CASE REPORT

Brucella endocarditis: an occupational hazard!

Sanjeev Kumar Agarwal,¹ Ali Raza Rajani,¹ Kosar Hussain,²
Mangesh Manoharrao Dande¹

¹Department of Cardiology,
Rashid Hospital, Dubai Health
Authority, Dubai, UAE

²Department of Internal
Medicine, Dubai Health
Authority, Dubai, UAE

Correspondence to
Dr Kosar Hussain,
koshussain@dha.gov.ae

SUMMARY

A young man presented with a 2-month history of fever and malaise. Cardiac auscultation revealed the presence of a diastolic murmur. Subsequently, a cardiac echocardiogram was done, which showed a large vegetation adherent to an anterior mitral leaflet. The blood culture was positive for *Brucella* species. The patient was given antibiotic therapy for brucellosis and referred for surgery. *Brucella* endocarditis is one of the rarest, yet most notorious complications of this infection. This condition requires a high degree of clinical suspicion in order to facilitate prompt diagnosis and treatment.

BACKGROUND

Brucella endocarditis is a rare complication of human brucellosis. However, it is one of the most serious complications that accounts for the main cause of mortality in this disease. It requires a high degree of clinical suspicion based on epidemiological information. This allows the physician to recommend specific diagnostic tests which facilitate early diagnosis.

CASE PRESENTATION

A 34-year-old man residing in Dubai presented with a 2-month history of low-grade fever associated with sweating, arthralgia and malaise. There were no other associated respiratory or cardiac symptoms. There was no history of previous antibiotic use. His medical and surgical history was unremarkable. He was a non-smoker and was employed in the animal-rearing industry. He admitted to occasionally consuming raw milk.

On general examination, he appeared unwell. His blood pressure was 100/60 mm Hg, heart rate was 95 bpm and temperature was 40°C. Cardiac auscultation revealed a loud second heart sound with a rumbling mid-diastolic murmur in the mitral area. There were no apparent peripheral signs of infective endocarditis. The remaining systemic examination was non-contributory.

INVESTIGATIONS

ECG showed sinus rhythm and signs of left atrial dilation (figure 1).

His labs included: white blood cell count $7.7 \times 10^3/\mu\text{L}$, haemoglobin 10.8 g/dl (normocytic and normochromic), platelet $124 \times 10^3/\mu\text{L}$, D-dimer 1.31 mg/L, erythrocyte sedimentation rate <10 mm/1 h, C reactive protein 49 mg/L, procalcitonin 0.33 ng/ml, PT 14.6 s (international normalised ratio 1.21) and troponin 0.03 ng/ml. Other laboratory tests included: alanine transaminase 52 U/L, aspartate aminotransferase 51 U/L, alkaline phosphatase 96 U/L, albumin

3.7 g/dl, creatine 0.8 mg/dl, urea 21 mg/dl, sodium 133 mmol/l and potassium 4.3 mmol/l. HIV and hepatitis serology were negative.

The chest x-ray showed mild hilar congestion; however, the cardiothoracic ratio was within the normal range (figure 2). Transthoracic echocardiography (TTE) revealed moderate mitral stenosis, possibly of rheumatic aetiology. The mitral valve surface area was 1.3 cm^2 with a mean gradient of 13 mm Hg. There was a large dense vegetation attached to the anterior mitral leaflet (figure 3). It also showed a grade I mitral regurgitation (figure 4) and left atrial dilation (5 cm). The left ventricular ejection fraction was 50%. Transoesophageal echocardiography confirmed the findings of TTE. It showed a large vegetation measuring $12 \text{ mm} \times 7 \text{ mm}$ in size and patchy calcification of both mitral leaflets (figure 5).

Three different sets of blood cultures were drawn from different sites, each 30 min apart. No antibiotics were given prior to blood culture collection. Once blood cultures were sent, the patient was started empirically on antibiotics for infective endocarditis. All three cultures grew Gram negative coccobacilli on the third day. Our laboratory identified them as *Brucella* species. However, owing to the inability of specialised kits, it was not possible to identify the species.

Since Duke's diagnostic criteria were met in this patient, a diagnosis of infective endocarditis due to *Brucella* species was thus established.

DIFFERENTIAL DIAGNOSIS

- ▶ Subacute bacterial endocarditis
- ▶ Brucellosis infection
- ▶ Tuberculosis
- ▶ Typhoid fever
- ▶ Connective tissue diseases

TREATMENT

The patient was treated initially with empiric antibiotic regimen for infective endocarditis. However, once the blood culture identified the causative organism as *Brucella*, the antibiotics were changed to include gentamycin, doxycycline, rifampicin and cotrimoxazole. After the initiation of antibiotics, he became afebrile and his general condition improved. The remaining of his hospital stay was uneventful. He was not given any antithrombotic medications. Meanwhile, he was referred to the cardiothoracic surgeons for their opinion. They recommended surgical intervention due to the large size of the vegetation; however, the patient refused surgery as he wanted to go in for further treatment in his native country.

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Figure 1 ECG showing a sinus rhythm and signs of left atrial dilation.

OUTCOME AND FOLLOW-UP

He was discharged after 2 weeks of treatment and advised to continue doxycycline, rifampicin and cotrimoxazole for a total of 3 months. He was subsequently lost to follow-up.

DISCUSSION

Brucellae are Gram negative, aerobic, uncapsulated coccobacilli, which are the commonest cause of zoonotic infections worldwide.¹ They are transmitted to humans by contact with infected secretions, inhalation of contaminated aerosols or ingestion of unpasteurised dairy products.

The Middle East is regarded as an endemic region. In fact, it contains 5 of the top 10 countries with the highest incidence of human brucellosis.¹ This highlights the importance of history-taking for physicians dealing with travel medicine.

Brucellosis is often a challenging diagnosis to make as it presents with non-specific signs and symptoms. This often delays

the correct diagnosis and treatment. The most commonly cited manifestations include fever and arthralgia.^{2–4} The *Brucella* pathogen can affect many organ systems: the gastrointestinal tract and the hepatobiliary, musculoskeletal, nervous, genitourinary, skin and haematological systems.

Although cardiovascular involvement accounts for fewer than 2% of the cases, it accounts for the main cause of mortality in brucellosis.^{3 5 6} *Brucella* endocarditis most commonly involves the aortic valve.^{6–8} The median duration of symptoms in such cases is reported to range from 3 to 5 months.^{6 8} In our case, the aortic valve was free of vegetation.

In cases of suspected infective endocarditis, three sets of blood culture should be drawn half an hour apart.⁹ Various diagnostic tests are currently available for *Brucella* endocarditis. These include blood culture, serology, immunohistology and PCR of surgical material. Blood culture is the gold standard diagnostic test in diagnosis of brucellosis, but unfortunately it has a relatively low diagnostic yield. In a study by Esmailpour *et al*,⁸ only 22.2% of cases with *Brucella* endocarditis had a positive blood culture. Therefore, various serological tests are

Figure 2 Chest x-ray (posteroanterior view).

Figure 3 Transthoracic view of an echocardiogram showing a bulky vegetation attached to the anterior mitral leaflet.

Figure 4 Transthoracic echocardiography colour Doppler images from an apical view.

now gaining diagnostic importance as they have a higher sensitivity.^{10 11}

Brucella endocarditis is a relatively uncommon condition; thus, experience in this subject is limited to scattered case reports and case series in the literature. This condition is conventionally managed by a combined medical and surgical approach.^{7 12–14} Surgical intervention includes valve replacement with adequate debridement. A review of the 308 cases reported in the literature showed that surgical intervention improved the clinical outcome in patients with *Brucella* endocarditis. It decreased the death rate from 32.7% in the medical treatment only group to 6.7% in the combined surgical and medical treatment group ($p < 0.001$).¹⁵ However, there is recently a growing trend to manage selected patients with antibiotics alone.¹⁶ The presence of endocarditis mandates a more prolonged course of antibiotics as dictated by the clinical condition.^{16 17} In general, human brucellosis infection is conventionally treated with a combination of doxycycline plus aminoglycosides or rifampicin. However, the European Society of Cardiology guidelines for infective endocarditis advocate the use of doxycycline, cotrimaxazole plus rifampicin orally for

more than 3 months, with the use of aminoglycoside being optional for the first 2 weeks of therapy. There is no recommendation regarding the routine use of antithrombotic medications during the acute phase of infective endocarditis in the absence of other compelling indications (like left atrial thrombus, atrial fibrillation or venous thromboembolism).¹⁸

Learning points

- ▶ Consider a diagnosis of brucellosis in a febrile patient living in an endemic region.
- ▶ *Brucella* endocarditis should be suspected in cases of endocarditis with negative blood cultures and a risk of exposure (dietary, occupational or travel).
- ▶ Always perform meticulous cardiac examination in patients with brucellosis during the initial assessment, follow-up and in cases that relapse.
- ▶ *Brucella* endocarditis requires a long course of antibiotics and may need surgery in order to prevent relapse and reduce mortality.

Competing interests None.

Patient consent Obtained.

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Figure 5 Transoesophageal echocardiogram showing a large vegetation (green arrow) measuring 12 mm×7 mm with patchy calcification on both anterior mitral leaflets (AML, anterior mitral leaflet; LA, left atrium; LV, left ventricle; PML, posterior mitral leaflet; RV, right ventricle).

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