Nocardia asteroides Native Valve Endocarditis

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A 39-year-old man with a history of injection drug abuse was given a diagnosis of Nocardia asteroides native aortic valve endocarditis, and he required valve replacement therapy, despite having received potent antimicrobial therapy. This is the first reported proven case of native valve endocarditis due to Nocardia species.

Nocardiosis is primarily an opportunistic infection. It occurs, in particular, in patients with underlying malignancies, chronic lung disease, or disorders of cell-mediated immunity, including HIV infection; those who receive long-term corticosteroid therapy; and those who undergo organ transplantation. It also occurs in injection drug abusers. We present what we believe is the first published case report of native valve endocarditis due to Nocardia species that occurred in an immunocompetent patient who had abused injection drugs.

A 39-year-old man presented with a 2-week history of fever, chills, and night sweats. He was a long-distance truck driver who occasionally self-injected amphetamines and reused needles, but who denied sharing needles. Needles were occasionally left uncapped in the cabin of his truck. He had no history of any cutaneous lesion occurring at the sites of injection. Physical examination revealed a temperature that spiked to 39°C, a heart rate of 92 beats/min, and a body weight of 75 kg. He had moderate hepatosplenomegaly. Heart murmur was not audible.

Laboratory studies disclosed the following values: hemoglobin, 13.7 g/dL; WBC count, 8.5 cells/mm³; platelets, 185 cells/mm³; and erythrocyte sedimentation rate, 45 mm/h. Findings on chest radiography were normal, and the results of tests for antibodies to HIV and hepatitis C virus were negative. Multiple cultures of blood specimens yielded Nocardia asteroides. The patient was treated simultaneously with iv meropenem (1 g q8h), iv amikacin (750 mg q12h), iv ceftriaxone (2 g q12h), and iv trimethoprim-sulfamethoxazole (TMP-SMZ; TMP, 560 mg q8h, and SMZ, 2800 mg q8h). Transthoracic echocardiography revealed an echodense aortic valve with a definite echodense lesion (size, 0.9 cm × 0.9 cm) at the junction of the right and left coronary cusps, which prolapsed into the outflow tract. A jet of aortic regurgitation was visible on Doppler sonography. Transesophageal echocardiography confirmed the presence of this abnormality, which appeared to be attached to the left coronary cusp of the valve. The mitral and tricuspid valves were normal in appearance.

The patient’s course of disease was complicated by persistent fever and malaise. Cultures of blood samples were repeated after initiation of antibiotic therapy and yielded negative results. An ulcerative embolic lesion emerged on the left great toe, and a swab of the ulcer tested positive for N. asteroides on culture. Transesophageal echocardiography was repeated and revealed a perforated left coronary cusp and an aortic root abscess. Aortic valve replacement was undertaken 21 days after presentation. The operative findings were vegetation (size, 1.0 cm × 1.0 cm) at the junction of the right and left valve cusps, with perforation of both cusps and an associated small abscess in the annulus. The vegetation was removed with the valve leaflets, and the abscess was debrided. The aortic root did not require replacement, and the valve was replaced with a St. Jude’s prosthesis. The patient began receiving treatment with warfarin. Seventeen days after initiation of antibiotic therapy, cultures of valve specimens tested positive for N. asteroides.

MICs for key antibiotics were obtained by use of the E-test (AB Biodisk) method, for the original isolate obtained from culture of blood samples, and by use of the microdilution method, for the isolate yielded by culture of valve tissue specimens. The MICs obtained, by means of E-test and microdilution, respectively, were as follows: for cefotaxime, 0.5 μg/mL and 1.0 μg/mL; for amikacin, 0.5 μg/mL and 0.5 μg/mL; for TMP-SMZ, 8 μg/mL and 0.032 μg/mL; and for imipenem, 0.064 μg/mL (by microdilution only).

Treatment with meropenem and amikacin was discontinued ~2 weeks after surgery. The dosage of iv ceftriaxone was decreased to 2 g/day, and the dosage of TMP-SMZ was changed to TMP, 320 mg t.i.d., and SMZ, 1600 mg t.i.d. Four weeks after surgery, treatment with ceftriaxone was changed to treatment with cefpodoxime, 100 mg b.i.d., and TMP-SMZ therapy was continued. Cefpodoxime was subsequently discontinued 10 weeks after surgery, and the patient ultimately continued...
taking TMP-SMZ for a total of 6 months. He was in good health at a follow-up done 18 months after presentation.

*Nocardia* species are ubiquitous soilborne aerobic and saprophytic bacteria that form branched filaments [1]. *N. asteroides* is the predominant human pathogen and is most commonly introduced through the respiratory tract. The principal syndromes caused by *Nocardia* species include upper and lower respiratory tract disease and hematogenous dissemination to the brain, skin and subcutaneous tissues, eyes, liver, kidneys, joints, and bones. Although pulmonary disease may be self-limiting, disseminated disease progresses unless treated. Our patient probably acquired his infection percutaneously through the reuse of a contaminated needle. Despite a subacute presentation, well-preserved cardiac function, and extremely potent antibiotic therapy, it soon became clear that valve replacement would be essential for the patient’s survival.

This is the first reported proven case of native valve endocarditis due to *Nocardia* species. Cases of proven prosthetic valve endocarditis due to *Nocardia* species have been reported [2–8]. In a review by Dhawan et al. [2], 4 of 6 patients with prosthetic valve endocarditis due to *Nocardia* species died; the remaining 2 patients recovered while following regimens of antimicrobial agents, including imipenem [2]. Dhawan and colleagues also reported a case of native valve endocarditis in which *Nocardia*-like organisms were revealed on histological examination of mitral valve tissue specimens, but for which the results of cultures of the valve specimen and blood samples were negative. As with other forms of life-threatening nocardiosis, the use of antimicrobial therapy for endocarditis due to *Nocardia* species remains problematic because of the lack of standardized susceptibility testing methods [9]. In murine models of cerebral and pulmonary nocardiosis, imipenem and amikacin appear to be most-effective antimicrobial agents, although neither cefotaxime nor TMP-SMZ appears to be synergistic with imipenem [10]. However, synergy between imipenem and TMP-SMZ, imipenem and cefotaxime, and amikacin and TMP-SMZ has been demonstrated in vitro [11].

Native valve endocarditis due to *Nocardia* species is clearly an extremely rare disease. Appropriate antimicrobial therapy is likely to be delayed, given the rather indolent onset of and low level of suspicion for this disease. Valve replacement will very likely always be required, given the propensity of the organism for local tissue destruction, despite what would appear to be potent and adequate antimicrobial therapy.

**References**