Disseminated and Cerebral Infection Due to *Nocardia farcinica*: Diagnosis by Blood Culture and Cure with Antibiotics Alone

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Systemic infections with *Nocardia* species continue to be a serious threat to immunosuppressed hosts. Diagnosis of these infections can be difficult despite their known tendency for cerebral and subcutaneous involvement. We describe a patient who presented with nonspecific constitutional symptoms and was found to have subcutaneous and cerebral abscesses due to *Nocardia farcinica*. In addition, a blood culture yielded the organism. The patient responded remarkably to oral therapy; resolution of the cerebral disease was observed on serial magnetic resonance images. We discuss the important clinical features of *N. farcinica* infection, the rarity of positive blood cultures, and the importance of susceptibility testing of *Nocardia* species in selecting drug therapy.

Disseminated infection with *Nocardia* species is uncommon and occurs primarily in immunocompromised patients. Signs and symptoms of this infection are often nonspecific, delay in diagnosis is common, and invasive procedures are frequently needed to obtain appropriate tissue specimens. Unfortunately, *Nocardia* species are rarely identified in blood cultures. Timely recognition of the infection is important, since appropriate antibiotic treatment and surgical drainage may be lifesaving. We present a case of disseminated infection and cerebral abscesses that was due to *Nocardia farcinica* and that was diagnosed by means of blood culture and subcutaneous tissue biopsy and cured with oral antibiotic therapy.

Case Report

A 64-year-old male was seen in the emergency department for evaluation of a 2-week history of arthralgias in the shoulders and wrists; sharp pain involving the left anterior chest, left scapular region, and inner thighs; fatigue; and numbness of the left side of the face and left arm. He denied fever, chills, dyspnea, cough, or weight loss. The patient had diabetes mellitus type II, Wegener’s granulomatosis, and renal insufficiency due to focal segmental glomerulosclerosis. His vasculitis had been diagnosed 4 years earlier, and remission was obtained with a 9-month course of cyclophosphamide and prednisone. He had resumed prednisone therapy (80 mg/d) 4 months before the current visit because of the focal segmental glomerulosclerosis.

Physical examination revealed a temperature of 35.5°C and a respiration rate of 24; his blood pressure and pulse rate were normal. Other findings were unremarkable except for tenderness to palpation in the left parasternal region and over the left rhomboid muscles. The WBC count was within normal limits (with 12% band forms), and mild anemia was present. Findings on a chest radiograph were unremarkable. Blood for cultures and a antineutrophil cytoplasmic autoantibody (ANCA) determination was obtained, and the patient was discharged.

He was admitted to the hospital 8 days later because his symptoms persisted. Examination now revealed a firm, subcutaneous 2-cm mass over the left pectoral muscle. Aspiration yielded cloudy fluid consisting of WBCs and RBCs, but no gram stain or culture was performed on this fluid. The ANCA titer was reported as <10 U (normal titer, 0–10), the erythrocyte sedimentation rate was 113 mm/h, and serological studies for *Coccidioides immitis* infection were negative. A repeated chest radiograph showed no abnormalities. The patient also was noted to have a 2.5-cm area of induration on the right forearm.

Three days after admission, a weakly acid-fast, branching gram-positive rod, identified initially as *Nocardia* species, was reported to be growing in one of two blood culture bottles; the isolate was later confirmed to be *N. farcinica* by a reference laboratory with use of the criteria of Wallace et al. [1]. The following day, a surgical biopsy specimen obtained from the patient’s right forearm also yielded *N. farcinica* in culture.

Susceptibility studies with use of a commercial broth microdilution method (Scepter System; Becton Dickinson Microbiology Systems, Cockeysville, MD [2]) demonstrated that the organism was susceptible to amikacin, imipenem, trimethoprim-sulfamethoxazole (TMP-SMZ), ciprofloxacin, and minocycline but resistant to cefotaxime and ceftriaxone. Therapy with oral TMP-SMZ (160 mg/800 mg four times daily) was begun, with rapid improvement in the patient’s condition. A gadolinium-enhanced MRI revealed five ring-enhancing lesions involving the right thalamus, external capsule, and occipital and frontal deep white matter. The dosage of prednisone was rapidly tapered.
After 5 weeks of therapy with TMP-SMZ, the patient developed a diffuse rash, and treatment was changed from TMP-SMZ to minocycline (100 mg twice daily) and sulfadiazine (1,000 mg four times daily). An MRI obtained 3 months later demonstrated marked regression of the cerebral lesions, and another MRI obtained after 9 months of therapy showed complete resolution. The patient has now completed a 12-month course of antimicrobial therapy. Although his brain lesions were not aspirated, his clear response to therapy strongly supports the diagnosis of *N. farcinica* infection.

**Discussion**

Current microbiological studies support the separation of the *N. asteroides* complex into at least the following three species: *N. asteroides* sensu stricto, *N. farcinica*, and *N. nova*. Results obtained with molecular methods support the presence of additional distinct species or subgroups within the *N. asteroides* complex [3]. This distinction is important because the antimicrobial susceptibility patterns differ between the species, with *N. farcinica* characteristically showing resistance to multiple antimicrobials. For this reason, clinical isolates identified initially as *Nocardia* species should be evaluated further—in a reference laboratory, if necessary. In addition, case reports and series [4] suggest that *N. farcinica* has a propensity for causing disseminated disease and nosocomial infection, necessitating prompt and proper treatment.

The relative frequencies of the various *Nocardia* species are difficult to determine retrospectively and may vary geographically. Before the acceptance of *N. farcinica* as a species, Beaman et al. [5] reported that of 253 isolates recovered in the United States, 77.9% were *N. asteroides* and 9.5% were *N. brasiliensis*, and McNeil et al. [2] reported that of 121 isolates recovered in the United States, 81% were *N. asteroides* and 19% were *N. brasiliensis*. However, Wallace et al. [6] reported that 19% of 200 isolates collected between 1979 and 1989 in the United States were *N. farcinica*. Schaal and Lee [4] tested 131 isolates in Germany between 1979 and 1991 and found that 28.2% were *N. asteroides*, 60.3% were *N. farcinica*, 6.1% were *N. otitidiscaviarum*, and 3.8% were *N. brasiliensis*. Boiron et al. [7] reported that of 63 isolates recovered in France between 1987 and 1990, 66.7% were *N. asteroides*, 23.8% were *N. farcinica*, and 4.8% were *N. otitidiscaviarum*.

Blood cultures for patients with nocardia infection are rarely positive. Our search of the English-language literature disclosed only 29 previous case reports of nocardia bacteremia, and in only two of these 29 cases was *N. farcinica* reported as the isolate [8, 9]. Of these 29 bacteremic patients, only five also had CNS disease (four cases due to *N. asteroides* and one due to *N. otitidiscaviarum*), and nine had subcutaneous abscesses. One of the two previously described patients with *N. farcinica* bacteremia had an infected prosthetic heart valve alone, and the other had lung involvement alone. For our patient, one of two routine blood cultures performed with the Bectec 660 System (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD) was positive, while a blood culture performed with use of the Bectec media for fungi was negative. The final identification of *N. farcinica* was reported 17 days after blood for the initial culture was drawn.

Because routine blood cultures are usually reported as negative after 5–7 days of no growth but fungal blood cultures are normally held for 4 weeks, Roberts et al. [10] have recommended the performance of fungal blood cultures when nocardia infection is suspected. Vannier et al. [11] were able to detect *Nocardia* by using the Bectec system, but these investigators noted faster detection rates when the samples were subcultured early (on day 5) onto blood agar media. Recovery rates may be increased when the clinical suspicion of nocardia infection is communicated to the laboratory, lysis centrifugation, additional media, and increased incubation periods will then be applied.

On the whole, the treatment of nocardiosis remains empirical. Sulfonamides have been used most extensively, with good results when these drugs are tolerated. Wallace et al. [12] found that the agents most active in vitro against *N. asteroides* were sulfamethoxazole, minocycline, amikacin, imipenem, cefotaxime, and ceftriaxone. In a later study Wallace and colleagues [6] found that *N. farcinica* exhibits a high degree of resistance to the cephalosporins, ampicillin, aminoglycosides other than amikacin, and erythromycin but is usually susceptible to amikacin, ciprofloxacin, imipenem, and sulfamethoxazole. Because of the significant risk for adverse reactions to sulfonamides and because of the unique drug susceptibility patterns that distinguish the species comprising the *N. asteroides* complex, in vitro susceptibility testing of *Nocardia* species is recommended [12, 13].

Infections caused by the *N. asteroides* complex remain a diagnostic challenge and require prolonged antimicrobial therapy. Clinically significant isolates of *Nocardia* should be identified completely to the species level. Such identification allows elucidation of the clinical and epidemiological associations between *Nocardia* species and human disease. Therapy for nocardiosis may still be guided by susceptibility testing, which is best performed by experienced laboratories; however, results of such testing have not been well correlated with clinical outcomes.

**References**


