Case Reports

Nocardia brasiliensis Cellulitis in a Heart Transplant Patient

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Three months after undergoing heart transplantation, a 55-year-old man presented with N. brasiliensis *cellulitis resulting from a splinter wound acquired during yard work. Surgical débridement was necessary before the infection responded to medical treatment. Although pulmonary nocardiosis is a well-documented complication of immunosuppressive therapy, this is the 1st report of a nocardial infection associated with primary skin involvement in a heart transplant patient.* ***(Texas Heart Institute Journal 1990;17:133-5)***

Increased susceptibility to infection, especially infection with exotic pathogens, has long been associated with immunosuppression in transplant patients.[1] Not only are some opportunistic agents more commonly encountered in infected transplant patients, but the numbers of these agents have increased as the transplant population has expanded. Although pulmonary nocardiosis arising from inhalation is a well-described complication of heart transplantation, cutaneous disease resulting from direct inoculation is rare.[2] We report the case of a heart transplant patient in whom cellulitis associated with *Nocardia brasiliensis* resulted from direct inoculation with a splinter.

Case Report

A 55-year-old man underwent orthotopic heart transplantation for an idiopathic dilated cardiomyopathy. Immunosuppression was initiated with an oral regimen of cyclosporine (4 mg/kg/day), azathioprine (2 mg/kg/day), and a tapered regimen of prednisone, beginning at 40 mg/day. Seven days after transplantation, rejection was diagnosed on the basis of an endomyocardial biopsy, and the patient was treated with intravenous methylprednisolone, 1 g daily, in bolus form; 3 such doses produced good therapeutic response. No OKT3 or antilymphocyte globulin was given.

Three months after transplantation, the patient presented with pain, redness, and swelling of the left hand, radiating into the arm. His illness had begun 4 days earlier, when, after doing some yard work, he found a splinter in the 3rd finger of his left hand. Two days after the injury, redness and swelling developed at the site of the wound; over the next 12 hours, these symptoms spread to involve the dorsum of the hand and the forearm. The patient had no cough or dyspnea, but he was subjectively febrile and reported chills.

Upon admission, physical examination revealed a temperature of 38 °C, a pulse of 80 beats/min, respirations of 24/min, and a blood pressure of 110/60 mmHg. The chest was clear to percussion and auscultation, and the heart sounds were unremarkable. The patient's neurologic system was intact. His left hand showed marked erythema with diffuse margins, dorsal edema, a possibly fluctuant area over the proximal interphalangeal joint, and streaks typical of lymphangitis that radiated as far as the anterior surface of the forearm. Two 1-cm cutaneous nodules were present along one of the lymphangitic streaks, but there was no associated lymphadenopathy.

A hemogram was normal, as were the results of liver function studies and electrolyte analyses. The patient was admitted to the hospital; the cellulitis and finger lesion were aspirated. A gram stain of the aspirate from the finger disclosed granulocytes and fine, branching, gram-positive filaments that proved acid-fast on

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modified Kinyoun staining. The patient was placed on a regimen of oral sulfadiazine, 4 g/day. Three days later, cultures of the aspirate yielded *Nocardia* species. After 5 days of therapy, the patient remained febrile and developed a fluctuant area on the dorsum of his hand; the hand was surgically débrided, and 3 mL of serosanguinous fluid was drained. Over the next 24 hours, the cellulitis and associated fever resolved. Further testing of the isolate showed it to be *N. brasiliensis*, with intermediate sensitivity to sulfadiazine, so minocycline (200 mg/day, orally) was added to the regimen.

The patient was subsequently discharged from the hospital. His scheduled 6-month course of therapy was interrupted after 4 months, when he acquired a peripheral neuropathy thought to be associated with the sulfadiazine. The minocycline was continued for 2 more months, and there was no recrudescence of the disease.

Discussion

The nocardiae are members of the family Actinomycetaceae; 3 of its species are *N. asteroides*, *N. caviae*, and *N. brasiliensis*.[2] These gram-positive, fine-branching bacteria are acid-fast on modified Kinyoun staining. Optimal culture growth occurs, at 37 °C in the presence of 10% carbon dioxide, on sheep-blood agar, Sabouraud dextrose agar, or Löwenstein-Jensen culture medium. Cultures generally become positive within 2 to 5 days, but should be observed for at least 2 weeks when *Nocardia* infection is suspected.[3]

In comparison with the other species in this genus, *N. brasiliensis* is distinguished by its biochemical pattern of fermentation, its growth on diluted gelatin, and its relative resistance to the commonly used agent sulfadiazine.[3] *N. asteroides*, which causes the vast majority of nocardial infections, is widely distributed in the soil, whereas *N. brasiliensis* is a less common isolate usually found in the southeastern and southwestern regions of the United States.[2] Customarily, *N. asteroides* causes pulmonary disease in patients with defective immune systems, whereas *N. brasiliensis* causes soft-tissue infection in immunocompetent individuals. These distinctions, however, are not exclusive; both species have been shown to produce a spectrum of nocardial infections ranging from pneumonia to skin infection to disseminated disease. *N. brasiliensis* has caused pulmonary disease in heart transplant patients before, but ours is the 1st report of primary skin involvement.[4]

Lymphocutaneous disease—typified as in our case by cellulitis, lymphangitis, and nodule formation—begins in the normal host with an erythematous lesion secondary to a puncture wound, which may be acquired during farm or garden work. This injury is followed by the gradual evolution of lymphangitis and, finally, by the development of subcutaneous nodules along the superficial lymphatics. Our case involved an immunosuppressed patient, and the presentation differed from normal inasmuch as the disease evolved rapidly over a 48-hour period and involved the clinical finding of cellulitis. Due to the rapid onset of the infectious process, the presentation was clinically indistinguishable from that of cellulitis produced, more typically, by pyogenic bacteria; care should be taken, in similar cases, not to institute inappropriate empiric therapy.

Although dissemination of *N. brasiliensis* has occurred occasionally in individuals with no apparent immune deficiency, patients with impaired host defenses are more likely to develop systemic disease involving the lungs, central nervous system, bones, kidneys, or liver.[2,5] Conditions that predispose to systemic disease include hematologic malignancies, diabetes mellitus, and systemic corticosteroid use. Disseminated *N. brasiliensis* disease entails a poor prognosis, with a mortality that approaches 80%; therefore, early diagnosis of localized disease and prompt institution of therapy is imperative, especially in the immunocompromised patient.[2,5]

The sulfonamides, in addition to being the most effective agents for treating *N. asteroides* infections, are useful for managing *N. brasiliensis*.[2,6] Both sulfadiazine and sulfisoxazole have been used successfully as single agents in doses ranging from 4 to 12 g/day; the higher doses are used in more severe cases or in the treatment of resistant organisms. Sulfisoxazole, in combination with trimethoprim (e.g., Bactrim, Septra), has been proved effective. There is some doubt, however, regarding the contribution made by trimethoprim, and there have been reports of late relapses after discontinuation of treatment.[7-9] Minocycline and amikacin have both exhibited excellent in vitro action against *Nocardia* species, but little clinical experience has been accumulated with use of these drugs as single agents; therefore, their use is best reserved for sulfonamide-resistant disease that requires combination therapy. The appropriate duration of different treatment regimens has not been well established, but short courses have been associated with an increased incidence of relapse. Most practitioners suggest a treatment duration of 4 to 6 months, with meticulous attention to alkalizing the urine pH to prevent crystalluria.

Additionally, drug levels are recommended with a favorable therapeutic response associated with serum levels greater than 12 mg/dL.[2,6] We rechecked levels biweekly. As our case shows, chemotherapy should never be considered a substitute for thorough surgical drainage of an abscess.

Generally, *Nocardia* infections in heart transplant patients originate in the lung, involve secondary spread to the skin, and are caused by sulfonamide-

sensitive *N. asteroides*. We have reported the case of a patient with primary cutaneous nocardiosis caused by the relatively resistant pathogen, *N. brasiliensis*. This case shows that *N. brasiliensis* can primarily involve the skin, thus mimicking pyogenic cellulitis, and may necessitate surgical intervention before it responds to appropriate medication. Therefore, cardiac transplant recipients who have cellulitis associated with soil contact should be carefully scrutinized for *Nocardia* organisms; when these are encountered, consideration should be given to the presence of the unusual pathogen, *N. brasiliensis*.

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