IDCases 15 (2018) xxx–xxx

Contents lists available at ScienceDirect

IDCases

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

Case report

Simultaneous *Brucella* breast and pacemaker infection

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ARTICLE INFO

Article history:
Received 14 September 2018
Received in revised form 2 January 2019
Accepted 3 January 2019

Keywords:
Brucella
Pacemaker
Endocarditis
Breast abscess

ABSTRACT

Infection with *Brucella* spp. is endemic to the Middle East and the eastern Mediterranean basin. Brucellosis can mimic infectious and non-infectious febrile illnesses and therefore it can pose a diagnostic challenge. A wide range of deep-seated infections have been ascribed to brucellosis including breast abscesses and infections of prosthetic endovascular devices. The latter are usually rare but difficult to treat short of excision of the infected device. Here, we present the case of a middle-aged Lebanese woman who presented with simultaneous breast abscesses and a pacemaker infection due to brucellosis. To our knowledge, a similar manifestation has not been reported in the literature.

Introduction

Infection with *Brucella melitensis* is endemic to the Middle East and the eastern Mediterranean basin. It is colloquially known as the Malta fever in reference to the first cases reported in the medical literature [1]. Brucellosis is the most frequently encountered worldwide zoonotic disease [2,3]. It usually presents as a systemic illness [4]. However, brucellosis has a wide spectrum of clinical presentations mimicking a number of infectious and non-infectious diseases. Several complications have been reported particularly related to osteoarticular and neuro-brucellosis [5,6]. There have also been a few case reports on endocarditis, pacemaker infections and breast infections from different parts of the world, but not from Lebanon [7]. Here we report the unusual case of a simultaneous infection with *Brucella* species involving a cardiac pacemaker and the contralateral breast in a middle-aged woman from Lebanon with no significant previous medical problems.

Case presentation

A 52-year-old Lebanese woman presented to the emergency department of the American University of Beirut Medical Center (AUBMC) complaining of redness, pain and swelling at her pacemaker site on the upper left chest wall. The symptoms started one week earlier and had worsened over few days. She had no fever or chills that day. She was previously healthy except for an unclear history of an arrhythmia that occurred in 2005 necessitating the insertion of the cardiac pacemaker. The patient also complained of right breast pain, swelling and erythema of 3 days duration. Her primary care physician had prescribed amoxicillin-clavulanate for suspected mastitis. The patient also reported episodes of fever (temperature reaching 38.5 °C) and chills especially at nighttime for about three months prior to this current illness. She denied localizing signs or symptoms at the time.

On physical examination, the patient was hemodynamically stable and afebrile. Left chest wall erythema, induration and tenderness were observed. Erosion was noted at the skin overlying the pacemaker impulse generator and wires. The right breast was swollen, diffusely erythematous, and tender. No palpable masses were appreciated. The laboratory examination revealed a normal white Blood Cell count of 5400 per cu mm, (reference range: 4000–11000), polymorphonuclear cells were 50% (reference range: 40–65), and lymphocytes were 40% (reference range: 25–40). Her creatinine was 0.6 mg/dL (reference range: 0.5–1) but her C-reactive protein was elevated at 12.5 mg/dL (reference range: 0.0–2.5). A computed tomography scan of the chest wall with

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https://doi.org/10.1016/j.idcr.2019.e00485

intravenous contrast revealed three well-circumscribed rim enhancing fluid collections in the right breast the largest measuring 1.9 × 2 cm. There was overlying skin thickening and associated subcentimetric right axillary lymph nodes. A collection on the left side of the chest wall over the site of the pacemaker was also noted.

On the second day of admission, the pacemaker impulse generator and wires were removed. Purulent drainage was noticed in the pacemaker bed and sent for culture. The Gram stain showed numerous WBCs but no microorganisms. The patient received intravenous teicoplanin and amoxicillin-clavulanate empirically awaiting the culture results. An ultrasound-guided aspiration of the right breast abscess was also performed. The content was sent for microbiologic culture as well and cytologic evaluation to rule out an underlying malignancy. On the 5th day of admission, cultures from both the pacemaker bed and the right breast grew *Brucella* species. The titers for the direct serum tube agglutination (STA) as well as the indirect test (*Brucella* Capt., Vircell, Spain) were both ≥ 1:1280. Two sets of blood cultures done on VIRTUO Biomerieux blood culture automated system were negative.

Upon further questioning, the patient remembered eating unpasteurized cheese several months before. She also remembered an episode of breast tenderness, swelling and warmth after that. The symptoms resolved spontaneously but were followed by a period of night sweats and low-grade fever.

The patient received intravenous gentamicin (240 mg intramuscularly daily) for two weeks along with rifampin (600 mg orally daily) and doxycycline (100 mg orally twice daily) for three months. At the end of her treatment, the patient reported marked improvement in her condition and complete resolution of the fever and chills. Four months later, the patient was asymptomatic, with normal physical examination. Repeat *Brucella* serology showed a decrease in the direct STA titer (1:320) and indirect *Brucella* titer (1:640). The repeated blood cultures were negative at 14 days of incubation and the breast ultrasound did not reveal a residual abscess.

Discussion

Brucella are small, non-encapsulated, non-motile, facultative intracellular, aerobic, Gram-negative coccobacilli [1,8]. Brucellosis is almost invariably transmitted to humans from infected domestic animals and their contaminated products [9]. Infected animals excrete Brucellae in the urine, milk, placenta, and other products of miscarriages. In this way, the bacteria are disseminated and infect other animals and humans [10]. *Brucella* organisms can survive up to two days in milk at 8 °C, up to three weeks in frozen meat, and up to three months in goat cheese [10,11]. Even though a wide range of clinical manifestations and complications have been reported, only few reports describe *Brucella* breast infections or pacemaker infections, mainly from countries of the Mediterranean basin [3].

Brucella breast infections were mainly reported in women with a wide age distribution [12–16]. It is most likely due to hematogenous spread, as both breasts have been involved simultaneously. There were no associated underlying malignancies. Drainage culture was required to establish the diagnosis [13,15,17]. Blood cultures were not all positive [14,15]. *Brucella* serology was reported positive in one case most likely due to relying on direct agglutination test only and not using more sensitive tests such as the indirect titers, *Brucella* CAPT or ELISA [8,13] (Table 1).

Symptoms may last for several weeks before the diagnosis of *Brucella* mastitis is established if there are no associated systemic manifestations. In 1991, Gasser et al. reported a case of *Brucella* mastitis and posterior uveitis that improved markedly on antimicrobial treatment [16]. Failure of treatment response with first line antimicrobials used for common causes of cellulitis and skin and soft tissue infection should prompt suspicion of infection

Table 1
Breast infections with brucellosis.

Study/year	Patient/age	*Brucella* preceding and associated infections	*Brucella* blood culture	Miscellaneous cultures	Antimicrobials	Treatment duration	country
Gasser et al. [16]	52 year old woman	Acute presentation with uveitis	No	Abscess culture	Doxycycline streptomycin	45 days 15 days	Spain
Al Abdely et al. [12]	39-year-old /woman	No information	N/A	Breast abscess	Doxycycline & TMP/SMX	3 months	Saudi Arabia
Tsironi et al. [13]	77 year old/ woman	Yes, acute illness 5 days	No	Breast abscess	Doxycycline & streptomycin (1st infection)	8 weeks 3 weeks	Greece
Erdem et al.	63-year-old female	No information	No	Breast abscess	Tetracycline & rifampin	1 year	Turkey
Gurleyik et al. [17]	46 year old woman	3 months acute illness and spinal (L5-S1) abscess	No	Negative spinal and breast abscess culture	TMP-SMX Later Streptomycin Rifampin + tetracycline	2 weeks 4 months	Turkey
Akay et al.	52-year old woman	No information	No	None	Rifampin 600 mg/day and doxycycline 200 mg/day	8 weeks	Turkey
Ibis et al. [14]	48 year old/ man	2 years night sweats. Bilateral breasts.	No	Abscess culture positive	Doxycycline & rifampin	Not specified	Turkey
Nemenqani et al. [15]	6 cases women						Saudi Arabia
With permission	45 year old woman	Bilateral abscesses three weeks	N/A	N/A	Rifampin & Tetracycline	7 weeks	
	35 year old woman	L breast abscess. Systemic illness preceding	Surgical drainage & Antimicrobials	N/A		N/A	
	20 year old woman	R breast abscess	N/A		TMP / SMX	2 months	
	32 year old woman	Breast Abscess	N/A	Surgical drainage & Antimicrobials		N/A	
	48 year old woman	L breast abscess	N/A	N/A	Doxycycline and Streptomycin	N/A	
	32 year old woman	Left Breast abscess	N/A	N/A	Rifampin & Tetracycline	N/A	

with *Brucella* in the correct endemic context [12]. Subsequently, successful response was achieved in patients receiving doxycycline and trimethoprim-sulfamethoxazole doxycycline and streptomycin [13] or doxycycline and rifampin [14] (Table 1).

Brucella pacemaker infection is also a rare entity with only few reported cases in the literature (Table 2). In 2013, a study by Osmonov et al. focused on cardiac-device related endocarditis (CDE) in one large hospital in Turkey. One of 23 cardiac devices infection was caused by *B. melitenis* [18]. Similarly, in 2014, a study by Simsek-Yavuz et al. looking at infective endocarditis in 325 cases in Turkey revealed one case of CDE infection due to *B. melitensis*. No information was found in the article on the patients' characteristics, treatment, and prognosis [19]. In our review of published cases (Table 2), all of patients were men; the age range was 38-71 years, with the mean of 61.8 years. The pacemaker had been inserted for a mean of 7 years (duration range from 2 to 20 years) for various cardiac indications. Several of these men had direct occupational contact with sheep [20,21].

Eradication of the infection and complete resolution are possible only after complete extraction of the device and leads [22]. In some instances, the *Brucella* infection presented as device infection. The first case of *B. melitensis* pacemaker infection was reported by de la Fuente et al. in 1997 in a 63-year-old sheep herder who initially had a pacemaker implanted in 1994 who developed *B. melitensis* pacemaker infection [21]. Similarly, other patients developed *B. melitensis* infection months or years after the implantation of a cardiac device, presumably leading to the seeding of the device with the organism [20,21,23]. Cardiomyopathy, valvular vegetation and abscess formation at the pacemaker site were described in those instances. Treatment included antimicrobials and removal of the pacemaker or defibrillator and leads. *B. melitensis* pacemaker infection presented as recurrent skin papules at the site of the device in one report [24]. Two years after the first onset of the lesions, the pacemaker was removed. In other cases, patients suffered recurrent systemic *Brucella* infections several years after the implantation of the cardiac devices, suggesting that those organisms have the potential to seed the cardiac device at any point after implantation and establish a focus for recurrent episodes [25,26]. It took several recurrences of the illness before the extraction of the device and leads. In one case the transesophageal echocardiography was negative for endocarditis, yet the pacemaker leads were removed despite lack of infectious signs [25]. Culture of the leads is usually positive for *B. melitensis*.

The present case is the first concomitant mastitis and pacemaker infection with brucellosis. There are only six cases of *Brucella* breast abscesses in the literature, only eight case reports of pacemaker endocarditis. Our case, as in other cases, highlights the insidious nature of this infection. Such findings reflect the importance of awareness about the disease in endemic areas to establish early diagnosis and treatment and avoid serious complications.

In this report, we emphasize the role of brucellosis in complicated infections especially that this disease remains endemic to the Middle East and East Mediterranean basin. *Brucella* infection can have a myriad of clinical presentations; prolonged undulating fever and night sweats comprise the most classical signs and symptoms, usually lasting days to weeks before recognition [4]. Complications of *Brucella* infection are varied and include orchitis and/or epididymitis, spondylitis and osteoarticular involvement, endocarditis, myocarditis, endarteritis, uveitis, central nervous system infection, as well as less frequently hepatitis, pneumonitis, or splenic abscess [6]. Such complications are preceded by a bacteremic phase and hematogenous seeding of an organ. Those organs usually serve as a focus and lead to the recurrences and relapses witnessed by patients [27]. Inflammation of those organs is the only clinical manifestation of ongoing infection with *Brucella* in the absence of other systemic symptoms. In our patient and after the initial infection, fever and night sweats resolved spontaneously and she remained asymptomatic for several weeks before presenting with the dramatic erosion at the pacemaker site. A certain threshold of suspicion for *Brucella* infection should be kept even for usual presentations in the right geographic context.

In our patient, the infection was most likely acquired after ingestion of unpasteurized cheese; she likely developed a

Table 2
case reports of brucellosis involving pacemakers and cardiac devices.

Study/year	Patient/age	Pacemaker type of device and time since implantation	*Brucella* preceding	*Brucella* blood culture	Miscellaneous cultures	Pacemaker and leads removed	Antimicrobials	Treatment duration	country
De la Fuente et al. [21]	63-year-old /man	2 years	Yes, one year preceding	No	Pacemaker, leads, pus, necrotic tissue	Yes	Doxycycline & rifampin Streptomycin	45 days 21 days	Spain
Francia et al. [25]	71 year old/ man	5 years	Yes, based on positive serology Sacroilitis 2 months later And two recurrences	No	Pacemaker and leads. No obvious signs on exam. Negative TEE.	Yes	Doxycycline & streptomycin (1^{st} infection) Doxycycline & Rifampin (2^{nd} infection)	6 weeks 8 weeks	Spain
Ulkar et al. [23]	68 year old/ man	1 year (patient had previous pacemaker for 7 years)	No	Yes, positive	Abscess culture positive	Yes	Doxycycline & rifampin	6 weeks	Turkey
Miragliotta et al. [22]	No information	No information	Yes, relapsed	No information	No information	No information	No information	No information	Italy
Dourakis et al. [20]	70 year old/ man	7 years	Yes, 25 years prior to presentation	Yes positive	TEE showed mass on tricuspid, Pacemaker and leads had vegetation	Yes	Doxycycline, Ciprofloxacin & Rifampin	12 months	Greece
Al-Majid et al. [26]	38 year old/ man	20 years/pacemaker	Relapsing *brucella* three times in one year	Yes positive	Yes leads positive	Leads removed	Doxycycline & Rifampin	6 weeks	Saudi Arabia
Gungor et al. [24]	61 year old	2 years Pacemaker	No	Yes	Skin abscess	Yes	Doxycycline & Rifampin	6 weeks	Turkey
Osmonov et al. [18]	NA	6 months pacemaker	NA	Yes positive	Yes leads positive Echocardiography positive	Leads and pacemaker removed	NA	NA	Turkey

bacteremia and seeded the breast area since the pacemaker abscess was noted after the development of the breast abscess. This suggests that the breast abscess served as a nidus for the infection to later spread hematogenously and colonize the pacemaker leads. Clumping development is a complex process that is initiated when bacteria attach to a surface using exopolysaccharide polymers or other adhesins and develop into microcolonies. Because bacterial clumping is one of the initial steps of biofilm formation, the clumping phenotype in *B. melitensis* was described giving evidence that this alpha-proteobacterium could form biofilms during its lifecycle and cause hardware infection [28].

Treating and managing such infections entails the drainage of the breast abscesses, removal of the pacemaker and its leads and a prolonged course of antimicrobials. In our case, and as reported in the literature, the pacemaker and leads were extracted for this patient. *Brucella* cardiac device endocarditis is a relapsing disease if the leads and pacemaker are not extracted, together with a prolonged treatment with antimicrobials. The insidious presentations and complications of *Brucella* infections remain a major diagnostic challenge. Infections with brucellosis should figure in the differential diagnosis of complicated infections, as noted in this rare case of simultaneous infection of breast and pacemaker device, especially in endemic areas.

Author statement

All authors contributed to the conceptualization and preparation of this manuscript.

Dima Ibrahim and Helene Dabbous contributed equally

Dima Ibrahim: Writing: original draft and tables

Helene Dabbous: Writing: original draft and tables

Yasmina Abi-Aad: Writing: original draft and review

George Araj: Writing: review and editing

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Disclosure

Authors declare no conflict of interest.

No financial support was needed to write the review.

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