CASE REPORT

Implantable cardiac defibrillator infections: the emerging importance of *Mycobacterium fortuitum*

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SUMMARY

Infection is a clinically relevant complication associated with intracardiac devices. Atypical mycobacteria, particularly *Mycobacterium fortuitum*, have been increasingly implicated in cardiovascular implantable electronic device (CIED) infections. We present a case of *M. fortuitum* CIED infection in a patient with ischaemic cardiomyopathy occurring approximately 3 weeks after insertion. The recognition and adequate treatment, including device removal, tissue sampling and the determination of antimicrobial sensitivities, are essential in the proper management of these patients.

BACKGROUND

Cardiovascular implantable electronic device (CIED) infections are a significant source of morbidity in patients with usually advanced chronic medical conditions, such as heart failure, arrhythmias, diabetes, renal failure and so on. CIED infections secondary to atypical mycobacteria are an increasingly reported aetiology.¹ Prompt diagnosis requires a high index of suspicion, particularly because initial microbiological testing may be negative and their clinical presentation may be acute, subacute or chronic. Adequate recognition and treatment, including device removal, tissue sampling and the determination of antimicrobial sensitivities, are important in the proper management of these patients.

CASE PRESENTATION

A 59-year-old Hispanic man presented with 1 week of tenderness and erythema at the pocket site of his implantable cardiac defibrillator (ICD). Four weeks prior, he had ICD placement for prevention of sudden cardiac death in the setting of ischaemic cardiomyopathy with a low left ventricular ejection fraction (LVEF) of 20%. He also had undergone aortocoronary bypass (ACB) surgery 5 months prior. His medical history also included hypertension, type II diabetes mellitus, hyperlipidaemia, chronic kidney disease stage 3a and hypothyroidism. Transthoracic echocardiography (TTE) performed right before his ACB surgery demonstrated a LVEF of 18%. His medications at the time of presentation included aspirin, lisinopril, hydrochlorothiazide, atenolol, spironolactone, pravastatin, levothyroxine and insulin (detemir and aspart). He did not have a history of any previous mycobacterial infection.

On admission, physical examination was remarkable for obesity (body mass index 32.1 kg/m²), blood pressure 125/75 mm Hg, heart rate 82 beats/min, respirations 18 respirations, normal oral temperature and oxygen saturation 98%. His pocket site showed erythema with bloody, yellow secretion and was tender to palpation. Overall, he felt well and denied fever, chills, shortness of breath, chest pain, syncope or noticeable ICD discharges.

INVESTIGATIONS

His initial testing revealed a white cell count (WBC) of 7.0 k/ μ L (69% neutrophils, 12% lymphocytes and 13% monocytes), red cell differential width at 16%, haemoglobin 10.2 g/dL, glucose 274 mg/dL, bicarbonate 22 mmol/L, anion gap 10, sodium 133 mmol/L, potassium 4.9 mmol/L, creatinine 0.9 mg/dL, blood urea nitrogen 19 mg/dL, lactic acid 1.1 mmol/L, erythrocyte sedimentation rate 53 mm/h and C-reactive protein (CRP) 3.4 mg/dL (normal <0.5 mg/dL). Urinalysis was normal. HIV testing was negative. Initial Gram stain of the pocket showed numerous WBCs and no organisms. Blood cultures (3/3 bottles) were reported negative at 5 days. His ECG showed a sinus rhythm and QRS complex and QTc segment durations of 146 and 432 ms, respectively.

The patient had transoesophageal echocardiogram (TEE) showing no valvular vegetations and was taken for ICD system removal, incision and drainage of pocket site. The ICD pocket was left open and then closed 3 days after removal. Initially, the patient was treated with empiric intravenous vancomycin. Tissue cultures (3/3) and cultures of tip of RV lead all demonstrated beaded Gram-positive rods at day 5. Pending final identification, intravenous levofloxacin was added to his regimen. *Mycobacterium fortuitum* was identified, sensitive to amikacin, ciprofloxacin, clarithromycin, doxycycline, linezolid and moxifloxacin. Resistance or intermediate sensitivity was reported for cefoxitin, imipenem and trimethoprim/sulfamethoxazole. A TEE performed after lead removal did not show any vegetations or abscess.

DIFFERENTIAL DIAGNOSIS

The aetiology of ICD infection include skin flora organisms, mainly *Staphylococcus aureus* and coagulase-negative staphylococci, in up to 75% of cases. Other less frequent causes include *Streptococci*,

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Corynebacterium sp, *Cutibacterium acnes*, Gram-negative bacilli, *Aspergillus* and *Candida* sp and rarely, species of mycobacteria.

TREATMENT

Our patient received 23 weeks of oral levofloxacin and clarithromycin; he had only generalised pruritus as a significant side effect. During this period, he used a wearable cardiac defibrillator (WCD, LifeVest; Zoll Corporation, Pittsburgh, Pennsylvania, USA) and had no shocks delivered.

OUTCOME AND FOLLOW-UP

He had reimplantation of ICD 1 month after completing antibiotics. His CRP decreased to 1.1 mg/dL just before reimplantation and to 0.7 mg/dL 2 months after reimplantation. At 4-month and 12-month follow-up, the patient did not have signs or symptoms of ICD infection.

DISCUSSION

The placement of CIEDs has increased substantially through widespread use of pacemakers (PMs) or ICDs). Infection is a clinically relevant complication associated with ICD placement. In a large study using National Cardiovascular Registry Data, the rate of infection was reported at 1.7% overall. Notably, the infection rate differed depending on the number of leads placed. In this same study, the infection rate for single, dual, and biventricular ICDs was 1.4%, 1.5%, and 2.0%, respectively.² The rate of infection seems to be higher for ICDs compared with PMs.³

The vast majority of CIED infections are due to Gram-positive bacteria, mainly coagulase-negative *Staphylococcus* sp, followed by *S. aureus*. These two groups account for approximately 70% of all CIED infections.⁴ As was discovered in our patient, the aetiology of CIED infections also includes rapid growing mycobacteria, principally *M. fortuitum*, which has been reported in approximately 50% of all cases of CIED infections involving rapid growing mycobacterium.⁵

In addition to CIED infections, other cardiovascular infections associated with *M. fortuitum* are sternal wound infections^{6,7} and endocarditis,^{8,9} both after cardiac surgery. *M. fortuitum* is not part of normal skin flora but it can be a transient coloniser; it can also be found in tap water and other environmental reservoirs. It is a so-called 'rapid growing' mycobacteria due to its ability to grow mature colonies at the relatively faster rate of 7 days in culture media.¹⁰ The rapid growing group of mycobacteria causing human disease are mostly found in the *M. fortuitum* group (*M. fortuitum*, *M. peregrinum*, *M. senegalense*, *M. setense*, *M. conceptionense* and third biovariant complex), the *M. chelonae-abscessus* group (*M. chelonae*, *M. abscessus*, *M. immunogenum*, *M. bolletii* and *M. massiliense*) or the *M. smegmatis* group (*M. smegmatis*, *M. goodii* and *M. wolinskyi*).¹¹

There are currently no published guidelines specifically addressing the treatment of mycobacteria-related CIED infections. The most recent American Heart Association (AHA) statement regarding CIED infections does recommend that both tissue and the lead tip should be cultured for fungi and mycobacteria if the initial Gram stain is negative. Additionally, it is recommended that mycobacteria and fungal stains also should be obtained on resected pocket tissue. In our case, both the catheter tip and the tissue culture helped make the final diagnosis. Acid fast bacilli stains, however, were repeatedly negative on our patient's wound secretion and tissue specimens.⁴

The treatment of CIED infections due to atypical mycobacteria is also challenging. It is important to identify the specific

species of mycobacteria and perform susceptibility testing to guide antibiotic therapy. The length of treatment is also a matter of debate but is usually several months. Specifically for *M. fortuitum*, current infectious disease guidelines recommend a minimum of 4–6 months of therapy with at least two agents, as well as removal of all foreign materials associated with the infection site.¹²

Our patient responded well to a two-drug regimen and had only minor side effects (generalised pruritus) that did not limit therapy. As both macrolides and quinolones can produce QTc prolongation, it is important to check serial ECG during therapy and monitor renal function and electrolytes. This is particularly important in patients with depressed EF, as in our patient who fortunately did not have any significant changes in QTc or arrhythmias. The use of a WCD as bridge therapy until another ICD can be implanted is currently a class IIa recommendation per AHA guidelines.¹³ The timing of reimplantation is not well determined. British guidelines suggest that signs of active infection should be absent at the time of reimplantation.¹⁴ Our patient used a WCD for a prolonged period of 23 weeks given the persistence of mild elevations in CRP, but likely re-implantation may be considered sooner if markers of infection have cleared. As the use of subcutaneous ICDs increases, these devices may also be of consideration in a patients like ours. Further research regarding the timing of device reimplantation is needed, particularly in patients with mycobacterial infections.

Learning points

- Mycobacteria have been implicated with implantable cardiac defibrillator (ICD) infections, and with increasing device implantation, the incidence is likely to increase.
- The diagnosis of Mycobacterium sp's ICD infections require a reasonable level of suspicion coupled with timely procurement of stains/cultures of secretions, tissue and foreign material (lead tips).
- As the antimicrobial agents used to treat Mycobacteria sp can produce cardiac side effects (ie, QTc prolongation), it is important to check serial ECG, monitor renal function and electrolytes during therapy.
- The use of a wearable cardiac defibrillator is reasonable as bridge therapy until the infection has resolved and a permanent ICD can be re-implanted.

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Competing interests None declared.

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