Corynebacterium jeikeium pacemaker infection associated with antineutrophil cytoplasmic antibodies: a single positive blood culture could be sufficient for diagnosis

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Corynebacterium jeikeium, a member of the non-diphtheria corynebacteria, has been rarely reported as being responsible for cardiovascular-device infection. Here, we report what is believed to be the first case of C. jeikeium pacemaker infection associated with the presence of proteinase-3 antineutrophil cytoplasmic antibodies. The diagnosis was established based on the positivity of a single positive blood culture and led to pacemaker extraction. This observation highlights the difficulty in the diagnosis of cardiac-device infection in the presence of a single positive blood culture with a fastidious microorganism that could be considered as a contaminant. It also underscores the need for device extraction to ensure healing.

Introduction

Corynebacterium jeikeium is a member of the non-diphtheria corynebacteria formerly known as Corynebacterium group JK and designated C. jeikeium since 1987 (Jackman et al., 1987). It is a pleomorphic, non-motile, non-sporulating, Gram-positive rod that constitutes a major component of the bacterial flora of the human skin. This micro-organism particularly colonizes the axillary, rectal and groin regions of hospitalized patients, and can cause infection after disruption of the skin by surgery (cardiac or orthopaedic surgery) or invasive procedures (Soriano et al., 1988). C. jeikeium may cause various types of infections (Funke et al., 1997), and is implicated in native, prosthetic or catheter-related endocarditis (Belmares et al., 2007; Mookadam et al., 2006). However, this micro-organism has only been rarely observed in cardiovascular-device infection (pacemaker or implantable defibrillator). We report a case of C. jeikeium pacemaker infection associated with the presence of proteinase-3 antineutrophil cytoplasmic antibodies (PR3-ANCA).

Case report

In June 2007, a 72-year-old man presented with a 6 week history of fever. He was known to have a brady–tachy syndrome with bifascicular block, which led to a dual-chamber-pacemaker implantation in 1996. The pulse generator was replaced in September 2006 (with a Medtronic Adapta L ADDRL1). His physical examination showed normal results. A radiological examination, including transoesophageal and transthoracic echocardiography, and laboratory investigations were unremarkable. However, the level of PR3-ANCA was positive at 1053 IU ml\(^{-1}\) (normal range \(<20\) IU ml\(^{-1}\)) without clinical evidence for localized eye, nose and throat involvement or systemic Wegener’s granulomatosis. During his hospitalization, the patient developed right external popliteal nerve palsy. No evidence of vasculitis was observed on neuromuscular biopsy. One out of twelve sets of blood cultures yielded a growth-deficient Corynebacterium sp. after 11 days of incubation, with a small-colony morphology on blood agar medium. Species identification using 16S rRNA gene amplification and sequencing (Lécuyer et al., 2007) revealed the isolate to be C. jeikeium. The strain was only susceptible to tetracycline, pristinamycin, vancomycin and rifampicin. A decision was taken to treat...
the patient for possible pacemaker-related endocarditis. Vancomycin (3 g intravenously per day for 9 days) associated with gentamicin (300 mg intravenously per day for 6 days) was administered, followed by teicoplanin monotherapy (600 mg intravenously per day) for 2 weeks. Teicoplanin was then replaced by linezolid (1200 mg orally per day) due to a presumed allergic skin rash, then by vancomycin (3 g intravenously per day) due to linezolid-related thrombocytopenia for 2 weeks, followed by doxycycline (200 mg orally per day) for 6 weeks.

In November 2007, 3 weeks after the discontinuation of antibiotics, the patient was readmitted for relapsing fever. Physical examination results remained normal, except for a discrete left-foot motor deficit. Laboratory tests were otherwise normal. One out of ten sets of blood cultures yielded _C. jeikeium_ again after 5 days of incubation, with the same antibiotic susceptibility as the initial isolate. The patient’s pacemaker was removed by percutaneous extraction and vancomycin treatment (3 g intravenously per day) was initiated. The culture of the pacemaker pulse generator grew _C. jeikeium_ in enriched liquid medium after 9 days of incubation with the same antibiotic susceptibility phenotype as the original isolate. The culture of the pacemaker leads was negative. The patient received the intravenous vancomycin for 2 weeks, followed by doxycycline (200 mg orally per day) associated with rifampicin (1200 mg orally per day) for 4 weeks. After a 19 month follow-up, it was found that the serum PR3-ANCA had decreased to 30 IU ml⁻¹.

Comparison of the three strains of _C. jeikeium_ isolated from the pacemaker and the blood in June and November 2007 was realized with a PCR typing method as described before for _Corynebacterium diphtheriae_ (De Zoysa et al., 2008). Analysis of the genomic fingerprints of the three strains obtained after random amplification by PCR showed that they were highly related (Fig. 1).

**Discussion**

Pacemaker-related infection can be divided into pocket infection, lead infection or pacemaker-related endocarditis. Incidence rates of permanent pacemaker device infection vary from 0.13 to 19.9 % (Baddour et al., 2003). Most of the published reports documented coagulase-negative staphylococci and _Staphylococcus aureus_ as the predominant micro-organisms, which account for more than two-thirds of cardiac-device infections (Sohail et al., 2007). Non-diphtheria corynebacteria have been implicated in cardiac-device infection (permanent pacemaker or implantable cardioverter-defibrillator) (Belmares et al., 2007; Sohail et al., 2007) but to October 2010, only three pacemaker-related infections due to _C. jeikeium_ have been reported (Federmann et al., 1996; Gronemeyer et al., 1980; Heltberg et al., 1986).

Secondary procedures, such as pacemaker pulse-generator replacement, are one of the most important risk factors for infection (Klug et al., 2007). Our patient developed _C. jeikeium_ infection 18 months after the first generator replacement, which probably represented the portal of entry for the infectious micro-organism. This observation highlights the following: firstly, the isolation of a fastidious micro-organism, like _C. jeikeium_, should lead to consideration of the isolate as a possible cause of the infection and not just as a contaminant bacterium, particularly in the presence of a foreign device; secondly, the early relapse provides further evidence that infected cardiac devices should always be removed to ensure healing. Antibiotic therapy alone has been associated with a high rate of mortality and failure of infection control (Sohail et al., 2007).

Moreover, _C. jeikeium_ is one of the most resistant _Corynebacterium_ spp. with respect to antimicrobial agents. The majority of _C. jeikeium_ clinical isolates are resistant to antibiotics such β-lactams and macrolides, and often remain susceptible only to glycopeptides (Riegel et al., 1996; Weiss et al., 1996). Therefore, vancomycin should be considered as the drug of choice for the treatment of _C. jeikeium_ infection until the results of antibiotic susceptibility testing are obtained.

![Fig. 1. DNA fragment banding pattern after acrylamide gel electrophoresis of PCR products obtained by random amplification of polymorphic DNA with two primers, P5 and P1 (De Zoysa et al., 2008), and silver staining. Lanes: 1, 2 and 3, control strains of _C. jeikeium_ CIP103337, K411 and CIP82.51, respectively; 4 and 5, _C. jeikeium_ isolated from the pacemaker and the blood culture in November 2007, respectively; 6, _C. jeikeium_ isolated from the blood culture in June 2007; L, DNA ladder (the molecular sizes are indicated on the right in bp).](#)
Antineutrophil cytoplasmic antibodies (ANCA) directed against either proteinase-3 or myeloperoxidase have been rarely associated with subacute infectious diseases, and particularly subacute infective endocarditis, which are mainly due to *Staphylococcus* spp. and *Streptococcus* spp. (Choi et al., 2000). Subacute infective endocarditis and systemic vasculitis share many clinical manifestations, including fever, constitutional symptoms, and possible cutaneous and renal involvement. In our patient, the reversion of positive levels of ANCA to values approaching normal [30 IU ml⁻¹ (normal range <20 IU ml⁻¹)] with the treatment of endocarditis, and the absence of ANCA-associated systemic vasculitis (micropolyangiitis and Wegener’s granulomatosis) despite long-term follow-up, are evidence for subacute infective endocarditis associated ANCA. Awareness of ANCA positivity in subacute bacterial endocarditis may avoid unnecessary diagnostic procedures.

To our knowledge, this report is the first observation of a *C. jeikeium* pacemaker infection associated with ANCA and highlights the difficulty in the diagnosis of cardiac-device infection in the presence of a single positive blood culture with a fastidious micro-organism that could be considered as a contaminant. It also underscores the need for device extraction to ensure healing.

**References**


