

Nocardial endocarditis of an aortic valve prosthesis

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SUMMARY The organism responsible for endocarditis of a prosthetic aortic valve was identified as *Nocardia asteroides*. The patient was treated with intravenous amikacin (250 mg four times a day) and intravenous imipenem (1.5 g four times a day). The valve was replaced under this new antibiotic regimen. This is the first report of survival after prosthetic valve nocardiosis.

Two cases of endocarditis of a prosthetic valve resulting from *Nocardia asteroides* infections have been reported.^{1 2} Both patients died before specific treatment could be established. We report a case of nocardial endocarditis that followed aortic valve replacement.

Case report

A 61 year old man with severe calcific aortic valve disease was given a Medtronic Hall valve prosthesis in March 1984. Fever developed after operation and he was treated with the antibiotic cefadroxil because an exacerbation of chronic emphysematous bronchitis was suspected. The patient was transferred to the medical department 21 days after operation. Physical examination was normal and the prosthetic heart sounds were clear. A chest x ray indicated emphysema without pulmonary infiltrates; the heart was of normal size. Abdominal sonography and cholangiography showed small stones in the gall bladder and in the cystic duct. The erythrocyte sedimentation rate (56 mm per hour), the neutrophil count ($5.7 \times 10^9/l$) (with an increased proportion of unsegmented neutrophils (11%), serum iron ($<25 \mu g/dl$), and copper ($240 \mu g/dl$) were compatible with a systemic infection. When antibiotic treatment was withdrawn the patient's oral temperature rose to $40^\circ C$. After two weeks of incubation at $37^\circ C$ blood cultures showed growth of a Gram positive filamentous micro-organism. This organism was identified as biovar B of the *Nocardia asteroides* complex³ or *Nocardia farcinica*.⁴ Sputum cultures were always negative for nocardiae and urine cultures contained no micro-organisms.

TREATMENT

Intravenous treatment with amoxycillin (2 g three times a day) was started followed by a combination of mezlocillin (5 g three times a day) and tobramycin (80 mg twice a day) because blood cultures remained negative for two weeks. When *Nocardia asteroides* was identified as the aetiological agent treatment with sulphadiazine 12 g a day was started. But the dose of 24 tablets per day produced unacceptable gastrointestinal side effects. Intravenous treatment with amikacin and a combination of amoxycillin plus clavulanic acid (Augmentin) was started at dosage of 250 mg two to four times a day and 5.5 g three times a day (5 g amoxycillin + 0.5 g clavulanic acid) respectively. In vitro susceptibility tests⁵ showed that the *Nocardia* strain was sensitive to amikacin at a minimal inhibitory concentration (MIC) of $\mu g/ml$ and moderately sensitive to amoxycillin plus clavulanic acid (MIC 8-16 $\mu g/ml$) and the trimethoprim derivative, imipenem (MIC 8 $\mu g/ml$). Oral dosages of imipenem (1.5 g four times a day) and amikacin (500 mg four times a day) were chosen to maintain the bactericidal concentrations in the serum that were obtained during infusion of both drugs. This regimen reduced fever to $37-38^\circ C$ and reduced the proportion of unsegmented neutrophils.

Six weeks after admission, moderate signs of cholangitis were seen and a cholecystectomy was performed in the eighth week. Cultures from the removed gall bladder, the bile, and blood were negative. Body temperature declined and remained normal for four weeks and the patient was discharged on the thirteenth postoperative day without antibiotic treatment.

The patient was readmitted to the medical department on 30 July 1984 because of recurrent septic fever. Blood cultures again produced *Nocardia asteroides* (*N farcinica*) which was still sus-

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ceptible to amikacin, imipenem, and co-trimoxazole in vitro. Clinical investigation, especially prosthetic valve sounds and laboratory tests including chest x ray, bronchoscopy, abdominal sonography, and bone marrow histology did not indicate any systemic malignant disease. On the second day of amikacin treatment (500 mg four times a day) and imipenem (1 g four times a day) fever levelled off and remained at 36.5–37.5°C. The patient was transferred to the department of surgery. At operation an intact aortic valve prosthesis was found but there was an aneurysm of the non-coronary sinus of Valsalva. Cultures from the removed valve produced *Nocardia asteroides* (*N farcinica*). The sinus of Valsalva and the base for the valve were locally disinfected and a Medtronic Hall aortic valve prosthesis was implanted. Postoperative recovery was good. Amikacin had to be withdrawn because of rapid deterioration of hearing. Treatment with imipenem (1 g four times a day) was continued for three weeks after operation. Then the patient was treated with oral trimethoprim and sulphamethoxazole (160 and 800 mg twice a day respectively). Before discharge transmission computed tomography and scintigraphy with indium-111 labelled leucocytes did not detect any cranial abscesses. The patient remains well without any laboratory evidence of infectious disease.

Discussion

Nocardiosis is a rare disease with an unfavourable prognosis which occurs predominantly in severely compromised patients with systemic malignant disease or in those on immunosuppressive treatment.⁶ So far two cases of nocardiosis of prosthetic valves have been reported.^{1,2} Vlachakis and associates reported the death of a 34 year old women four months after mitral valve replacement.² Falk and coworkers reported the death of a 64 year old woman from nocardial endocarditis six months after replacement of an aortic valve.¹ Both patients had multiple abscesses and in the absence of other sites of entry the lungs were the most likely portal for systemic nocardiosis.⁶ In our patient body temperature declined to normal immediately after cholecystectomy; however, an infectious agent was not cultured from the resected gall bladder and cholangitis or cholecystitis have not been reported as primary manifestations of nocardiosis. The possibility of false negative cultures must be considered; however, the mode of infection remains unclear. Possibilities include intraoperative infection and activation by the operation of an infection that was acquired preoperatively.⁷

This is the first report of the survival of a patient

with nocardial endocarditis after valve replacement. In our opinion the favourable outcome in this case depended on the following factors: (a) the causative agent (*Nocardia asteroides*, biovar B = *N farcinica*) was identified early; (b) abscesses did not occur in vital organs; (c) an antibiotic regimen that was effective in vivo was found; and the patient could be brought to reoperation.

Nocardiosis was diagnosed in our patient from a blood sample obtained on the twenty-sixth post-operative day. Because we found that only screening for *Nocardia* gave positive results, we wonder whether the high numbers of "unknown" agents in prosthetic valve endocarditis⁸ may be partly accounted for by nocardiae. Early diagnosis is essential because nocardiosis tends to spread and produce disseminated, especially cerebral, abscesses.^{6,7} Prevention of these abscesses was probably the major effect of the antibiotic treatment that we used. We used a regimen of amikacin and amoxycillin plus clavulanic acid because experimental⁵ and clinical⁹ results with these agents have been reported to be better than standard sulphadiazine treatment. The *Nocardia* strain in the present case was sensitive to amikacin but only moderately sensitive to amoxycillin plus clavulanic acid (Augmentin) and fever was not suppressed by this combination. Augmentin was, therefore, replaced with the thienamycin derivative imipenem which has also been reported to be effective in some isolates of *Nocardia asteroides*.^{10,11} Imipenem appeared to be as effective or slightly more effective against the patient's *Nocardia* strain than amoxycillin plus clavulanic acid. Very high doses were required to achieve bactericidal plasma concentrations and after the replacement of the valve prosthesis the side effects of amikacin (deterioration of hearing) limited the use of this drug. Antibiotic treatment could not be expected to effect a cure in the presence of an infected valve prosthesis. The positive cultures obtained from the removed aortic valve prosthesis and the rapid recovery of the patient after replacement of the valve confirmed the diagnosis of nocardial endocarditis. The contribution of the aneurysm of the sinus of Valsalva in this case is not known. Cultures obtained from this aneurysm were negative and we do not know whether it was a consequence or a cause of the endocarditis.

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