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Case report

Brucella myocarditis with unusual clinical features & abnormal cardiac MRI: A case report

Mohammadreza Salehi [a], Hossein Khalili [b], Meysam Khoshavi [c], Reza Mollazadeh [c], Bahare Jahanshahi [d], Mahnaz Sadat Hosseini [b,*]

[a] Research Center for Antibiotic Stewardship and Antimicrobial Resistance, Imam Khomeini Hospital Complex, Department of Infectious Diseases, Tehran University of Medical Sciences (TUMS), Iran
[b] Department of Clinical Pharmacy, School of Pharmacy, Tehran University of Medical Sciences (TUMS), Tehran, Iran
[c] Department of Cardiology, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran
[d] Tehran University of Medical Sciences, Cardiovascular Department, Tehran, Iran

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ABSTRACT

Brucellosis is a zoonotic disease that remains an important public health problem in developing countries. It can affect almost all organs, including the heart. While cardiac complications of brucellosis are not common, they usually manifest as endocarditis. Brucella myocarditis, on the other hand, is a highly rare complication of brucellosis. In this case report, we present the case of a 35-year-old woman who was admitted to the hospital with severe palpitations, fever, and fatigue. Due to the patient's long history of brucellosis and clinical symptoms, she underwent cardiac evaluation, including cardiac magnetic resonance imaging, which was a promising method to diagnose Brucella myocarditis. Hopefully our patient responded well to Rifampin and Doxycycline with gentamicin. It is important to raise awareness of this rare but potentially serious complication of brucellosis and to emphasize the value of early diagnosis and treatment.

Introduction

Brucellosis is a bacterial disease that remains an important public health problem with endemic characteristics in many countries [1]. It is a worldwide zoonosis, with high numbers of human cases reported in recent years in Yemen, Iran, Syria, Turkey, and Saudi Arabia, particularly in the Middle East [2]. Almost all organs and systems of the human body can be affected by brucellosis [3]. Although cardiac complications are not common and occur in only 0%– 2% of patients [1], endocarditis is the most common cardiac complication, while myocarditis is a rare presentation [4]. Some cases of Brucella myocarditis have been reported from endemic countries [4,5]. In this report, we present an unusual case of myocarditis caused by Brucella species.

Case presentation

A 35-year-old single woman without known history of cardiac disease presented to the emergency department of Imam Khomeini Hospital Complex in Tehran, Iran with complaints of severe palpitations, fever, and fatigue that had persisted for two weeks. The patient had been diagnosed with brucellosis six months prior, and tests related to the diagnosis are detailed in Table 1.

A year ago, the patient had experienced symptoms of fever and fatigue, but did not seek regular medical care and did not receive a definitive diagnosis during that time. During the first episode, the patient took doxycycline (100 mg twice daily) and rifampin (300 mg twice daily) for two weeks, but her symptoms did not improve. She was subsequently admitted to the local hospital and received cotrimoxazole, ceftriaxone, and ciprofloxacin injections for two weeks, but her symptoms only slightly improved. Upon discharge, the patient was prescribed doxycycline (100 mg twice daily), ciprofloxacin (500 mg twice daily), and cotrimoxazole (2 tablets twice daily).

After two weeks, the patient returned to the hospital with palpitations and fever. Her medication was changed to doxycycline (100 mg twice daily) and rifampin (300 mg twice daily). On examination, the patient's blood pressure was 100/75 mm Hg, pulse rate was 90 beats per minute, temperature was 36.7 degrees Celsius, and respiratory rate was 18 per minute. She appeared ill and pale but was not toxic upon initial

* Corresponding author.
E-mail addresses: salehi.mohamad3@gmail.com (M. Salehi), khalilih@tums.ac.ir (H. Khalili), Meysamkhoshavi@yahoo.com (M. Khoshavi), mollazar@yahoo.com (R. Mollazadeh), Bahareh1jahanshahi@gmail.com (B. Jahanshahi), mahnazsadat.h1376@gmail.com (M.S. Hosseini).

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Table 1
Patient's lab data at Brucellosis diagnosis time.

Test	value	Normal Range	Unit
WBC	5.5	4.4–11	× 1000/mm^3
N%	61		
L%	28		
RBC	3.79	4.2–5.4	Million/mm^3
Hgb	12.4	12–15	Million/mm^3
MCV	97.9	80–100	fL
MCH	32.7	27–31	Picograms/cell
PLT	230	150–450	× 1000/mm^3
CRP	2.7	1	mg/dl
ESR	3	0–20	mm/h
LDH	218	105–333	IU/L
Brucella Ab. IgG	1	< 9	Index
Brucella Ab. IgM	11.6	< 9	Index
Wright agglutination test	1/320	< 1/160	Titer
Coombs wright agglutination test	1/320	< 1/160	Titer
2ME Brucella agglutination test	1/160	< 1/40	Titer
Tuberculin test	< 2	< 5	mm
Anti-toxoplasma (IgG)	2.6	< 9	Index
Anti-toxoplasma (IgM)	< 3	< 6	Au/ml
ACE (angiotensin-converting enzyme)	34	8–65	U/L
C3	81	90–180	mg/dl
C4	15	10–40	mg/dl
Anti-ds DNA	20.3	< 30	U/ml
Ferritin	47	10–124	ng/dl
cortisol	17.6	5–23	pg/ml

WBC: White blood cell count, Hb: hemoglobin, PLT: Platelet Count, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, PT: Prothrombin time, PTT: Partial thromboplastin time, INR: international normalised ratio, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, BS: Blood sugar, LDH: lactate dehydrogenase, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin

Table 2
Patient's lab data at the admission time.

Test	Value	Normal Range	Unit
WBC	5800		× 1000/mm^3
RBC	3.98	4.2–5.4	Million/mm^3
Hgb	13	12–15	Million/mm^3
MCV	96	80–100	fL
MCH	32.7	27–31	Picograms/cell
PLT	167	150–450	× 1000/mm^3
CRP	1	1	mg/dl
ESR	25	0–20	mm/h
AST	18		U/L
ALT	15		U/L
Bill T/D	0.3/0.2	1.2/0.2	mg/dl
Cr	0.7	0.7–1.2	U/L
urea	27	5–20	U/L
Na	137	135–145	meq/L
K	4.1	3.5–5.2	meq/L
Mg	1.9	1.7.2.2	meq/L
Ca	8	8.6–10.3	meq/L
Troponin-I	< 0.034	0–0.04	ng/ml
N-pro-BNP	< 20	< 125	pg/ml
INR	1	1	
PT	14.5	14.5	Second
PTT	26	25–35	Second
FBS	96	< 100	mg/dL
LDH	315	105–333	IU/L

WBC: White blood cell count, Hb: hemoglobin, PLT: Platelet Count, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, PT: Prothrombin time, PTT: Partial thromboplastin time, INR: international normalised ratio, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, BS: Blood sugar, LDH: lactate dehydrogenase, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin

clinical examination. A general review of her system and physical examination did not reveal significant abnormalities. Her laboratory data at the time of admission are shown in Table 2, and both viral markers and rheumatological markers were negative. Serological tests for Influenza and nasopharynx swab for SARS-CoV2(Covid-19) were negative.

Electrocardiography (ECG) revealed a sinus rhythm without any noticeable abnormalities, and the chest x-ray showed no significant abnormalities. Echocardiography showed interventricular septal wall hypokinesia, mild left ventricular systolic dysfunction (left ventricular ejection fraction 50%), and normal right ventricular function with a left ventricular ejection fraction of 50%. Due to the patient's history of brucellosis infection, accompanied by symptoms such as fever, fatigue, and heart palpitations, a diagnosis of myocarditis was suspected. Therefore, a cardiac magnetic resonance image (MRI) was performed, show that there is an increase in the T2 Signal Intensity ratio in the basal inferior septal segment of the left ventricle, which indicates localized myocardial inflammation. There is also evidence of reduced LVEF (left ventricular ejection fraction) of 54% and reduced global LV (left ventricular) longitudinal strain of 18.5 with mild pericardial effusion, but myocardial fibrosis is not entirely clear. These findings suggest that there is active myocarditis (Fig. 1 A, B,C). Assessment of the morphology and function of the cardiac valves revealed mild mitral regurgitation, trivial aortic regurgitation, and mild tricuspid regurgitation.

The patient was started on treatment with oral rifampicin (600 mg once daily), doxycycline (100 mg twice daily) along with intravenous gentamicin (160 mg once daily) for four weeks. In the fourth week of treatment, although her palpitations decreased, she still complained of intermittent palpitations. Twelve-lead ECGs were unremarkable, so a 48-hour ambulatory ECG holter monitoring was performed (Fig. 2), which showed periods of bigeminal premature ventricular contraction (PVC), correlating with the time of palpitation feeling of the patient, otherwise unremarkable. On the day of discharge, all laboratory tests were normal, and she was discharged with propranolol 10 mg TDS and colchicine 1 mg daily. She mentioned occasional palpitations with less intensity and frequency. Following treatment, the patient was clinically improved. She had gained 3 kg and the palpitations relieved at the 3-month follow-up. Palpitations are not usually considered strongly suggestive of myocarditis, although this has been reported [6]. After eight months, a follow-up cardiac MRI was conducted to reduce myocardial inflammation in the T2-weighted images. The results show evidence of subepicardial delayed hyperenhancement in the basal to mid inferior, inferior lateral, and anterior lateral LV segments. There is also evidence of improvement in the LVEF (now at 60%) and global LV longitudinal strain of 21. However, minimal pericardial effusion is still visible (Fig. 1D, E, F). Overall, based on these findings, it is suggestive that the myocarditis has healed.

Discussion

Infection from Brucella species can cause complications involving the musculoskeletal, genitourinary, gastrointestinal, hematologic, nervous, respiratory systems, skin, and mucous membranes [7]. Brucellosis rarely affects the heart, and when it does involve the cardiovascular system, endocarditis is the most common [8]. Myocarditis is a rare complication of brucellosis in adults, which can be detected by echocardiography and cardiac MRI [4,9]. MRI has been used in some studies to diagnose and confirm Brucella myocarditis [9,10]. Cardiovascular Magnetic Resonance (CMR) is an established and highly valuable clinical tool in the diagnostic work-up of patients with clinically suspected myocarditis [11]. CMR is the most important noninvasive imaging modality for the evaluation of myocarditis and is preferred over cardiac biopsy due to the invasive nature of the procedure and associated risks, as well as its low sensitivity compared to cardiac explants at autopsy [12].

According to the 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR

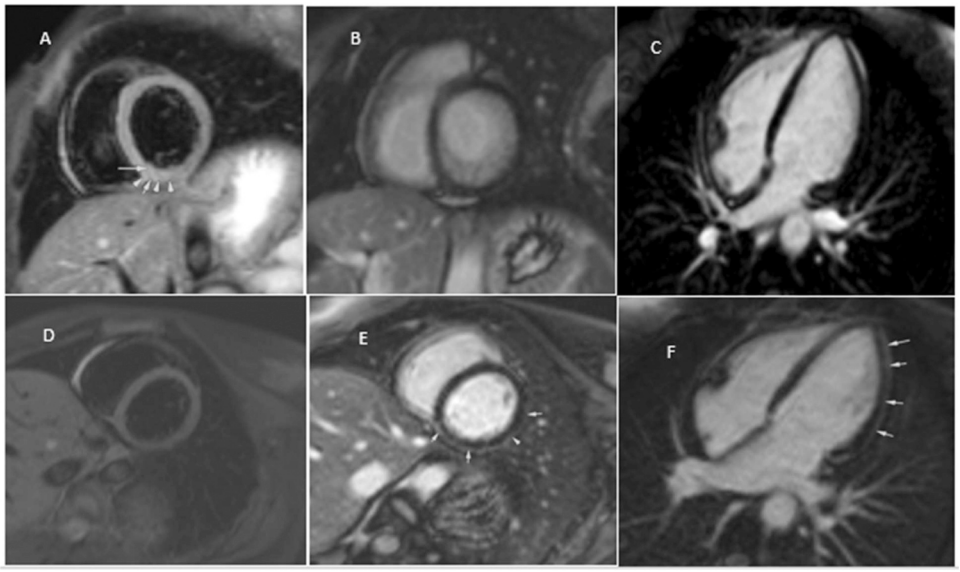

Fig. 1. The top panel displays the initial MRI images, while the bottom panel shows the MRI scans taken 8 months later. (A)short-axis view, T2 Weighted Image, showed myocardial edema present in the basal inferior septal LV segment, (B, C) in the short-axis and 4ch view, there was no evidence of late gadolinium enhancement, (D)another short-axis view with a T2 Weighted Image, showed improvement in myocardial inflammation, (E, F), late enhancement images revealed evidence of sub-epicardial fibrosis in the basal to mid inferior, inferior lateral and anterior lateral LV segments, which suggest the presence of post myocarditis scar.

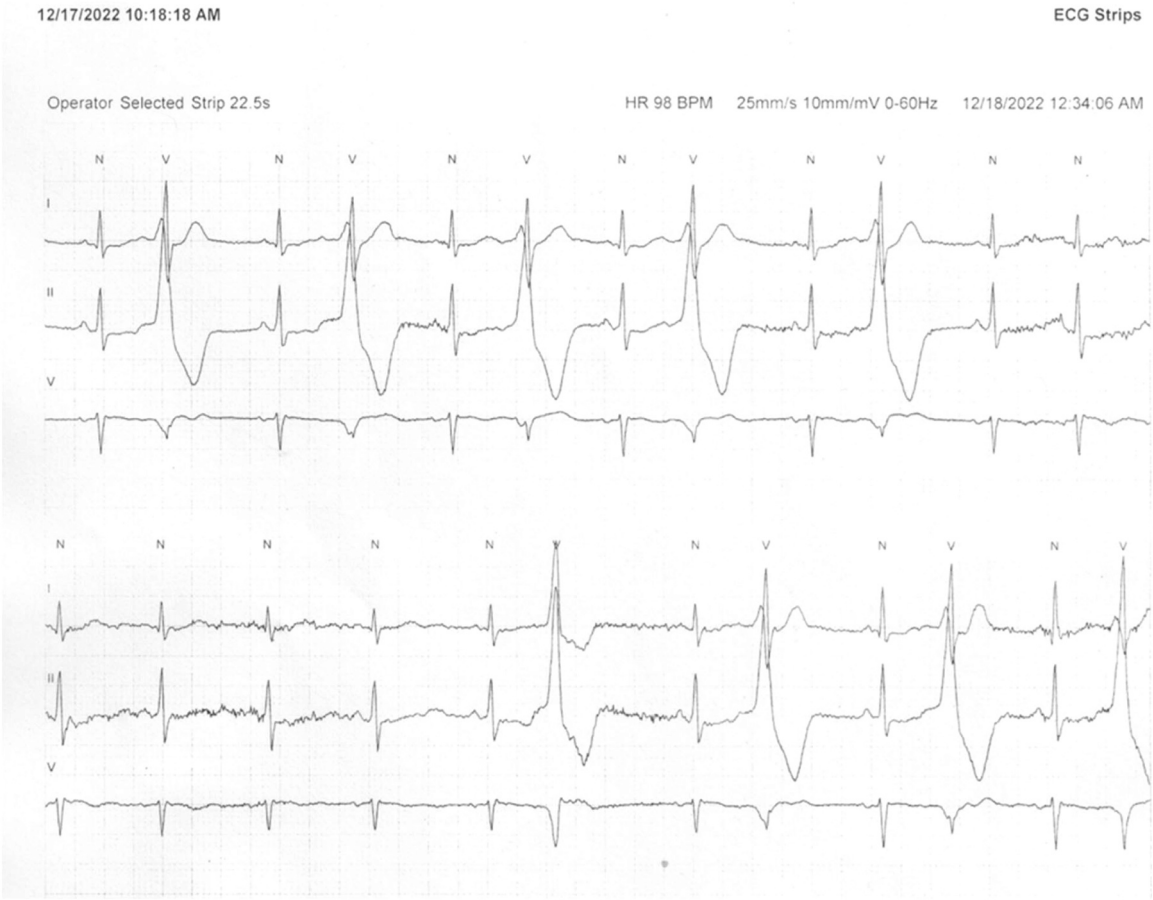

Fig. 2. Three channel ECG Holter monitoring of the patient showed bigemenic PVC and normal sinus beats (indicated as V and N respectively).

Guideline for the Evaluation and Diagnosis of myocarditis, CMR is useful in distinguishing myocarditis from other causes of acute chest pain in patients with myocardial injury who have nonobstructive coronary arteries at anatomic testing and to determine the presence and extent of myocardial or pericardial inflammation and fibrosis [6,13,14]. Diagnostic criteria in CMR include new regional wall motion or global systolic or diastolic function abnormality, with or without ventricular dilatation, with or without increased wall thickness, with or without pericardial effusion, with or without endo-cavitary thrombi, edema, and/or hyperemia, and/or late gadolinium enhancement of classic myocarditis pattern [11].

In our case, the diagnosis was made according to T2-based criteria for myocardial edema, which include regional high T2 signal intensity, global T2 signal intensity ratio equal to or greater than 2.0 on T2-

Table 3
Published case reports referring to Brucella myocarditis.

Publication	Gender	Age	Treatment	Follow-up
Gur et al.	Woman	25 y	Streptomycin and tetracycline	Relapse after 4 months
Lubani et al.	Boy	10 y	Tetracycline for 2 weeks Streptomycin for 3 weeks	Two-year follow-up showed no relapse
Jubber et al.	Man	55 y	Doxycycline and rifampicin	No follow-up
Efe et al.	Woman	51 y	Streptomycin for 3 weeks Doxycycline for 6 weeks	3-month follow-up: asymptomatic
Elkiran et al.	Girl	3 months	Gentamycin, Bactrim, and rifampicin	Four-month follow-up: no relapse
Pandit et al.	Woman	32 y	Streptomycin and doxycycline	Worsened and died due to pulmonary odema
Gatselis et al.	Man	34 y	Streptomycin for 3 weeks Doxycycline and rifampicin	One-year follow-up: no symptoms, no relapse
Gatselis et al.	Man	17 y	Streptomycin for 3 weeks Doxycycline and rifampicin	One-year follow-up: no symptoms, no relapse
Adid et al.	Man	32 y	Streptomycin for 2 weeks Doxycycline and rifampicin for 12 weeks	3-month follow-up: no relapse
Abid et al.	Man	20 y	Cotrimoxazole and rifampicin	No follow-up
Khorasani and Farrokhnia	Man	22 y	Cotrimoxazole, doxycycline, and rifampicin for 3 months	Two-month follow-up: asymptomatic
Pandit et al.	Man	27 y	Doxycycline, rifampicin for 12 weeks, and gentamycin for 10 days	After several months, the patient was asymptomatic
Wendt S et al.	Unknown	27 y	rifampin and doxycycline plus gentamicin for 10 days	recovered completely after several months
Bhatty S et al.	Mam	30 y	long-term rifampin and doxycycline plus streptomycin for 2 weeks	symptoms regressed rapidly after initiation of treatment
He Y et al.	Woman	35 y	long-term rifampin, doxycycline, and trimethoprim/sulfamethoxazole plus gentamicin for 4 weeks	6-month follow-up: no relapse and resolved symptoms
Lagadinou M et al.	Man	21 y	long-term rifampin and doxycycline plus gentamycin for 10 days	No follow-up
Our case	Woman	35 y	long-term rifampin and doxycycline plus gentamycin for 30 days	8-month follow-up: no relapse and resolved symptoms

weighted images, or regional or global increase of myocardial T2 relaxation time [12].

Some case reports of Brucella myocarditis have been published in the past. PubMed database search for articles published until July 2023 using keywords myocarditis and Brucella revealed only some reports with myocarditis in the absence of endocarditis (Table 3). Wendt S and colleagues reported a case of brucellosis myocarditis treated with long-term treatment of rifampin and doxycycline plus gentamicin for 10 days, and the patient recovered completely after several months [10]. In 2020, Bhatty S et al. reported a case of brucellosis myocarditis treated with long-term rifampin and doxycycline plus streptomycin for 2 weeks, and the patient's symptoms regressed rapidly after initiation of treatment [4].

In the current case, myocarditis secondary to Brucella infection was diagnosed, and involvement of the cardiac valves and minimal Pericardial was observed. The diagnosis of Brucella myocarditis was based on the patient's long history of untreated brucellosis, typical symptoms, myocarditis inflammation on CMR, typical symptoms, and myocardial involvement. The mechanism of cardiac damage from brucellosis is not clear, but it can be caused by the direct effect of the microorganism, local deposits of immunocomplexes, and inflammatory cytokines such as interleukin-6 [5,15].

Brucella myocarditis usually responds well to antibiotic therapy [16]. The guidelines recommend two regimens, both of which involve doxycycline for six weeks. They may be combined with streptomycin for two to three weeks or rifampin for six weeks. The second regimen is especially recommended for those with endocarditis. Triple antibiotic therapy using doxycycline plus rifampin for three months in combination with streptomycin for up to three weeks is recommended [4,17]. In the present case, the patient was treated with triple antibiotic therapy (gentamicin, rifampin, and doxycycline), although there was no endocarditis. Myocarditis is considered a dangerous complication of brucellosis, which is associated with a worse prognosis. The patient had symptoms of brucellosis for more than one year, and her diagnosis was delayed. After 4 months of diagnosis, ciprofloxacin, doxycycline, and cotrimoxazole were prescribed, which were not first-line drugs for the treatment of brucellosis. Currently, the patient has been receiving antibiotics for more than 6 months. After the diagnosis of myocarditis, the patient received rifampin (600 mg once daily) and doxycycline (100 mg twice daily) along with intravenous gentamicin (160 mg once daily). Gentamicin was administered for a total of 30 days. In previous studies, gentamicin was used for myocarditis caused by brucellosis for 10 days, but in this patient, gentamicin was used for a longer period at our discretion [10]. He Y et al. published a case of brucellosis myocarditis and pneumonitis treated with long-term rifampin, doxycycline, and trimethoprim/sulfamethoxazole plus gentamicin for 4 weeks, and the patient resolved symptoms after 6 months [18]. Due to the lack of clear guidelines for the treatment of Brucella myocarditis, the patient had been treated for Brucella for more than 6 months, and she was discharged with propranolol 10 mg TDS and colchicine 1 mg daily. This management was done by multidisciplinary team of Imam Khomeini Hospital Complex.

Conclusions

Cardiac evaluation should be considered if a patient with brucellosis has palpitations and does not respond to conventional treatment. CMR can be a promising method for diagnosing Brucella myocarditis. Patients with Brucella myocarditis usually respond well to combination therapy with gentamicin.

Ethical approval

Not applicable.

Consent

All authors consent to the publication of the article.

Conflicts of interest

The authors report there are no conflicts of interest to declare.

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