaneous nodules, and development of pustulant abscesses	Bacterial culture isolated from pustule followed by gene sequencing	Lymphocutaneous nocardiosis	Two weeks of amoxicillin potassium clavulanate infusion therapy and oral trimethoprim-sulfamethoxazole followed by one month of oral trimethoprim-sulfamethoxazole
Acevedo et al. 2021 (12).	Unknown insect bite	Painful swelling of the face and neck, as well as an ulcerated plaque over the right temple	Culture from the biopsy showed growth of <i>Nocardia</i> and 16S rRNA gene sequencing identified <i>Nocardia brasiliensis</i>	Primary cutaneous nocardiosis	Initial treatment of Trimethoprim-sulfamethoxazole followed by 3 months of oral amoxicillin/clavulanic acid
Lovecchio et al. 2022 (13).	Unknown insect sting	Fever along with erythema and ulcer formation on the right lower extremity	Lesion biopsy with subsequent culture weakly positive for actinomycetes	Primary cutaneous nocardiosis	Intravenous linezolid and intravenous sulfamethoxazole and trimethoprim, followed by oral therapy with amoxicillin/clavulanate and linezolid. Amoxicillin/clavulanate for an additional 5 months

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