

Cardiovascular implantable electronic device-related endocarditis: A rare cause of chronic brucellosis

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ABSTRACT

Brucellosis is a zoonotic disease that can progress with organ involvement, relapses, and treatment failures and can mimic many diseases. Determination of organ involvement is very important for appropriate treatment planning and prevention of recurrence. Endocarditis is the most common cardiovascular complication. Mortality in brucellosis is mostly attributed to endocarditis. Cardiovascular implantable electronic device (CIED)-related infections are the most important cause of morbidity and mortality in CIED implantations. CIED-related endocarditis (lead or valvular vegetations, or both) develops in approximately 10% to 23% of these cases. In this case report, we present a 73-year-old male patient with CIED-related endocarditis due to *Brucella spp.* which is very rare in the literature.

Keywords: Brucellosis, endocarditis, pacemaker-related endocarditis.

Brucellosis is a zoonotic disease that can present with various clinical symptoms and can involve organ damage, relapses, and treatment failures. The disease is endemic in our country where unpasteurized milk and dairy products are frequently consumed, and it is particularly more common in regions with livestock farming. According to the data from the General Directorate of Public Health in Türkiye, as of the year 2016, the number of brucellosis cases is 6,457, with a morbidity rate of 7.99 per 100,000 population.^[1] The disease is classified into three categories based on the onset time: acute (<8 weeks), subacute (8-52 weeks), and chronic (>52 weeks).^[2] Organ involvement is observed in more than 50% of the patient population.^[3,4] One of these involvements is cardiovascular involvement, most commonly

presenting as endocarditis. Endocarditis is observed in approximately 1% of all brucellosis cases and is the complication with the highest mortality rate.^[4-6]

The frequency of pacemaker implantation is increasing day by day, and as a result, the incidence of cardiovascular implantable electronic device (CIED)-related infections is also on the rise. Despite being less common with today's procedural advancements, CIED-related infections remain the most significant cause of morbidity and mortality in pacemaker implantation cases.^[7-9] The incidence of CIED-related infections has been reported as 0.13% to 19.9%.^[10,11] Among these cases, approximately 10-23% develop CIED-related endocarditis (valve vegetation, lead vegetation, or both).^[12,13]

In this case report, we aimed to present a case of CIED-related endocarditis that occurred in a patient with chronic brucellosis, which is rarely encountered in the literature.

CASE REPORT

A 73-year-old male patient, engaged in livestock farming, prepares and consumes

Received: June 16, 2021

Accepted: November 06, 2021

Published online: August 29, 2023

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Cite this article as:

Önder T, Akça A, Alkan S, Güçlü Kayta SB, Doğan E, Şener A. Cardiovascular implantable electronic device-related endocarditis: A rare cause of chronic brucellosis. D J Med Sci 2023;9(2):63-67. doi: 10.5606/fng.btd.2023.48.

his own cheese at home without undergoing pasteurization. In 2013, he had a non-ST-segment elevation myocardial infarction with ventricular tachycardia (NSTEMI+VT) attack, and as a result, an implantable cardioverter defibrillator (ICD) was implanted (Figure 1). Due to complaints of fever, chills, and shivering a Wright tube agglutination test was conducted, which showed a positive titer of 1/1,280. Consequently, in August 2015, the patient was diagnosed with brucellosis. Subsequently, with similar complaints, he had a total of four relapses, and on each occasion, antibiotic treatment was administered for periods ranging from six weeks to six months. The patient, who presented with complaints of chills, shivering, and weakness in October 2017, was admitted to the hospital for a diagnosis of chronic brucellosis. The Wright tube agglutination test showed a titer of 1/1,280, and the Wright test examined by 2-mercaptoethanol test showed a titer of 1/320. Physical examination did not reveal any inflammatory signs in the area of the pacemaker generator pocket. Due to the detection of a 3/6 systolic murmur at the tricuspid focus, transthoracic echocardiography was planned. Blood cultures were also obtained. During the transthoracic echocardiography, a vegetation of 5×5 mm in size, adherent to the pacemaker electrode, was detected in the right atrium. To evaluate the heart valves, transesophageal echocardiography (TEE) was planned. However, during the TEE, no infective involvement of the heart valves was found.

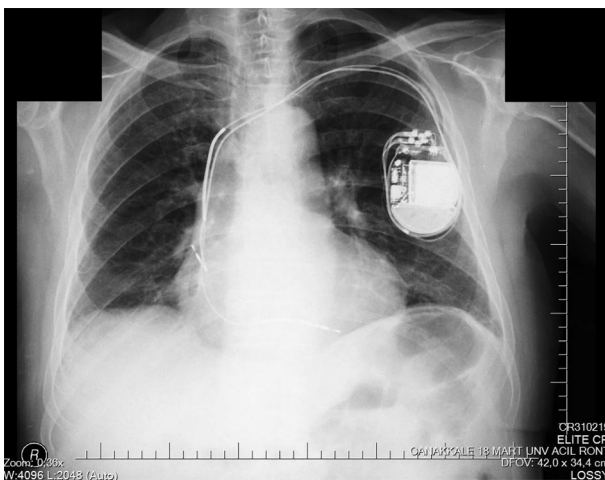


Figure 1. Pacemaker appearance on X-ray.

Based on this, the patient was diagnosed with CIED-related endocarditis, which had only vegetation on the electrode. Blood cultures revealed the presence of *Brucella* spp., and as a result, the pacemaker was removed. Subsequently, the cultured pacemaker electrode tip showed growth of vancomycin-resistant enterococci (VRE). A 42-day antibiotic treatment plan was initiated, consisting of intravenous (IV) ceftriaxone 2 grams twice daily, IV gentamicin 80 mg three times daily, and oral linezolid 600 mg twice daily. After the removal of the pacemaker, blood cultures were taken, and no bacterial growth was observed. Following the completion of the 42-day antibiotic therapy, during which the patient's symptoms and findings improved, the patient was discharged.

DISCUSSION

Brucella spp. are small, non-motile, non-spore-forming, gram-negative bacilli that multiply intracellularly. They are catalase-positive, but their oxidase, urease, and hydrogen sulfide production may vary among species. While *Brucella* spp. generally grow in aerobic conditions, and some species are capnophilic.^[5] Brucellosis is the most common zoonotic disease worldwide, capable of affecting multiple organs and tissues.^[14] Endocarditis is one of the manifestations of this disease and is associated with mortality rates of up to 13%.^[5,6] The aortic and mitral valves are the most commonly affected areas in the heart. In the treatment, in addition to medical therapy, surgical treatment is also recommended for selected patient groups. Surgical intervention should be considered in cases of congestive heart failure, valvular regurgitation, uncontrolled infection with antibiotics, embolic complications, and the presence of large vegetation.^[6,15] Although there is no standard recommendation for medical treatment, combinations containing aminoglycosides are commonly used.^[6] CIED-related infections are the most significant complication observed after pacemaker implantation. According to the time of onset, these infections are categorized as early (<6 months) and late (>6 months) infections.^[16] Early infections typically present with inflammatory signs in the pacemaker generator pocket, while late infections often

manifest as positive blood cultures without inflammatory signs in the generator pocket. Staphylococci are the most commonly identified pathogens in these infections.^[17,18] Other identified pathogens in pacemaker-related infections include gram-negative bacteria, enterococci, streptococci, micrococci, *Candida* spp., and *Aspergillus fumigatus*.^[10] CIED-related infections caused by *Brucella* species are quite rare, and there are reported cases in the literature.^[19-23] If a patient develops a fever after six months of pacemaker implantation, blood cultures should be obtained, and if blood culture positivity is detected, TEE is recommended. For identifying the causative agent, cultures from the pacemaker electrode tip are also frequently used.^[24-26] However, since the electrode may get contaminated during removal, it is recommended to perform the removal using a sterile technique (via a protective sleeve) or by making an incision in a different area from the generator pocket and then extracting the pacemaker. In the treatment, complete removal of the pacemaker is advised due to the formation of biofilms on foreign bodies and poor response to medical treatment alone.^[10,27-29]

In our case, the transmission of *Brucella* spp. was associated with the consumption of unpasteurized dairy products and livestock farming. The Wright tube agglutination test showed a titer of 1/1280, and the Wright test examined by 2-mercaptoethanol test showed a titer of 1/320. Blood cultures confirmed the presence of *Brucella* spp. No inflammatory signs were detected in the pacemaker generator pocket. Transesophageal echocardiography did not reveal any vegetations on the heart valves, but vegetations were found on the pacemaker electrode. As soon as the diagnosis was made, the pacemaker was removed. The cultured pacemaker electrode tip showed growth of VRE. As recommended in the literature,^[6] an aminoglycoside combination therapy was initiated, and linezolid was added to this combination due to the presence of VRE growth in the cultured electrode tip. After 42 days of antibiotic therapy, all symptoms and findings were completely resolved, and no relapse was observed during follow-up.

In the literature presented by Dourakis et al.^[21] and Al-Adsani et al.,^[22] similar to our case, no inflammatory signs were detected

in the pacemaker generator pocket. In our case of late-onset CIED-related infections, as well as in the literature, there were no inflammatory signs in the generator pocket. In Dourakis et al.'s case of early-onset CIED-related infections, no inflammatory signs were observed in the generator pocket either. Their case showed vegetations on the tricuspid valve and pacemaker electrode, while in Al-Adsani et al.'s case, no vegetations were found on the pacemaker electrode, only on the Eustachian valve. It is possible that the cultured pacemaker electrode tip in our case was not appropriately collected, and the VRE growth might not be the actual pathogen. However, due to the severity of the patient's condition, and considering it a life-threatening situation, linezolid was still added to the antibiotic therapy. In Dourakis et al.'s case, the pacemaker was removed two weeks after starting antibiotic therapy, while no specific data about pacemaker removal were mentioned in Al-Adsani et al.'s case. In our case, clinical improvement occurred within six weeks, while Dourakis et al.'s case showed improvement in nine months and Al-Adsani et al.'s case in five months. The rapid clinical improvement observed in our case, with the pacemaker being removed immediately upon diagnosis and the absence of valve involvement but only vegetations on the pacemaker electrode, could be the reasons for the speedy recovery. The most common cause of chronic brucellosis is poor compliance with antibiotic treatment.^[2] Organ involvement and antibiotic resistance are also other reasons for chronic brucellosis.^[30]

In conclusion, our case developed chronic brucellosis due to previously undetected organ involvement. Therefore, it is crucial to thoroughly evaluate the presence of organ involvement before initiating treatment in patients diagnosed with brucellosis to minimize mortality and morbidity with appropriate therapy. In patients who have undergone pacemaker implantation and present with fever, blood cultures should be obtained even if there are no signs of inflammation in the pacemaker generator pocket. If blood culture positivity is detected, TEE should be performed, and CIED-related endocarditis should be considered in the current clinical picture. It is essential to remember that brucellosis can present

in various clinical forms, especially in endemic regions like our country.

Patient Consent for Publication: A written informed consent was obtained from the patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: All authors contributed equally to the article.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

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