Cardiac device infections due to *Mycobacterium fortuitum*

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Two cases of cardiac device infection due to *Mycobacterium fortuitum* are reported along with a discussion of their clinical management. Long-term therapy and removal of the infected device is needed. The slow progression and absence of systemic signs and symptoms suggest a low pathogenicity of *M fortuitum*.

Key Words: *Cardiac device;* Mycobacterium fortuitum

Les infections au *Mycobacterium fortuitum* causées par un appareil cardiaque

Deux cas d'infections au *Mycobacterium fortuitum* causées par un appareil cardiaque sont déclarés et suivis d'un exposé de leur prise en charge clinique. Une thérapie à long terme et le retrait de l'appareil infecté s'imposent. La lente progression et l'absence de signes et symptômes systémiques laissent supposer une faible pathogenèse du *M fortuitum*.

Mycobacterium fortuitum is a rapidly growing mycobacteria that is ubiquitous in soil and water. It is an opportunistic pathogen, and usually causes skin, skeletal or catheter-related infections (1,2). To date, no cases of *M fortuitum* infection of pacemakers or implantable cardioverter defibrillators have been reported.

CASE PRESENTATIONS

Case 1

A 72-year-old man with a history of diabetes mellitus type 2 and hypertension had a pacemaker implanted in December 2000 for sinus node disease. Two weeks later, a surgical site infection with abscess formation at the site of pacemaker implantation was observed. The abscess fluid grew a coagulase-negative staphylococcus, which was treated with ciprofloxacin over four weeks. *M fortuitum* was also isolated, but was interpreted as a possible contamination. One year later, the patient was hospitalized for 11 days for exploration of the pacemaker site due to subcutaneous nodules and chronic drainage. He developed a postoperative fever, but blood cultures were negative. Parenteral teicoplanin and ceftriaxone were administered for three weeks. Two months later, treatment with ciprofloxacin, trimethoprim-sulfamethoxazole and clarithromycin was started and then changed to amikacin and ciprofloxacin once the antimicrobial susceptibility pattern for the isolated *M fortuitum* was available. Susceptibility testing was performed in the clinical microbiology laboratory with the agar disk elution method for amikacin, tobramycin, ciprofloxacin, doxycycline, cefoxitin, imipenem and trimethoprim-sulfamethoxazole, and by a disk diffusion method for clarithromycin, azithromycin, erythromycin and tetracycline. The isolate was susceptible only to amikacin and ciprofloxacin. Ceftriaxone was not tested. All subsequent cultures remained sterile, but the patient was again hospitalized for 23 days for pacemaker removal. Further postoperative fever delayed the implantation of a new pacemaker by 14 days. An echocardiography showed no vegetations. Ciprofloxacin was continued for six months after pacemaker replacement, and amikacin was discontinued after 15 days due to injection site problems and the development of hearing impairment. At three years follow-up, the patient was well with no evidence of recurrence.

Case 2

A 61-year-old man had an implantable cardioverter defibrillator in July 2000 for severe coronary artery disease and multiple episodes of ventricular tachycardia. At routine follow-up in December 2001, he presented with evidence of a cutaneous infection overlying the generator. *M fortuitum* was isolated from culture. Treatment with ciprofloxacin was initiated but

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discontinued by the patient at 14 days. He refused replacement of the cardiac device. He had a continuing follow-up at the pacemaker unit because of chronic drainage of the area, but was referred for further management only after two years. The patient was subsequently hospitalized and the device removed. Cultures of the leads, the area around the generator, the pocket and granulomas isolated M *fortuitum*. Sensitivity testing included tobramycin, amikacin, ciprofloxacin, imipenem, trimethoprim-sulfamethoxazole, cefoxitin and doxycycline (tested by the agar disk elution method); tetracycline, azithromycin and amoxicillin/clavulanate (tested by the disk diffusion technique); and erythromycin, linezolid, levofloxacin, clarithromycin, teicoplanin and vancomycin (by E-test). An echocardiography showed no vegetations. Immunoglobulin levels were normal and screening for HIV was negative. There was mild renal insufficiency and previously diagnosed chronic anemia. He was not receiving any immunosuppressive treatment.

Treatment with levofloxacin and amikacin was initiated, to which the organism was susceptible. The creatinine value was 102.54 µmol/L before initiating treatment, and increased to 183.87 µmol/L after 10 days of amikacin. Amikacin was discontinued and renal function subsequently recovered (100.77 µmol/L). An ultrasound-guided puncture of the involved area obtained after two weeks of treatment showed no acid-fast bacteria and was negative for mycobacteria on culture. The patient continues on levofloxacin (500 mg/day) monotherapy.

DISCUSSION

M *fortuitum* causes human infection primarily by direct inoculation, including primary skin and soft tissue infections, surgical wound infections and catheter-related sepsis. Other infections, such as keratitis, pulmonary disease, endocarditis and cervical lymphadenitis are rarely observed. In a retrospective study of M *fortuitum* infections in Sweden (3), 86 isolates were recovered but none from an intravascular source. To our knowledge, no cases of M *fortuitum* infection of cardiac devices have been previously described.

M *fortuitum* was isolated from granulomas in contact with the pacemaker generator in one patient, and from the intravascular electrode leads and subcutaneous abscess in the other. The clinical presentation was consistent with surgical site infection with subsequent fistula formation and chronic drainage. Neither patient had fever, leukocytosis or other signs of systemic infection. Blood cultures remained negative in both cases, although M *fortuitum* was isolated from the intravascular electrode lead in one patient. Endocarditis was excluded by absence of clinical signs and symptoms (absence of fever, no cardiac murmur and no septic embolism), sterile blood cultures and negative echocardiography. Although the duration of the infection exceeded two years, the infection remained localized and blood cultures sterile, with no progression to systemic signs.

Bacteremia due to M *fortuitum* is uncommon but has been attributed to long-term central venous catheters in cancer patients (4,5). Colonization of the breast and adjacent skin has been reported (5). This could also be possible for cardiac devices implanted via a subclavian vein. Hospitalization was required in both patients to remove the infected device and re-implant a new one. These procedures require monitoring in critical care with substantial expense. While other authors (3) have questioned the pathogenicity of M *fortuitum*, we believe it was the infection agent in our patients based on chronicity of infection, isolation from sterile sites and response to therapy.

Acquisition of infection was most likely at the time of the surgical procedure. Both patients had their cardiac devices implanted in the same pacemaker laboratory. Environmental sources could include contaminated medical instruments or fluids (6). Because the patients were referred several years after the initial infection, environmental cultures to identify the origin of M *fortuitum* were not performed. Additional infections were not identified in any other patients.

The optimal antimicrobial regimen is unknown, given the few cases, types and sites of infection. M *fortuitum* is also resistant to conventional antituberculous drugs. Some fluoroquinolones have been reported to have excellent activity against mycobacteria. It is not recommended, however, that they be used as monotherapy because of the emergence of resistance leading to possible relapse (7). In our patients, other options were not possible because of renal toxicity from the amikacin and resistance of the isolate to other antibiotics.

Our strains showed a more resistant antimicrobial susceptibility pattern than those reported previously (8-10). It is recognized that erratic results are achieved with clarithromycin (11). The resistance pattern in our isolates confirmed the need for antibiotic susceptibility testing of all clinically significant isolates.

We agree with previous reports (12) that initial treatment should include at least two appropriate antibiotics selected on the basis of susceptibility results as well as the removal of the affected electrode lead and/or abscess. In a study describing catheter-related infections (5), bacteremic patients in whom catheters were not removed uniformly relapsed or failed treatment. Thus, the removal of foreign material is crucial. Full debridement of abscesses or fistulas is also necessary, and surgery should also be considered in those patients in which resistant organisms exist (13). While our patients have done well, previous reports have suggested that recurrences are frequent, even with optimal therapy (12).

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