





Klebsiella sp. carbapenem-resistant pocket infection of an Implantable Cardioverter Defibrillator (ICD)

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ABSTRACT

Infections associated with Implantable Electronic Cardiac Devices (IECD) have an incidence of up to 3.4% and a notable impact on patient morbidity and mortality. Gram-positive bacteria, especially *Staphylococcus* sp. represent 60-70% of isolated agents. In turn, gram-negatives account for up to 9% of cases. We report an Implantable Cardioverter-Defibrillator (ICD) generator pocket infection by a Carbapenem Resistant *Klebsiella* sp., in a young male patient, whose challenging diagnosis of certainty was only possible after surgical exploration and culture of the material from the ICD pocket, given the oligosymptomatic clinical presentation. Although already described, *Klebsiella* sp. are rare in this context and to our knowledge, this is the first report of an IECD infection by a carbapenem-resistant enterobacterium.

Keywords: Implantable cardioverter defibrillators, Carbapenem resistant enterobacteriaceae, *Klebsiella* infections.

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INTRODUCTION

The rate of cardiac implantable electronic devices (CIED) has increased considerably worldwide, and approximately 1.5 million patients have CIED implanted every year¹. However, device-associated infections have an incidence of up to 3.4% and have a significant impact on morbidity as well as mortality, which can be as high as 8% in 30 days².

The main pathophysiological mechanism of this complication is the contamination of electrode leads and/or generator during the implantation or subsequent handling. Colonization of generator pocket material can spread through the leads and result in systemic infection. Hematogenous spread from other infection sites has also been described^{2,3}.

Gram-positive bacteria are the most important agents of these infections, of which 36.7 % correspond to Coagulase-negative *Staphylococcus* and 30.8% to *Staphylococcus aureus*²⁻⁵. Gram-negative agents comprised about 6-9% of the isolated, and they belong to the genus *Enterobacteriaceae* in up to 3% of the cases^{2,3,5}. Similarly, fungal and mycobacterial infections have also been described²⁻⁶.

We reported an infection from a Transvenous Implantable Cardioverter-Defibrillator (T-ICD) generator pocket, which had a carbapenem-resistant *Klebsiella sp.* agent isolated in the culture. In this case, there has been a significant diagnostic challenge in view of oligosymptomatic clinical presentation and precocity of manifestations.

CASE REPORT

A 21-year old male medicine student experienced persistent bleeding in surgical wound as of the fourth post-operative day of the T-ICD elective implantation due to the diagnosis of genetically determined desmoplakin (DSP) mutation cardiomyopathy. The patient denied any other signs or symptoms, including fever. During the anesthetic induction for antimicrobial prophylaxis, Cefazolin 2 grams had been administered. He was using Prednisone 20 milligrams daily for a prior diagnosis of recurrent Myopericarditis.

Upon clinical examination, the surgical wound did not show inflammatory signs or purulent drainage. However, there was slight dehiscence of the edges laterally. There was no erythema, edema or ecchymoses on the skin adjacent to the generator pocket. (figure 1). Moreover, the physical examination did not show any

changes. Therefore, conservative management and clinical surveillance were chosen.



Figure 1. Dehiscence in the lateral region associated with bleeding on the surgical wound, although neither signs of inflammation nor drainage of purulent content were observed.

However, after five days under conservative measures, although the patient was not febrile, bleeding was still persistent; therefore, a surgical re-evaluation was decided. Before the procedure, samples were collected for blood cultures. Vancomycin (15 mg/kg) was administered as prophylaxis and the patient experienced pruritic maculopapular erythema on the neck, chest, and extremities compatible with Red Man Syndrome. The rash subsided with the use of antihistamine.

During the intra-operative, necrotic and friable tissue was noted in generator pocket. Therefore, due to the suspicious of pocket infection, the complete extraction of the device was conducted. The ICD electrode leads fragments and tissue samples were submitted for culture. The patient remained hospitalized, clinically stable with empiric use of Teicoplanine (6 mg/kg/day) due to Vancomycin reaction, while waiting for microbiological results.

Pocket culture evidenced *Klebsiella sp.* Carbapenem-resistant (CR), sensitive to gentamicin alone on antibiogram (figure 2). Both blood culture samples and electrode lead cultures were negative. In addition, there were no vegetations on Transesophageal Echocardiography (TEE) (figure 3). Therefore, infectious endocarditis (IE) was ruled out and antibiotic therapy was scaled up to Polymyxin B (25000 IU/kg 12/12h) and Gentamicin (5 mg/kg/day).

However, after the infusion of the first dose of Polymyxin B, the patient exhibited paresthesia on the face, bilaterally. Consequently, the patient showed a strong desire to suspend the drug. After deliberation and clarification to the patient regarding the Gentamicin monotherapy, it was decided to discontinue Polimixin, as his clinical condition was stable.

CULTURA BACTERIANA

Material: Loja

RESULTADO: *Klebsiella* sp

AG. TERAPÊUTICO	SENSIBILIDADE	AG. TERAPÊUTICO	SENSIBILIDADE
AMICACINA.....	: Resistente	ERTAPENEN.....	: Resistente
GENTAMICINA	: Sensível	CEFEPIME.....	: Resistente
CEFOTAXIMA.....	: Resistente	PIPERACILINA TAZOBACTAM..	: Resistente
CIPROFLOXACIN.....	: Resistente		
IMIPENEM.....	: Resistente		
MEROPENEM.....	: Resistente		
CEFTAZIDIMA.....	: Resistente		

NOTA: Antibióticos testados de acordo com tabela CLSI Atualizada

Data de Coleta: 01/05/2018 às 07:08 - Material entregue ao laboratório.

Código de segurança:cb0f59963cc0ea04e1eec03d994e7813

Data: 06/05/18 10:22

CULTURA - 2ª amostra

Material: Ponta

RESULTADO: NEGATIVO

Figure 2. Generator pocket culture evidenced Carbapenem resistant (CR) *Klebsiella* sp. Negative electrode cable tip culture.

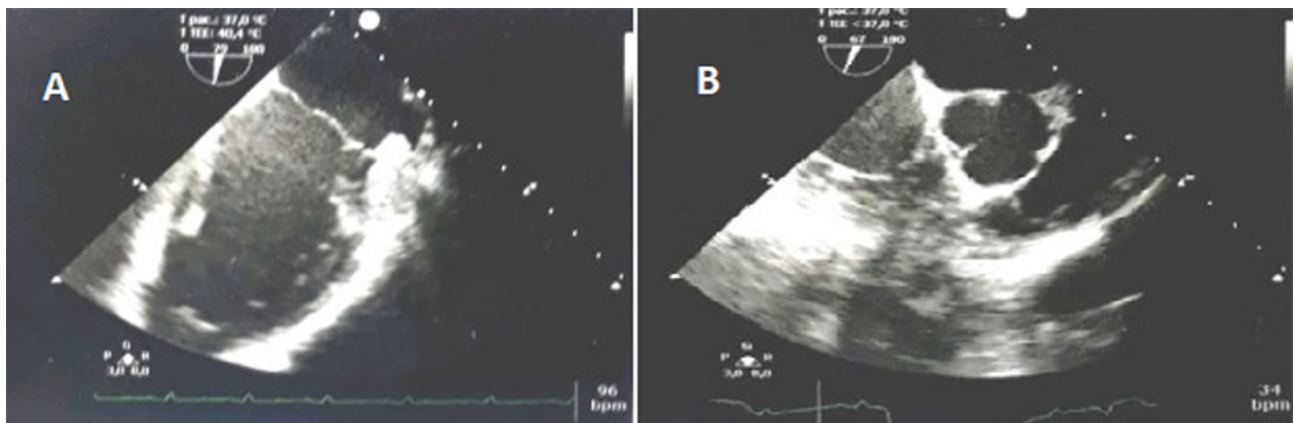


Figure 3. A – No lesions in the mitral valve are observed; B- Aortic and tricuspid valve with no evidence of vegetation.

This therapeutic regimen was administered for 14 days and the patient remained in good clinical progression. No new complications of the operative wound or adverse effects were found and the patient was discharged from the service by the end of the second week.

Finally, three months later, the patient implanted a subcutaneous ICD (S-ICD) and remained free from complications. On that occasion, preoperative skin swabs were collected, which were all negative, and the patient was instructed to take chlorhexidine bath in the preoperative period.

DISCUSSION

The European Heart Rhythm Association (EHRA) recently published a consensus² which summarizes the main recommendations for diagnosis, treatment, and prevention of infections in CIED.

In indication process of a CIED is essential to assess the risk factors^{2,4}. These can be changeable or unchangeable. Dialysis Chronic Kidney Disease was strongly associated with infections, likewise the use of corticosteroids². In our report, the patient was using Prednisone 20 mg per day, which may have contributed to its complication.

The greater complexity of the device, such as dual-chamber T-ICD and resynchronizers, is another risk factor. Finally, the longer procedures duration and the need for a new intervention (hematomas, for example) increase device-related infections²⁻⁶.

Clinically, the CIED infection presents a variable spectrum from superficial incision infections to infectious endocarditis. Pocket infections are the most common and they manifest with edema, erythema, dehiscence, and secretion at the store site. In turn, systemic infections can occur in the absence of a generator pocket infectious process. This makes the diagnosis more challenging and there should be high suspicion in case fever, chills, night sweats, and septic embolic phenomena are present²⁻⁷.

The diagnosis is based on CIED 2019 international infection criteria, including microbiological, radiological, and clinical aspects². This case shows the diagnostic difficulties of oligosymptomatic patients. Recently, fluorine 18-labeled positron emission tomography (18F-FDG PET-CT) emerged as a promising adjuvant diagnostic method. With an emphasis on establishing a differential diagnosis between pocket infections and post-surgical inflammation, or in case of high suspicion of systemic infection but the TEE is negative^{2,3,8}.

TEE is recommended to assess infection in electrode leads and CIED-associated IE. Following device extraction, the TEE can be considered so as to identify potential complications in the tricuspid valve, right ventricular function, and device residues²⁻⁵.

Pocket needle aspiration, to establish the etiological agent, is not recommended due to low sensitivity and theoretical possibility of contamination³. Therefore, samples of the pocket tissue should be collected for culture, as well as the leads fragments if the device extraction is deemed necessary. At least three blood culture samples are recommended if infectious endocarditis is suspected²⁻⁶.

The isolation of resistant pathogens is of concern in this scenario and in 33.8% of infections, Methicillin-resistant *Staphylococcus* were isolated in CIED. Furthermore, Vancomycin-resistant *Enterococcus* strains correspond to 1.4% of the agents isolated in North America². As for the infection etiology of this report, *Klebsiella* sp. are rare in this context, although they have been previously described⁹. To our knowledge, this is the first report of Carbapenem-resistant *Klebsiella* sp ICD infection.

At the service where this procedure was performed, the rate of Healthcare Associated Infections (HAI) in implantation month was 2.7%. This index is found to be acceptable considering the prevalence between 5.7% to 19.1% of HAI in developing countries according to the World Health Organization¹⁰. Moreover, there has been no report of aseptic technique breakage or contamination of the surgical field in the intraoperative period.

As for the treatment, device removal is strongly recommended. The exception consists of superficial skin infections, which should be treated with oral antibiotics, such as flucloxacillin or amoxicillin-clavulanate for at least one week^{2,3}. In turn, pocket infections require 10-14 days of antibiotic therapy after extraction. The choice regimens are Vancomycin (or Daptomycin) alone or combined with a third generation cephalosporin or Gentamicin, particularly if systemic symptoms are present. For deep infections, such as IE, 4-6 weeks of antimicrobial agents are necessary^{2,3; 5-7}.

The antibacterial envelope releases rifampicin and minocycline and is indicated in situations where the infection is most likely, such as re-operation, device upgrade, cardiac resynchronization therapy,

and high-risk patients. However, its ability to prevent infections by multi-resistant agents is uncertain^{2,11}.

Finally, patients with previous T-ICD extraction due to infection can be eligible for S-ICD, which does not require transvenous leads and, therefore, reduces the risk of more serious events, such as IE, and electrode lead-related complications. In this patient population, there was no increased risk of *de novo* infection after S-ICD re-implantation¹².

This case should warn against the possibility of multidrug-resistant bacteria as potential etiologic agents of CIED infection in addition to the urgent need for adjuvant methods to prevent them and control bacterial resistance. Finally, a high index of suspected infection is necessary when facing perioperative complications of CIED to establish a timely diagnostic and therapeutic approach and improve the patient's prognosis¹³.

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