

## Case Report

# Two rare cases of *Brucella*-induced endocarditis and myopericarditis: challenges in diagnosis

Dalila Šačić<sup>1</sup>, Olga Petrović<sup>1,2</sup>, Branislava Ivanović<sup>1,2</sup>

<sup>1</sup> Clinic for Cardiology, University Clinical Center of Serbia, Koste Todorovića 8, 11000, Belgrade, Serbia

<sup>2</sup> Faculty of Medicine, University of Belgrade, Dr Subotića 8, 11000, Belgrade, Serbia

### Abstract

**Introduction:** Brucellosis is one of the most common zoonotic infections in the world. Cardiac complications of the disease are usually in the form of endocarditis, and, to a lesser extent, in the form of myopericarditis.

**Case:** We report the case of a 34-year-old female admitted with signs of fever, nausea, and headache. The patient came from Libya, where she drank unpasteurized milk. Wright-Coombs test and blood confirmed *Brucella* species infection, while transthoracic echocardiogram revealed a thrombotic mass on the tricuspid valve that required cardiac surgery and antibiotic treatment, leading to complete recovery. The second case was a 37-year-old male admitted with suspected acute coronary syndrome, where further diagnostics excluded occlusions of coronary arteries and found *Brucella* species infection and signs of myocardial and pericardial involvement that reacted well on treatment (combination of doxycycline and rifampicin).

**Discussion:** Brucellosis is commonly seen in people working with farm animals or using unpasteurized milk but is still often misdiagnosed.

**Conclusions:** Tricuspid valve endocarditis, as well as isolated myopericarditis, are rare complications of Brucellosis, which can be fatal if not diagnosed and treated on time.

**Key words:** Brucellosis; zoonosis; endocarditis; myocarditis; pericarditis; case report.

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### Introduction

Brucellosis is a systemic infection caused by a pathogen species from the genus *Brucella* (*B. melitensis*, *B. abortus*, *B. suis*, *B. canis*), a Gram-negative, intracellular coccobacillus [1]. It continues to be reported in Mediterranean and Middle Eastern regions, making it one of the world's most common zoonotic infections. The method of transmission to humans is through direct contact of body tissues with the fluids, milk, and dairy products of infected animals or through breastfeeding from infected mothers to infants. Brucellosis is a frequent occupational disease in people dealing with cattle and cattle products, such as shepherds, slaughterhouse employees, food handlers, veterinarians, dairy industry specialists, and staff members in microbiology labs [1]. The disease is characterized by an acute or insidious onset of fever and one or more of the following: night sweats, arthralgia, headache, fatigue, anorexia, myalgia, weight loss, arthritis/spondylitis, meningitis, or focal organ involvement (endocarditis, orchitis/epididymitis, hepatomegaly, splenomegaly) [2]. Brucellosis rarely results in death; nearly half of deaths are caused by

*Brucella* endocarditis. Endocarditis is the most common cardiac complication, while acute pericarditis and myocarditis without endocardial involvement are uncommon [3].

A female with *Brucella* endocarditis and a male with *Brucella* myopericarditis are the two cardiac brucellosis patients we present here.

### Case reports

#### *Brucella* endocarditis

The first patient was a 34-year-old woman who was admitted to the hospital with headache, nausea, and a fever of 40°C. The patient denied ever having had a respiratory, gynecological, or urinary infection before. She also denied using intravenous drugs. The patient was working in Libya and reported having drunk unpasteurized milk.

A physical examination revealed a regular heart rate of 100 beats per minute, a systolic murmur over the apex and Erb's point, and an arterial blood pressure of 100/60 mm Hg. The right knee was subtly swollen, and there was slight inflammation. On admission, the patient did not have a fever.

Laboratory tests showed elevated parameters of inflammation; erythrocyte sedimentation rate was 36 mm/h, fibrinogen 3.9, C-reactive protein 9.1 mg/L, red

**Figure 1.** Transoesophageal echocardiogram representing unusually large, irregular, uneven mass, attached to the middle of the front leaflet of the tricuspid valve.



blood cells count  $3.71 \times 10^{12} \mu\text{L}$ , hemoglobin 106 g/L, hematocrit 0.327, iron  $4.0 \mu\text{mol/L}$ , Gamma-GT 68 U/L, IgA 3.88 g/L, Ig G 23.8 g/L. Antibiotic therapy was started after blood cultures revealed *Brucella spp.* and *Streptococcus agalactiae*. The Wright-Coombs serotype test was positive with a titer of 1:160, but repeated blood cultures did not reveal any signs of infection.

The electrocardiogram (ECG) showed no abnormalities or changes in the ST segment and T wave. Transthoracic echocardiography was performed, and it showed a mass around 4 cm long on the tricuspid valve. Doppler echocardiography showed minor tricuspid regurgitation. A transoesophageal echocardiogram confirmed the finding and revealed an unusually large, irregular, uneven mass, attached to the middle of the front leaflet of the tricuspid valve (Figure 1). Magnetic resonance imaging showed a mass with two parts: one of them spreading to the apex of the right ventricle, 45 mm long, and the other (37 mm) spreading to the pulmonary valve.

Antibiotic treatment was started with a combination of doxycycline (100 mg, twice a day), and rifampicin at 15 mg/kg/day to treat *Brucella*, while ceftriaxone (2 grams per day) was administered for the treatment of *Streptococcus agalactiae* infection. The patient was afebrile on the second day of hospitalization.

Due to the size of the vegetation on the tricuspid valve, the patient was referred for cardio-surgical treatment, in order to debride the affected valve. A biopsy of the mass revealed a thrombus consisting primarily of fibrin, a few granulocyte cells, and a few eosinophils. The thrombus was also covered by connective tissue in one sample.

Anti-microbial treatment was administered two weeks prior and a month after a cardiovascular medical procedure. During a one-year follow-up, the patient demonstrated no disease recurrence and had completely recovered.

### *Brucella myopericarditis*

The second patient was a 37-year-old male farm worker admitted to the hospital with suspected acute coronary syndrome. The patient complained of chest pain, nausea, and vomiting, accompanied by ECG changes suggestive of ST-elevation myocardial infarction (STEMI) (ST-segment elevation in leads I, II, III, aVL, aVF, V3-6), and elevated cardiac biomarkers (troponin and creatine kinase). Additionally, three days before admission, he had a fever with a temperature of 38°C. His physical exam revealed normal blood pressure and a heart rate of 76 beats per minute. The

coronary arteries were found to be without any signs of significant stenosis or spasm when urgent coronary angiography was performed.

Laboratory findings showed an elevated erythrocyte sedimentation rate of 80 mm/h, C-reactive protein 32.8 mg/L, ALT 249 IU/L, AST 67 IU/L, with normal blood cell count. An abdominal ultrasound examination revealed no significant abnormalities.

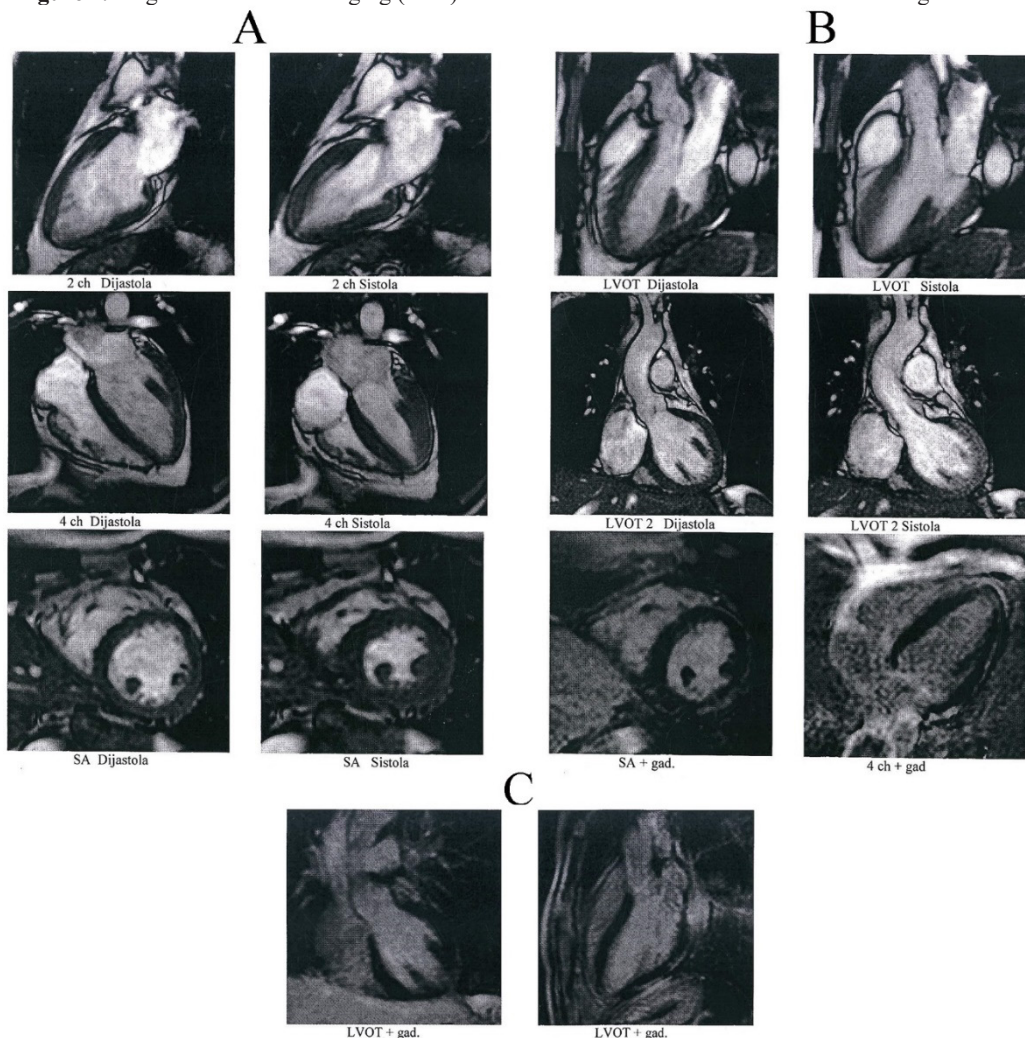
The patient underwent serological testing for the following infectious agents after consulting with an infectious disease specialist: *Mycobacterium tuberculosis*, *Mycoplasma pneumoniae*, *Brucella*, *Borrelia burgdorferi*, and the following viruses: Epstein-Barr, Coxsackie, Influenza, Parainfluenza, Herpes, Adenovirus, Cytomegalovirus, Hepatitis A and B. There were only elevated antibodies against *Brucella*: IgM (12.2 U), and IgG (4.5 U). IgM levels were lower (8.9 U) and IgG levels were slightly higher (4.8 U) in subsequent tests. Anti-microbial treatment was begun

including doxycycline (200 mg, two times every day) and rifampicin (600mg each day) for 45 days.

Initial echocardiogram showed an enlarged left ventricle (EDD 63mm, ESD 47mm), with normal thickness of the walls, hypo-akinesia of the medial and apical segment of the anterior wall, and hypokinesia of the whole septum. There was spontaneous echo contrast in the left ventricle. Ejection fraction was 31%. There was also an increase in echogenicity and discrete pericardial effusion.

Additionally, a heart magnetic resonance imaging (MRI) was performed: In the posterolateral segment of the left ventricle, smaller zones of enhanced signal that were localized intramyocardially and subepicardial were observed following the intravenous administration of gadolinium. After using a contrast agent, smaller areas of the amplified signal were found, which suggested myocarditis (Figure 2 A-C). Four days later, a control echocardiogram revealed that the left ventricle

**Figure 2.** Magnetic resonance imaging (MRI) of the heart after intravenous administration of gadolinium.



had recovered, with a 70% ejection fraction and normalization of segmental kinetics.

The patient was sent home, and at one-year follow-up, there was no disease recurrence.

## Discussion

Brucellosis is a relatively common zoonosis but is often misdiagnosed [4]. Brucella endocarditis is one of the most overseen clinical infections, as it is extremely rare and requires strong clinical suspicion [5]. Furthermore, endocarditis of the tricuspid valve in patients not using intravenous drugs is seldom recognized [6].

Symptoms of Brucella endocarditis vary widely, and range from asymptomatic, to mild, and even severe disease. Diagnosis is easier in countries where the incidence of brucellosis is high. The incidence in Serbia is 3.3 per 100,000 inhabitants, which is lower than in the surrounding countries, like Northern Macedonia (18.6 per 100,000) or Albania (25 per 100,000) [6]. According to a previously published study [7] the number of reported cases of brucellosis in Serbia in the period from 1980, when the disease was imported to our country, to 2008 was 1521, but since it is commonly classified as a ‘fever of unknown origin’ the true number of cases is probably higher than officially reported [7]. The male population in Serbia is at higher risk of infection due to the fact that brucellosis is often an occupational disease in male-dominated occupations such as farming, shepherds, and abattoir workers [1], in accordance with a higher incidence of brucellosis in males in other countries [8]. Farming was the probable cause of infection in our patient with myopericarditis. While the majority of those infected come into contact with domestic animals, transmission through the use of unpasteurized milk and cheese, which is common in Mediterranean countries is also frequent, as demonstrated in our first patient who worked in Libya.

Although gastrointestinal, hematological, urogenital, or cardiovascular symptoms are uncommon, brucellosis can affect many organs and organ systems as a systemic infection. It typically affects the spleen, liver, or bone marrow, which are rich in reticuloendothelial cells [6,7].

Vascular involvement is uncommon and encompasses blood vessel aneurysms, apoplexy, or vasculitis [9-15]. The most common sign of cardiac involvement is endocarditis [3], which most often affects the aortic valve and necessitates its immediate surgical replacement. Myocardial involvement in brucellosis without concurrent endocarditis has only been reported a few times [3]. The precise mechanisms

of the damage to the myocardium, if myocarditis develops independently of endocarditis, are unknown, but they may be associated with the immune-mediated mechanisms or the direct effect of *Brucella*. Antibiotic therapy typically works well for Brucella myocarditis [3].

Establishing a diagnosis when endocarditis is the manifestation of brucellosis may be challenging because the clinical presentation is unspecific and includes chills, weight loss, and loss of appetite, but heart murmurs could also be found in almost 85% of patients. Other unspecific signs include laboratory signs of infection [5]. The standard procedure for diagnosis of Brucella endocarditis is to identify the microorganism through blood culture, serology, immunohistology, and polymerase chain reaction (PCR) test of surgical material. The gold standard is still the isolation of the organism from blood cultures, but false negative results should be taken into consideration if there is a strong clinical suspicion [5]. Blood culture has variable specificity (17% and 85%) depending on the condition of the culture, treatment, or time between the occurrence of symptoms and diagnosis [8].

Transthoracic echocardiography is the imaging method of choice when suspecting Brucella endocarditis; if the finding is normal/ non-specific, then further imaging techniques should be employed such as transesophageal ultrasound (TEE). TEE’s sensitivity goes up to 100%. In our first case, transthoracic echocardiography revealed vegetation on the tricuspid valve leaflet. Surgical treatment, which includes tissue debridement and valve replacement if it is necessary, is often advised, right after medical treatment, as was the case with our first patient. In most cases, this condition may necessitate immediate heart surgery without waiting for the action of antibiotic therapy.

Transthoracic echocardiography and MRI with gadolinium may help demonstrate myocardial involvement if there is a clinical suspicion of Brucella myocarditis.

It is challenging to select the antibiotics and treatment duration for brucellosis treatment. It is necessary to use antibiotic drugs, which have low minimum inhibitory concentrations against brucellosis, and which are transferred into the cells since this infective agent is located intracellularly. The use of combined tetracyclines and aminoglycoside drugs favors better drug-to-cell transitions. Since 1986, the World Health Organization has recommended the use of doxycycline and rifampicin for six weeks to treat uncomplicated forms of brucellosis, while some studies

suggest doxycycline (six weeks) plus streptomycin (two or three weeks) regimen [16].

Brucellosis can mimic a large number of diseases that manifest with a febrile state. Our first patient blood cultures revealed *Brucella spp.* and *Streptococcus agalactiae* (group B streptococcus, GBS). GBS infection can also result in a wide spectrum of clinical diseases, including endocarditis, but this infection is usually seen in pregnant women, neonates, the elderly, or patients with chronic disorders. Also, it is often presented with altered mental status, or signs of skin infections or wounds [17], which was not the case with our patient. Similarly, we discussed the possibility of stress-induced cardiomyopathy [18] in our second case. There were no specific signs of that type of Takotsubo cardiomyopathy (ballooning of the cardiac apex, or hypokinetic apex with hyperkinetic basal heart segments), heart MRI had not shown myocardial edema, and dimensions and function of the left heart ventricle were normal. On the other hand, patient history (farming, fever three days prior), as well as serological testing pointed us to diagnosis and treatment.

## Conclusions

Adequate anamnesis, including occupational and socio-epidemiological history, and clinical suspicion followed by proper diagnostic procedures could be of the utmost importance in *Brucella* infection diagnosis. These two case reports describe rare complications of brucellosis, such as infectious endocarditis and myopericarditis, that were successfully treated after appropriate and prompt diagnosis.

## Authors' contributions

Šačić D. first author, most of the writing, literature review; Petrović O. Collection of data, writing review and correction; Ivanović B. Collection of data, writing review and correction

## Statement of consent

The authors have obtained written informed consent from the patients.

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## Corresponding author

Dalila Šačić, M.D.  
Alekse Nenadovića 2, 11000 Belgrade, Serbia  
Tel: +381656412564  
Email: dalilasrad1@gmail.com

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