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Mycobacterium phlei, a previously unreported cause of pacemaker infection: Thinking outside the box in cardiac device infections

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Abstract

The increased use of cardiac rhythm management devices has led to an increase in cardiac device-related infections (CDI). Staphylococcus aureus *and* epidermidis *account for the vast majority of CDI. CDI due to rapidly growing non-tuberculous mycobacteria is very rare, with only about ten cases having been reported. We report a case of pacemaker pocket infection with* Mycobacterium phlei. *There are only three published reports of human infection involving this typically non-pathogenic organism. To the best of our knowledge, this is the first report of CDI with* Mycobacterium phlei. (Cardiol J 2011; 18, 6: 687–690)

Key words: cardiac device infection, non-tuberculous mycobacteria, pacemaker pocket infection, *Mycobacterium phlei*

Introduction

Expanding clinical indications and the growing burden of cardiovascular disease has led to increased implantation of cardiac rhythm management devices (CRMD) which include permanent pacemakers, implantable cardioverter defibrillators and cardiac resynchronization therapy (CRT) devices [1, 2]. Between 1996 and 2003, implantation of CRMD increased by about 50% in the United States [3]. This was associated with a three-fold increase in hospitalization for cardiac device-related infections (CDI) [3]. *Staphylococcus aureus* and *epidermidis* account for the vast majority of CDI [3]. CDI due to non-tuberculous mycobacteria (NTM) is extremely rare, with only about ten reported cases [4]. We report a case of pacemaker pocket infection with *Mycobacterium phlei*. To the best of our knowledge, there are only three published reports of human infection involving this organism, and no prior reports of CDI [5–7].

Case report

A 73 year-old female with ischemic cardiomyopathy underwent implantation of a cardiac resynchronization therapy-defibrillator (CRT-D) device for NYHA class III heart failure. Medical history included diabetes, hypertension, prior anterior wall myocardial infarction, and coronary stent placement. Left ventricular ejection fraction was 30–35%, and QRS duration was 130 ms with left bundle branch block morphology. Medications included metoprolol succinate, lisinopril, aspirin, glipizide

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and furosemide. A CRT-D generator was placed in the left pectoral area and the leads were positioned in the right atrium and right ventricular septum by active fixation mechanism. The left ventricular pacing lead was positioned in the postero-lateral branch of the coronary sinus. Standard techniques were used and appropriate position and adequate pacing and capture thresholds of all leads were confirmed. The patient had a small post-operative hematoma which resolved over the following two weeks. The device was set to DDDR mode, VT and VF zones were programmed at 171 and 200 respectively. Post-operatively, she was started on warfarin as multiple episodes of paroxysmal atrial fibrillation (AF) were noted on device monitoring. Two weeks later, amiodarone was started following an inappropriate shock due to AF with rapid ventricular response. At one-month follow up, some serosanguinous discharge was noted at the pocket site. There was no local erythema, swelling, or tenderness and a small amount of fluid could be expressed from the medial aspect of the pocket. She was admitted to the hospital and treated empirically with intravenous vancomycin for presumed pocket infection. Blood cell counts were normal, blood and swab cultures remained sterile. Therefore, vancomycin was discontinued and the patient was discharged on oral minocycline. Two weeks later, a small fluid collection with surrounding erythema and induration was noted at the medial aspect of the pocket. She was readmitted, cultures were repeated, and intravenous vancomycin was restarted. She remained afebrile and WBC count was 9,500/mm^3. Exploration of the pocket site revealed a small amount of pus below the skin with communication to the pacemaker pocket. The device and leads were explanted and the pocket was thoroughly debrided. The pus was sent for microbiological analysis including acid fast bacilli (AFB) smear, Gram stain, fungal, aerobic and anaerobic cultures. On microscopy, rare beaded Gram positive bacilli, weakly positive on modified AFB (Kinyoun) stain were noted (Figs. 1–3). The infectious disease team was consulted and trimethoprim/sulfamethoxazole was added to cover for infection with Nocardia. Blood cultures remained sterile but fluid cultures yielded a moderate amount of mycobacteria. DNA sequencing confirmed the organism to be *Mycobacterium phlei*. It was susceptible to amikacin, clarithromycin, doxycycline, minocycline, and trimethoprin/sulfamethoxazole. Vancomycin was discontinued and doxycycline was added to the antibiotic regimen. Due to the indolent nature of the infection, we recommended prolonged antibiotic therapy for 12 months. Four weeks after

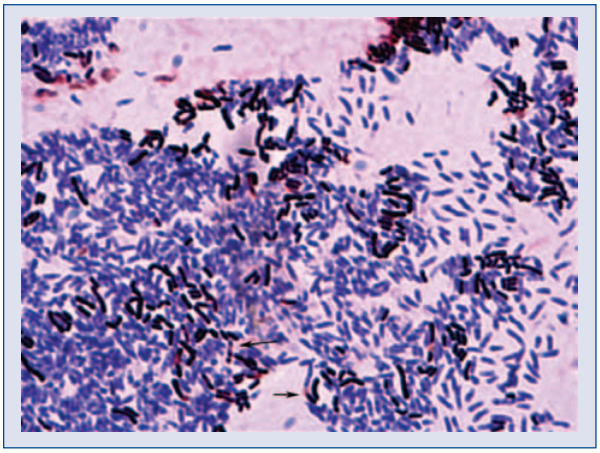

Figure 1. Gram stain of the case isolate (400×). Note the weakly staining gram positive rods with occasional beaded morphology (arrow).

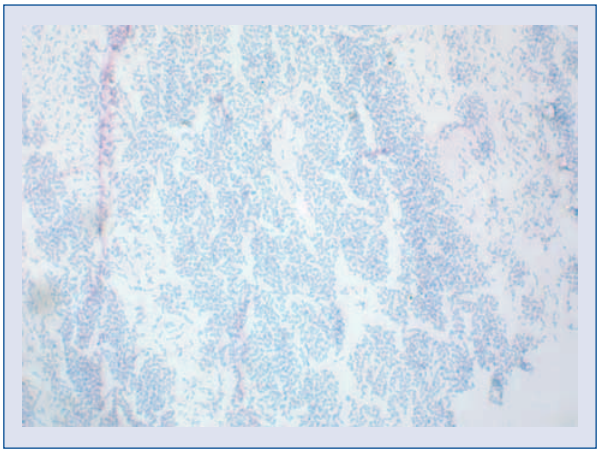

Figure 2. Routine Kinyoun acid-fast stain of the case isolate (400×). Note the sheets of acid-fast negative (blue) rods. Rapidly growing mycobacteria often stain negative by the routine AFB stain.

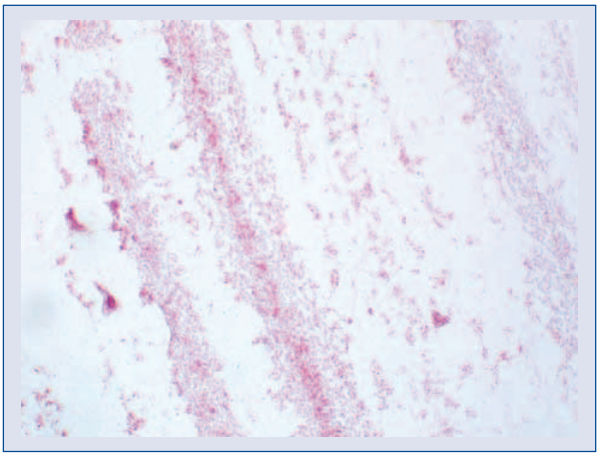

Figure 3. Modified Kinyoun's acid-fast stain of the case isolate showing sheets of acid-fast positive (pink) rods (400×). Modified AFB stain has a weaker decolorization step.

explantation, the patient underwent right sided CRT-D device implantation without complications. At six month follow-up, she remains asymptomatic on dual antibiotics and free of infection.

Discussion

Non-tuberculous mycobacteria are ubiquitous organisms that are found widely in the environment including tap water and soil [8]. Cardiac device related infection due to NTM is extremely rare with only about ten reported cases. The majority of these are caused by rapidly growing NTM, of which *Mycobacterium fortuitum* is the commonest [4]. *M. phlei* is a rapidly growing NTM which is typically non-pathogenic with only three reported cases of human infection [5–7]. There have been numerous reports of hospital/health care-associated infections with NTM, ranging from sternal wound infections following cardiac surgery, ocular infections following LASIK (laser-assisted in situ keratomileusis), and skin infections following plastic surgery to abscesses after intramuscular injections [8–10]. Though individual susceptibility is likely to be a crucial factor, specific clinical risk factors for infection with NTM have not been identified. Advanced age and the presence of diabetes in our patient are known risk factors for post-operative infections in general. However, given the rarity of NTM-related infections, it is unlikely that diabetes or age is a major factor determining susceptibility to these infections. Colonization of aqueous solutions used to mark the incision site before surgery and in hospital water systems has been incriminated in previous nosocomial outbreaks and is the only known risk factor [8—10]. In our case, no definite hospital source of infection was identified despite an extensive environmental investigation (including a review of surveillance cultures) by the infection control team. Furthermore, it is known that NTM have intermediate/high resistance to antiseptics and disinfectant due to the high lipid content and triple layered structure of their cell wall. However, glutaraldehyde and alcohol are effective, provided sufficient contact time is allowed. At implantation, a combination of chlorehexidine (2%) and iso-propyl alcohol (70%) was used in our patient. Interestingly, our patient was an avid fisher and had extensive aquatic contact. Whether this led to colonization of her skin with NTM and subsequent infection is unknown. Though some atypical mycobacterial infections like those related to *M. marinum* are known to be associated with aquatic contact, such an association has not been reported with *M. phlei*.

Diagnosis of NTM-related infections is difficult and often delayed as conventional microbiologic tests are inadequate [10]. The mean time to diagnosis in prior cases was approximately 34 days [4]. On Gram stain, NTM appear as Gram-positive bacilli and can be mistaken for *Nocardia, Rhodococcus* or *Corneybacterium*. Despite positive cultures, identification of specific species of NTM using traditional biochemical and phenotypic methods is difficult and genetic/molecular diagnostics like nucleic acid probes or PCR-restriction enzyme analysis are usually necessary. For CDI in general, current guidelines recommend complete hardware removal in the presence of blood stream or pocket infection. The duration of antibiotic therapy and optimal time of re-implantation are individualized based on the virulence of the causative organism and presence or absence of bacteremia, endocarditis etc. [11]. Due to the rarity of NTM-related CDI, there are no clear management guidelines as to the duration of therapy. Based on prior reports, a combination therapy of two or three drugs for six to 12 months appears necessary. The choice of antibiotics depends on the results of susceptibility testing.

Conclusions

This case highlights the growing concern over cardiac device infections with uncommon and fastidious organisms such as NTM. There is a potential for delay in diagnosis due to the rarity of the infection and the difficulties in microbiologic diagnosis. Physicians should consider NTM in evaluating patients with suspected CDI and negative aerobic and anaerobic cultures. Proper surveillance and strict adherence to infection control measures can potentially prevent NTM-related CDI. There is a need for further research into the appropriate choice and duration of antimicrobial therapy for NTM-related CDI.

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