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Case report

Corynebacterium striatum cardiac device-related endocarditis: A case report

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ABSTRACT

Corynebacterium striatum is an emerging Gram-positive bacillus associated with invasive infection in both immunocompetent and immunocompromised patients, especially associated with medical devices. Its ability to form biofilms has been demonstrated and it has been occasionally associated with cardiac device-related infective endocarditis with few cases described in literature. We report a case of *C. striatum* cardiac device-related infective endocarditis of complex management.

Introduction

Corynebacterium striatum is a Gram-positive bacillus belonging to the Corynebacterium genus. Although it is part of the normal commensal flora of the human skin and mucous membranes (and hence usually considered a contaminant when isolated in blood cultures), it has been increasingly associated with severe infections in both immunocompetent and immunocompromised hosts [1]. It is becoming an emerging agent, with the ability to form biofilms that can cause infection of endovascular devices [2]. It is occasionally associated with infective endocarditis and few cases of *Corynebacterium striatum* cardiac device associated endocarditis are described [3]. The authors present a case of recurrent *Corynebacterium striatum* bacteraemia due to infected pacemaker lead.

Case

We report a case of a 73-year old female, with a background history of obesity, arterial hypertension, type 2 diabetes mellitus, chronic kidney disease stage III - *Kidney Disease: Improving Global Outcomes* (KDIGO), and peripheral neuropathy due to diabetes. She had a pacemaker implanted 13 years ago, for a complete heart block. Due to previous transmetatarsal amputation, she was unable to walk by herself, moving in a wheelchair.

She presented to another hospital with a four day-history of fever, asthenia and confusion. On physical examination she was disoriented and febrile (T: 38,2 °C), showing haemodynamic stability (BP:125/54 mmHg; heart rate: 101 bpm) and low peripheral saturation on room air (SpO2: 88%). She had signs of hypervolemia (bilateral inspiratory rales on pulmonary auscultation and bilateral peripheral oedema to both knees) and a mall diabetic wound in the left foot with no signs of infection. Laboratory results revealed mild respiratory failure, anaemia, a white blood count of 8870/mm^2, a C-reactive protein (CRP) of 305 mg/L and a deteriorated renal function with creatinine of 3,5 mg/dL and 153 mg/dL of urea. A thoracic computed tomography (CT) scan showed a right lower lobe pneumonia and she was admitted to the general ward under intensive diuretic therapy and antibiotherapy with piperacillin/tazobactam. She developed refractory hypervolemia and was transferred to our hospital.

On admission, two sets of blood cultures were drawn and urgent haemodialysis was started. She remained afebrile, her respiratory status and serum CRP level improved. Both sets of blood cultures were positive for *Corynebacterium striatum* — susceptible to vancomycin and linezolid and resistant to ciprofloxacin and penicillin. Two

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sets of blood cultures were drawn after 48 h of therapy, which were also positive for *C. striatum.* Further reviewing previous admissions, there had been two previous episodes of *C. striatum* bacteraemia in the previous six months, the first treated with two weeks of linezolid and piperacillin/tazobactam and the second with two weeks of linezolid and piperacillin/tazobactam and one week of vancomycin.

In view of the recurrent bacteraemia in a patient with an intracardiac device, a trans-oesophageal echocardiogram was performed but did not reveal signs of infective endocarditis. Abdominal and head computed tomography scans had no evidence of embolic phenomenon and physical examination did not reveal Osler's nodules or Janeway's lesions. Urinalysis showed significant leuko erythrocyturia and there was also marked complement consumption and raised circulating immune-complexes — but a negative rheumatoid factor in the blood work. A diagnosis of intra-cardiac electronic device (ICED) associated systemic infection with secondary glomerulonephritis was assumed and vancomycin was started according to the susceptibility test.

Blood cultures cleared after seven days of vancomycin and CRP persistently dropped. A multidisciplinary discussion (Internal Medicine, Cardiology and Infectious Diseases) was held to decide the best treatment approach. A conservative approach with suppressive antibiotherapy was decided due to the high risk of pacemaker extraction in a patient with several comorbidities. After two weeks of therapy, renal function improved and haemodialysis was withdrawn. The patient was discharged at six weeks of vancomycin after first negative blood cultures, with renal function normalisation to the previous baseline. It was decided to continue therapy with linezolid with regular blood count surveillance. However, after three weeks of therapy, she developed myelotoxicity secondary to linezolid, which was withdrawn.

One month later, she was admitted to the emergency department due to acute confusion. Brain CT was normal and laboratory results only showed mild CRP elevation (65 mg/L) with no additional findings of interest. She spontaneously recovered and was discharged home, but surveillance blood cultures were again positive for *Corynebacterium striatum* and she was readmitted to the hospital and vancomycin was restarted. Trans-oesophageal echocardiogram revealed a small vegetation in the pacemaker lead. Therapeutic options were re-discussed and device extraction was decided. Pacemaker was extracted after negative blood cultures and a temporary pacemaker was placed. Culture of pacemaker generator was negative but pacemaker leads were positive for *Corynebacterium striatum*. A new echocardiogram was performed which excluded valvular involvement and a new pacemaker was implanted after negative blood cultures (drawn after device extraction). Due to diabetic foot lesions and high risk of bacteraemia, it was decided to implant a leadless pacemaker.

The patient was discharged after 14 weeks of vancomycin, six weeks after pacemaker extraction. Follow-up at two months, the patient is doing well and surveillance blood cultures are negative.

Discussion

The authors present a complex case of an ICED infection due to *C. striatum*. The use of ICEDs has increased in the last ten years due to technological advances, expansion of their indications and improved life expectancy of the recipient population [4]. This increment has been accompanied by a largely unforeseen increase in infectious complications affecting the devices [5]. ICED infections are considered in two categories: pocket infection and systemic infection. Diagnosis of the latter may be difficult due to heterogeneous clinical presentations and even diagnostic criteria and definitions, which vary depending on scientific societies. According to 2015 European Society of Cardiology (ESC) guidelines on infective endocarditis [6], diagnosis may be established according to the modified Duke criteria, which implies that a positive echocardiogram is not mandatory for the definite diagnosis. On the other hand, for 2015 British guidelines for the diagnosis, prevention and management of ICED infection [7], an echocardiographic involvement or culture, histology or molecular evidence of infection on explanted lead are required for the definite diagnosis of ICED infection. Although very similar, both classification criteria have small differences, with different results when applied to difficult cases — as in the present case report. Our patient would be classified as having an infective endocarditis according to European Society of Cardiology (ESC) guidelines from the first hospital admission, since she has one major criterion (persistent bacteraemia) and three minor criteria (fever, intracardiac device and immunological phenomena - glomerulonephritis and complement consumption). On the other hand, according to British guidelines, ICED lead infection diagnosis requires a positive echocardiogram or culture, histology or molecular evidence of infection on explanted lead, which only occurred in the second admission.

Previously seen as a contaminant agent, *Corynebacterium striatum* is emerging as an infectious agent in susceptible patients, being rarely identified as a pathogen in infective endocarditis. In a systematic review of *Corynebacterium* endocarditis [8], it was concluded that *Corynebacterium* endocarditis mainly affected the left side of the heart and was linked with nosocomial risk factors such as presence of prosthetic medical devices, invasive procedures, and intravascular access. Our patient had some risk factors such as a cardiac device and some degree of immunocompromise due to long-standing type 2 diabetes mellitus and chronic kidney disease.

One of the challenges in the treatment of *C. striatum* infections is the antibiotic choice, and there are currently no agreed guidelines to treat *C. striatum* endocarditis. Although initial studies indicated that *C. striatum* clinical isolates were susceptible to a wide range of antibiotics [9], recent reports have shown increased multidrug resistance [2,10,11]. Several reports have demonstrated that vancomycin has the lowest minimum inhibitory concentration (MIC) [10,11], and case reports have shown its efficacy in treatment of *C. striatum* endocarditis [12]. Our patient isolate was resistant to penicillin, clindamycin, tetracycline and ciprofloxacin, being susceptible to linezolide and vancomycin, and thus the later was the natural choice.

Our patient posed an additional challenge: the pacemaker. Intracardiac devices are susceptible to biofilm formation but, unlike other devices (such as intravascular catheters, prosthetic heart valves and some orthopaedic implants), infection eradication can rarely be achieved [13], and thus, international society guidelines recommend early removal [6,7]. Few cases of cardiac device-related infective endocarditis due to *C. striatum* have been described, and in all of them, early removal of cardiac device was done [3]. In our patient, pacemaker extraction was considered of high risk of mortality due to previous comorbidities and associated frailty along with the fact that her system was implanted in the right side of the heart thirteen years ago, being deeply adherent to endocardium and endovascular tissue, which increased the complexity of the procedure and the risk of wall rupture. Thus, a conservative approach with long-term antibiotherapy was considered the best treatment option. The initial strategy was to complete six weeks of vancomycin followed by long-term linezolid treatment since it was the only oral effective antibiotic. No prospective randomised studies have assessed the value of conservative antibiotic therapy alone, compared with combined device removal and administration of appropriate antibiotics, but few case series have shown a poor outcome with low cure rates using conservative antibiotic therapy in ICED infections [14,15]. Additionally long-term linezolid administration is commonly associated with thrombocytopenia, which is more common in patients with chronic kidney disease [16]. Thus, the likelihood of success of

this strategy was low and the patient eventually developed severe thrombocytopenia, which led to linezolid withdrawal and bacteraemia recurrence.

Despite the high mortality risk of device extraction, that was the only option for our patient due to failure of conservative approach. Leadless devices have shown a much lower infection rate than that of permanent pacemakers with transvenous leads in approval studies [17], even in high-risk patients. Our patient had some risk factors for recurrent infection such as long-standing diabetes, diabetic foot lesions and chronic kidney disease ant therefore, a leadless device was chosen to minimise the risk of future device infection.

This case illustrates the complexity of the diagnosis and management of intra-cardiac device infections, especially when difficult-to-treat pathogens are isolated. Cardiac devices indications are increasing and they are implanted, generally, in elderly patients. However, in these patients, management of cardiac device infection may be difficult because of complication risk with device extraction, which is the gold-standard approach. A multidisciplinary team for timely diagnosis and appropriate treatment is essential. Conservative approaches with long-term antibiotic therapy may be an option in selected cases but are dependent on effective and tolerable oral antibiotics.

CRediT authorship contribution statement

Nuno Melo: Writing – original draft, Writing – review & editing. **Cristina Correia:** Writing – review & editing. **Juliana Gonçalves:** Writing – review & editing. **Manuela Dias**: Writing – review & editing. **Raquel Mota Garcia**: Supervision. **Pedro Palma:** Supervision. **Raquel Duro:** Supervision.

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Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Conflicts of interest

The authors of this manuscript have no conflicts of interests.

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Nothing to declare.

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