Primary Cutaneous *Nocardia brasiliensis* Infection Isolated in an Immunosuppressed Patient: A Case Report

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Cutaneous nocardiosis is a rare infection that may manifest as a superficial skin lesion, lymphocutaneous infection, mycetoma, or diffuse cutaneous infection from a disseminated systemic infection. We report a case of a 65-year-old immunocompromised man with persistent primary cutaneous Nocardia brasiliensis *infection following a motor vehicle collision. A high degree of suspicion is needed to diagnose* Nocardia *infection because of its resemblance to other bacterial infections. Nocardiosis should be included in the differential diagnosis of chronic cutaneous infections, especially when the response to antibiotics is inadequate or when the patient is immunocompromised. Because* Nocardia *may take several weeks to grow in standard bacterial culture media, laboratories should be notified of the suspicion so that culture plates are held for longer time periods. Long-term therapy, usually with sulfonamides, often is necessary.*

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Case Report

A 65-year-old man who had previously received a renal transplant secondary to polycystic disease of the kidneys was hospitalized following a motor vehicle collision. Approximately 1 month after the accident, he developed multiple painful, draining, purulent nodules on his right arm; 2 weeks later, a painful 1.8×2.0-cm abscess developed on the right leg. Upper and lower extremity lesions were incised and drained, and empiric treatment with meropenem, trimethoprim-sulfamethoxazole, and caspofungin were initiated for presumed bacterial and possible deep fungal infection.

Subsequently, he had new onset of fevers, night sweats, fatigue, and intermittent headaches associated with left basilar crackles and decreased air exchange bilaterally. Two days later, he developed multiple indurated, red to violaceous nodules in a sporotrichoid distribution along the right upper extremity adjacent to a long, linear, granulating surgical incision site (Figure 1) and a tender fluctuant nodule (3 cm in diameter) on the right leg. There was no edema,

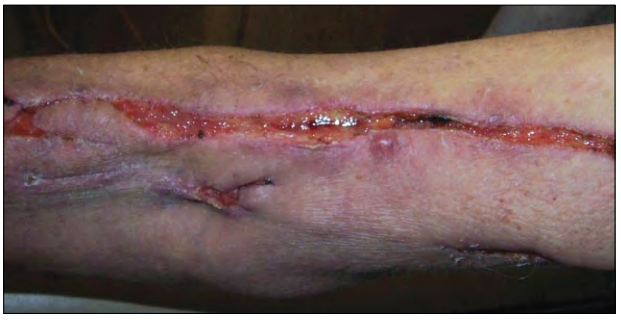

Figure 1. Multiple indurated, red to violaceous nodules (5–10 mm diameter) in a sporotrichoid distribution adjacent to a linear granulating surgical incision site.

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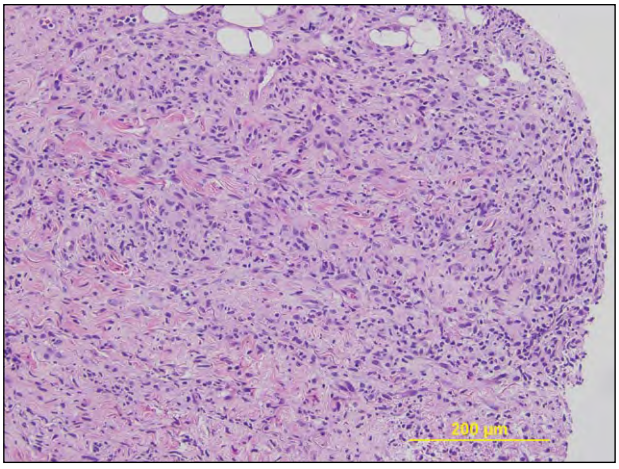

Figure 2. A nonspecific granulomatous inflammation including lymphocytes and histiocytes associated with dermal fibrosis (H&E, original magnification ×100).

purulent drainage, or tenderness. Immunosuppressive therapy was decreased to promote wound healing.

Gram stain of aspirate taken from the right lower extremity abscess revealed many polymorphonuclear leukocytes and many gram-positive branching organisms. A punch biopsy of the nodule and hematoxylin and eosin staining revealed acute, chronic, and granulomatous inflammation in the dermis (Figure 2). Gomori methenamine-silver stain revealed filamentous bacteria consistent with *Nocardia* species.

Computerized tomography showed no other abscesses in the chest, abdomen, or pelvis, and magnetic resonance imaging of the brain did not reveal any abnormalities.

Initial cultures from the upper extremity lesions grew *Nocardia brasiliensis* with susceptibility to linezolid, minocycline, trimethoprim-sulfamethoxazole, amoxicillin–clavulanate potassium, imipenem, and ceftriaxone, as well as resistance to ciprofloxacin and clarithromycin.

The patient was unable to tolerate trimethoprim-sulfamethoxazole or linezolid because of side effects and was started on amoxicillin–clavulanate potassium. The antibiotic treatment was continued for 1 year.

Two and a half months after the initial infection, the right upper extremity lesions were healing with healthy granulation tissue, and the open wound on the lower extremity was closed. Complete healing occurred and there were no recurrent lesions 6 months after discontinuation of antibiotic treatment.

Comment

Nocardiosis is a gram-positive bacterial infection caused by aerobic actinomycetes of the genus *Nocardia*, which causes systemic and/or localized infections.[1] Transplant recipients are at increased risk for nocardiosis and represent up to 13% of *Nocardia* cases in the United States. The risk for transplant recipients acquiring nocardiosis infection is greatest within the first year posttransplant, possibly because higher doses of immunosuppressants are used during this period.[1]

There are 4 clinical variants of cutaneous nocardiosis: superficial cutaneous infection, lymphocutaneous infection, mycetoma, and a disseminated form with cutaneous involvement. The majority of primary cutaneous nocardiosis cases occurs in immunocompetent patients and usually is caused by *N brasiliensis*.[2]

Nocardia species are ubiquitous in soil, decaying organic matter, and aquatic environments.[2,3] Superficial cutaneous infections result from direct inoculation of the organism into the skin, usually during gardening, farming, insect or animal bites, automobile accidents, or other trauma.[1,3] As in our patient, the injury often occurs weeks to months before the infection is apparent.[4] Superficial cutaneous infections resemble lesions produced by common pyogenic bacteria, such as *Staphylococcus aureus* and group A streptococci, and include ulcerations, bullae, pyoderma, cellulitis, nodules, or subcutaneous abscesses.[5-7] These infections tend to recur locally; therefore, prolonged therapy is necessary to prevent relapse.[5]

In up to one-third of cases, the initial cutaneous infection may progress to a lymphocutaneous syndrome consisting of advancing lymphadenitis with subcutaneous erythematous nodules along the lymphatics.[2] Nocardiosis differs from sporotrichosis because it has an acute onset, as well as rapid progression, tenderness, erythema of overlying skin, and highly inflammatory course.[4,7]

A mycetoma is a chronic, indurated, granulomatous tumorlike mass with draining sinuses,[3,5] which can be caused by fungi or actinomycetes. *Nocardia brasiliensis* is the most common cause of actinomycetomas in the United States, occurring in the southeast and southwest, as well as in South America and Australia.[2] The organisms in the tissue aggregate to form macroscopic granules.[5] The infection may remain localized or may progress to involve the underlying fascia, muscle, or bone.[3,7]

Disseminated nocardiosis, most commonly caused by *Nocardia asteroides*, predominantly affects severely immunocompromised patients and usually begins in the respiratory tract. Skin involvement in disseminated infection occurs in approximately 10% of patients.[5] Dissemination from a primary cutaneous site caused by *N brasiliensis* rarely occurs.[8] All patients with cutaneous lesions should be evaluated to exclude systemic involvement.

Nocardia infections are confirmed by positive culture of the abscess aspirate and by characteristic histology of biopsy specimens.[9] Laboratory notification of the clinical suspicion for *Nocardia* infection is important so that proper steps are taken to identify the organism. Gram staining is the most sensitive way to recognize *Nocardia* in clinical samples and may reveal gram-positive, thin, branching filaments surrounded by polymorphonuclear leukocytes. A presumptive diagnosis can be made if the modified Kinyoun stain shows partially acid-fast filamentous bacilli.[9] Histopathology also may show fibrinopurulent exudates, monocytic infiltrates, granuloma formation, chronic nodular dermatitis, microabscess formation, or sulfur granules.[1] Gomori methenamine-silver stain reveals fine branched filaments in fixed tissue.[10] Two to 4 weeks may be required before *Nocardia* growth is evident in culture.[7,11] This growth occurs on nonselective media, but culture plates may be prematurely discarded if the laboratory is not warned of this possibility.

Sulfonamides and sulfonamide-containing regimens are the treatments of choice for *Nocardia* infection.[1,11] Alternative therapies include minocylcine, aminoglycosides, third-generation cephalosporins, fluoroquinolones, imipenem, amoxicillin–clavulanate potassium, dapsone, and doxycyline.[1,3,11] The optimal treatment duration is uncertain, but prolonged courses are recommended because *Nocardia* infections tend to recur.[3] Primary cutaneous *Nocardia* infection in immunocompetent individuals usually is treated from 1 to several months,[1,12] and immunocompromised patients are treated for a minimum of 6 to 12 months.[1,3,12] Immunosuppressive therapies should be reduced doses, if possible.[3] Surgical intervention such as drainage or excision of abscesses may be required to eliminate the infection or to shorten the course of antibiotic therapy.[1]

As seen in our patient, cutaneous nocardiosis often is unsuspected and undiagnosed because of its resemblance to pyogenic bacterial infections and its slow growth on culture. Clinicians must have a high degree of suspicion to assist the laboratories in isolating and identifying the organism. *Nocardia* should always be considered in the differential diagnosis of immunocompromised patients with a history of trauma because they are at highest risk for acquiring the infection. Once the organism is recognized, patients must be properly treated and monitored for recurrence.

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