IDCases 13 (2018) e00431

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcr

Case study

Pacemaker lead endocarditis: A rare cause of relapsing brucellosis

Evgenia Tsyba[a], Enrique Gallego-Colon[b,*], Aner Zeev Daum[b], Evgeny Fishman[b], Yosefy Chaim[b]

[a] Infectious Disease Unit, Barzilai University Medical Center, Ashkelon, Israel
[b] Cardiology Department, Barzilai University Medical Center, Ashkelon, Israel

ARTICLE INFO

Article history:
Received 7 July 2018
Received in revised form 26 July 2018
Accepted 26 July 2018

Keywords:
Brucella melitensis
Relapsing brucellosis
Neurobrucellosis
Pacemaker induced endocarditis
Sick sinus syndrome

ABSTRACT

Implantable cardioverter-defibrillator endocarditis is a rare and potentially life threatening complication of brucellosis of difficult management for clinicians. We report an unusual case of pacemaker-related endocarditis due to *Brucella melitensis* in a patient with previous history of neurobrucellosis. Our patient was admitted to a hospital with severe swelling of his pacemaker pocket implanted 8 years earlier for sick sinus syndrome. Although pocket site cultures were positive for *Brucella* but blood cultures were not and serologic titer by the Rose Bengal test was positive. Transesophageal echocardiography showed two vegetations on the pacemaker leads. The patient was treated with doxycycline, rifampin and gentamicin with full recovery and the entire pacemaker apparatus was surgically explanted.

Interestingly, two year prior this admission, the patient presented with meningoencephalitis diagnosed with neurobrucellosis proven by positive growth of *Brucella mellitensis* from the CSF. The patient was treated with doxycycline, rifampin and gentamicin with full recovery and the pacemaker had been removed. Reports of *Brucella* infection of prosthetic implants and devices have increased over the past decade. Consequently, potential relapsing of the disease and occupational exposure to *Brucella* should be considered in the differential diagnosis and management of cardiac device infection.

Introduction

Brucellosis is the most frequently encountered world-wide zoonotic disease endemic at the Mediterranean, Middle Eastern, South Asia and South America regions. The disease is caused by a gram-negative, non-encapsulated, non-motile facultative intracellular coccobacilli of the genus *Brucella* [1]. Brucellosis is transmitted to humans by direct contact with infected animals through cuts, abrasions or aerosols. Additonally, transmission can occur by ingestion of unpasteurized milk and milk products from infected animals. Animals that are most commonly infected and can transmit the disease to humans include sheep, goat, cattle, swine [2]. Human brucellosis is a multisystemic disease that often presents with broad spectrum of clinical manifestations including fever and malaise, and complicated by focal involvement such as neurobrucellosis, endocarditis, and arthritis [3,4].

Endocarditis caused by infection of an automated implantable cardioverter- defibrillator (AICD) or pacer is a rare complication of brucellosis, which often leads to the removal of the device [4–6]. Diagnosis of pacemaker endocarditis is based on clinical findings, echocardiography, blood culture and serology. Neurobrucellosis is a complication of systemic brucellosis infection characterized by neurological complications including encephalitis, meningoencephalitis, subarachnoid hemorrhage, myelitis, radiculitis, psychiatric manifestations, peripheral and cranial neuropathies, and myelitis [7]. We report a case pacer infection by *Brucella melitensis* in a patient with previous history of neurobrucellosis. Additionally, we summarize previous reported cases of *Brucella*-mediated endocarditis.

Case report

A 41-year-old male presented to the pacemaker clinic with bulging of the left breast region at the pocket site of a pacer that was placed 8 years earlier due to sick sinus syndrome. The patient, who worked in slaughterhouse, denied fever, sweating, joint or muscle pain. The surgical scar appeared healed but the region was swollen, soft, non-tender and without regional lymph node enlargement. The patient's general non-infectious disease history was remarkable for diabetes mellitus managed by diet only and for untreated gout.

Diagnostic needle puncture of the pacemaker pocket revealed purulent fluid positive for *B. melitensis*. Blood cultures were

* Corresponding author.
E-mail address: enrique.gce@gmail.com (E. Gallego-Colon).

https://doi.org/10.1016/j.idcr.2018.e00431

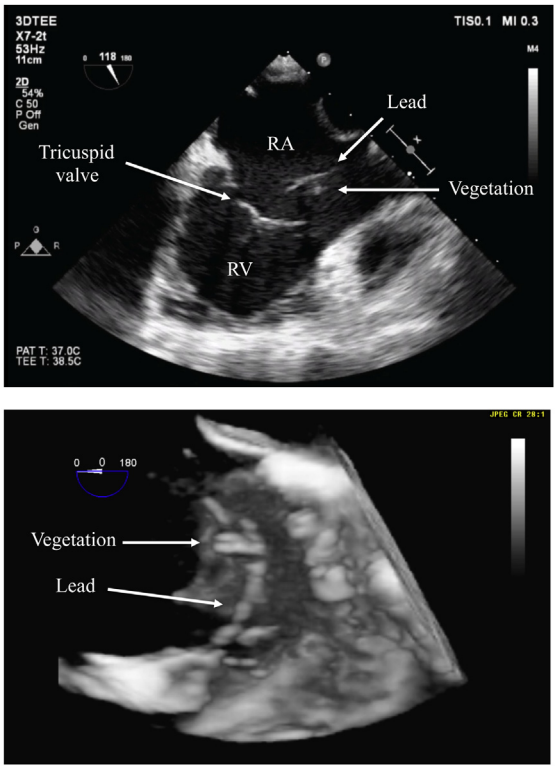

Fig. 1. Vegetations on pacemaker lead. Transthoracic echocardiography, parasternal long axis view showing a large vegetation in the pacemaker lead in a case of *brucella* infective endocarditis (A). 3D transesophageal echocardiography showing a pedunculated echodense mass in a portion of the lead (B). RA, right atrium. RV, right ventricle.

negative but serology titer for *Brucella* by Rose Bengal test was 1/2560. A transesophageal echocardiography (TEE) revealed two vegetations on the lead (8.0 x 3.0 mm and 6.0 x 3.0 mm) (Fig. 1). The results showed no evidence of vegetation at the cardiac valves. In light of these findings the patient was diagnosed with *Brucella*-induced pacemaker lead endocarditis and a three-drug regimen, gentamicin (240 mg/day), doxycycline (200 mg/day) and rifampin (600 mg/day) was initiated. Following recommendations the pacer was removed. The postoperative course was uneventful and the patient remained completely asymptomatic 3 months later with 1/40 serological titer. Three years after pacer removal, we performed our last follow-up, which was unremarkable, and device reimplantation was not considered.

Interestingly, two years prior presentation the patient was hospitalized for severe headache lasting 3 weeks. Neurobrucellosis was diagnosed by CSF analysis which revealed WBC 190 cells/mm^3, 76% PMN, protein 180 mg/dL, glucose 22 mg/dL and serology titer for *Brucella* of 1/160 by Rose Bengal. Blood cultures were negative. TEE, abdominal ultrasound and nuclear bone scan were unremarkable. The patient was started with a three-drug regimen with rifampin (600 mg/day) and ceftriaxone (4.0 g/day) for 4 weeks and doxycycline (200 mg/day) for 8 weeks. After 4 weeks, blood, CSF culture and serology were negative and within normal parameters. During hospitalization, pacer removal was considered, but given the absence of clinical evidence of pacemaker infection, sterile blood cultures, and the rapid clinical response to antimicrobial treatment, pacemaker was not eventually removed.

Discussion

Infection of the pocket and/or the leads of a pacemaker or AICD are complications representing 10% of all cases of endocarditis [8].

Table 1
Clinical characteristics of patients with ICD infection due to *Brucella melitensis*.

	Year	Age	Sex	Location	Device placement to symptoms (years)	Reason for ICD	Symptoms	Device removed	Co-morbidities	Antibiotics received
Patient A [13]	2018	70	M	Kuwaiti	1	SSS	Fever	No[&]	T2DM, HTN, A.Fib	Rifampicin, doxycycline
Patient B[§]	2018[§]	41	M	Israel	8	SSS	Swollen in the pacemaker region	Yes	N/A	Gentamicin, doxycycline, rifampin
Patient C [14]	2012	61	M	Greece	2	N/A	Papular lesions at pacemaker implantation site	Yes	N/A	Doxycycline, rifampicin
Patient D [15]	2008	70	M	Greece	7	SSS	Fever, back pain and night sweats,	N/A	Grave's disease, dilated cardiomyopathy	Doxycycline Ciprofloxacin, Rifampicin
Patient E [5]	2006	66	M	US	3	Non-ischemic cardiomyopathy	Mild malaise, local pain, redness, swelling at ICD site[*]	Yes	T2DM, COPD, dyslipidemias	Doxycycline, ciprofloxacin
Patient F [5]	2007	70	F	Italy	3	N/A	Malaise; pain, swelling	yes	N/A	Rifampin, minocycline, ciprofloxacin

SSS, sick sinus syndrome. T2DM, type 2 diabetes mellitus. HTN, hypertension. COPD, chronic obstructive pulmonary disease. [§]– Present case. [*]Authors did not reported vegetations. & Elderly patients with multiple comorbidities. Patient under continous follow-up. Year, year of publication. Number, corresponding reference.

Although rare, *Brucella* endocarditis is a life threatening complication of brucellosis [8,9]. The prevailing management is device removal and extended combination therapy with doxycycline and rifampin for 8–12 weeks, together with an aminoglycoside for the first 4 weeks of the treatment [10]. There are no specific guidelines regarding timing of new device reimplantation.

In the current case, neurobrucellosis was diagnosed two years prior to the pacemaker infection in a patient who was not bacteremic shown to be with no evidence of vegetations on TEE. The patient was optimally treated and remained asymptomatic until a relapse of *Brucella* infection was observed after 24 months. The patient did not report unpasteruzed milk consumption so the likelihood of the *Brucella* infection in this case was occupational. We hypothesized that disease relapse was due to biofilm formation either at the pocket with organisms traveling along the track to the lead tip, or at the lead [11,12]. Additionally, the intracellular location of the bacterium with occult bacteremia, too low to be detected in blood cultures, may also have played a role in hindering eradication. The recommendation for device extraction for infection include evidence of valvular or lead endocarditis, pocket infection, or occult staphylococcal bacteremia or persistent occult gram negative bacteremia despite appropriate antimicrobial therapy [6]. In our case, the patient did not meet the criteria for device extraction when first diagnosed with neurobrucellosis.

A literature review on endocarditis mediated by infection of the pacer provides some insights (Table 1). Interestingly, pacer infection leading to endocarditis can present at any time after pacer implantation. Upon infection patients required device removal. Additionally, we noted that half of the patients with pacer-endocarditis presented sick sinus syndrome as primary condition. Our current case raises the issue of timing of removal of the cardiac device, suggesting an early rather than late removal in the face of any brucellosis infection regardless of the presence or absence of bacteremia. Our case also suggests that routine serological follow-up is required in cases of systemic *Brucella* infection to not overlook the rare complication of infective endocarditis. Lastly, an unresolvable issue is the timing for insertion of a new pacer in a patient with unusual organisms. According to recent guidelines [6], the new implantation can be done after 72 h of repeated negative blood cultures on appropriate antimicrobial (recommendation Class IIa, level of evidence C). This refers to extracellular organisms, e.g., staphylococci. Additionally, this report highlights the need to review and update the current guidelines [6] for the care of patients with suspected or established pacer infections and include intracellular organisms such as *Brucella*.

Author Statement (CRediT) and contributions

Evgenia Tsyba – Conceptualization, writing (original draft).

Enrique Gallego-Colon – Investigation, conceptualization, writing (review and editing), visualization.

Aner Daum – Investigation, writing (Review and Editing) and data curation.

Evgeny Fishman – Writing (Review and Editing).

Chaim Yosefy – Supervision and funding acquisition.

All authors read and approved the final version of the manuscript.

Acknowledgement

This work was supported by the bacteriology laboratory of the Barzilai University Medical Center.

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