

A rare cardiac manifestation of Brucellosis (RCD code: VIII)

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Abstract

Brucellosis, a zoonosis caused by Gram-negative coccobacilli *Brucella*, is characterized by a systemic illness with vague symptoms. Though, cardiac involvement with *Brucella* is reported mostly as endocarditis, the occurrence of exclusive *Brucella* constrictive pericarditis without endocardium involvement is extremely rare. We report a case of a young patient from a countryside, who presented with low-grade fever, dyspnea and malaise with signs of right heart failure. He was diagnosed with constrictive pericarditis on 2-D echocardiogram and the diagnosis was confirmed by cardiac magnetic resonance. Pericardiectomy was performed to relieve pericardial constriction. The patient, however, continued to have low-grade fever and lethargy. A workup for chronic infections revealed strongly positive titers for *Brucella*, indicating that the patient was suffering from systemic brucellosis. The patient was treated with combination of antibiotics for six weeks and responded well to the treatment. The case highlights the fact that brucellosis has a wide array of clinical presentations and may present as an isolated exclusive constrictive pericarditis. The diagnosis of brucellosis should always be considered in patients presenting with chronic fever and a history of animal contact. JRCD 2017; 3 (4): 129–132

Key words: brucellosis, constrictive pericarditis, cardiac magnetic resonance imaging

Background

Brucellosis should always be considered as a differential diagnosis in patients presenting with chronic fever, with a history of contact with animals or animal products. Though endocarditis is a recognized complication of brucellosis, constrictive pericarditis is rarely associated with *Brucella* infections. The diagnosis of pericardial constriction can be done by visualization of characteristic features on 2D echocardiogram or cardiac magnetic resonance imaging (CMR) by offering a 3D image of the heart can confirm the echo findings. Treatment of pericardial involvement in such cases is centered upon the surgical excision of pericardium along with long duration of antibiotic therapy.

Case presentation

A 36 year-old married gentleman, school teacher from a countryside presented with symptoms of dyspnea, generalized weakness and low-grade fever for the past two years. The symptoms of dys-

pnea had worsened over the last six months with rapid weight loss of 10 kg over this period.

There was no relevant family history of heart disease. He denied any instance of unprotected sexual contact or previous exposure to individuals with tuberculosis. There was also no history of substance abuse. However, he had a history of drinking goat's and cow's milk which he had raised.

The patient had received treatment at a rural health centre with analgesics and empiric oral antibiotics, and then was referred for further investigation due to persistent symptoms.

On clinical examination the patient had a low-grade fever, bilateral pedal oedema, jugular venous distention and ascites. He was hemodynamically stable. Based on the history and examination a diagnosis of right heart failure was formulated. The patient was referred for an electrocardiogram (ECG) and transthoracic echocardiography (TTE).

The ECG showed normal sinus rhythm with infrequent atrial premature complexes and T-wave inversions (Figure 1). TTE showed a thick and shiny pericardium with normal left ventricular systolic function. Prominent septal bounce and significant respi-

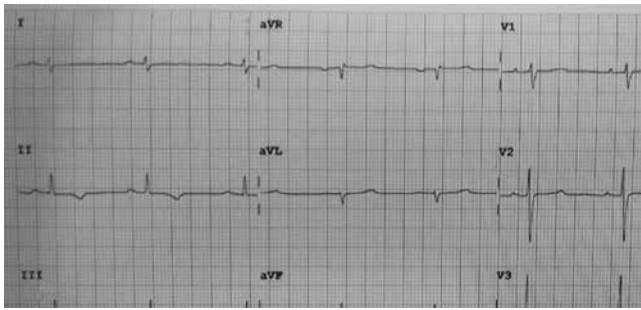


Figure 1. Baseline ECG showing normal sinus rhythm with infrequent atrial premature complexes and T-wave inversion

ratory variation in mitral inflow velocities were noted (Figure 2a). The inferior vena cava was dilated with loss of inspiratory collapse (Figure 2b). The mitral inflow showed large E wave with increased E to A ratio and an E/E' of 5 suggestive of normal myocardial relaxation but pericardial disease. On the basis of the echo findings, a diagnosis of constrictive pericarditis was formulated.

To confirm the echo findings, CMR imaging was performed. CMR showed 4–6 mm thickened pericardium with no evidence of pericardial effusion. Septal bounce and ventricular septal shift towards left ventricle during inspiration, suggestive of ventricular interdependence was noted (Videos 1 and 2). Delayed contrast enhanced imaging with gadolinium showed no area of myocardial hyperenhancement suggestive of myocardial fibrosis. The CMR images confirmed the diagnosis of constrictive pericarditis (Figure 3).

In the context of chronic low-grade fever with malaise and imaging evidence of constrictive pericarditis, the initial differential diagnosis was tuberculous pericarditis secondary to systemic tuberculosis, a disease endemic in subcontinent, chronic hepatitis, malignancy, brucellosis, connective tissue disorders and uremic pericarditis.

Review of literature

Brucella, a Gram-negative bacillus is the causative organism of brucellosis, a zoonotic systemic infection endemic to the Mediter-

ranean region [1]. The microorganism is transmitted to humans by infected animals primarily by secretions and animal products, especially unpasteurized milk [2]. Cardiac involvement in brucellosis can manifest as endocarditis, myocarditis or pericarditis. Due to the high fatality associated with *Brucella* endocarditis, surgical removal of the site of infection followed by aggressive antibiotics is indicated [3].

Rarely, *Brucella* may exclusively invade the pericardium causing an inflamed, thickened pericardium with pericardial effusions [4,5,6,7,8,9]. Ugartemendi'a et al. reported two cases of *Brucella* pericarditis with culture positive pericardial effusions [4]. Similarly Gomez-Huelgas et al. [5] and Rivera et al. [6] reported cases of *Brucella* pericarditis with pericardial effusions. Gatselis et al. [7] reported a blood culture positive *Brucella* pericarditis associated with pericardial effusion. Karagiannis et al. [8] reported a case of serology positive brucellosis presenting with cardiac tamponade requiring pericardiocentesis. Kaya et al. [9] in their review of literature on *Brucella* pericarditis presented four cases of *Brucella* pericarditis along with pericardial effusions.

However, a review of published English literature does not identify any case report of exclusive constrictive pericarditis associated with brucellosis.

The etiology of cardiac injury in brucellosis is unclear. It may be attributed to the direct effect of microorganism, as suggested by positive pericardial fluid cultures or by immune complexes deposition which may be seen in cardiac biopsies [7].

Chest pain, dyspnea and fever are the common symptoms in patients presenting with *Brucella* pericarditis. Pericardial friction rub may be auscultated. In our case, the patient had fever and dyspnea, while pericardial rub was absent. Variable ECG findings are seen in *Brucella* pericarditis patients [5,7]. Our patient had T wave inversions on ECG and atrial ectopic beats.

In cases of brucellosis, the diagnosis of *Brucella* infection is reached either by positive blood cultures or on the basis of serology. Blood cultures are the gold standard for laboratory diagnosis. However, positive blood cultures occur only in 10 – 70% of suspected infections. Relapsing or chronic infections are characterized by low blood culture yields [10]. In addition to bacterial cultures, serological tests such as the *Brucella* microagglutination test (BMAT),

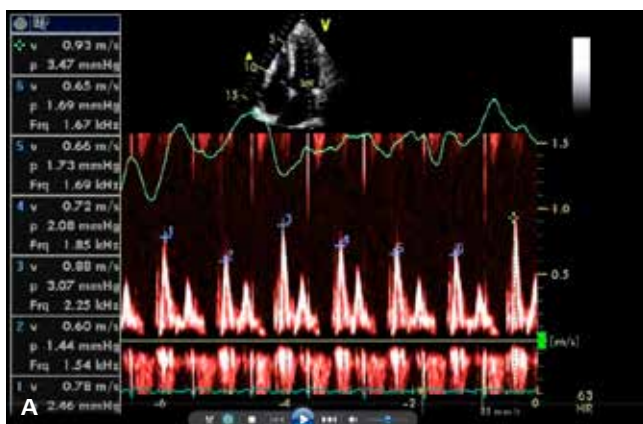


Figure 2. A. Transthoracic echo showing significant respiratory variation in mitral inflow velocities. B. Dilated inferior vena cava with loss of inspiratory collapse

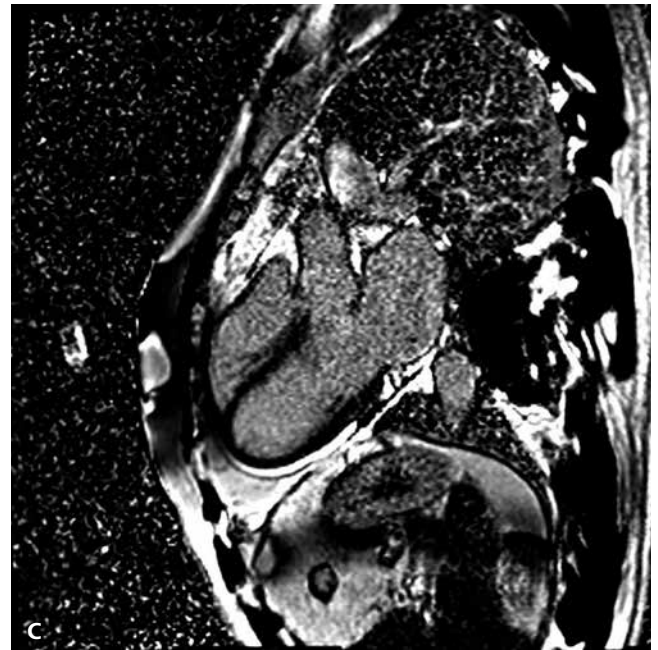
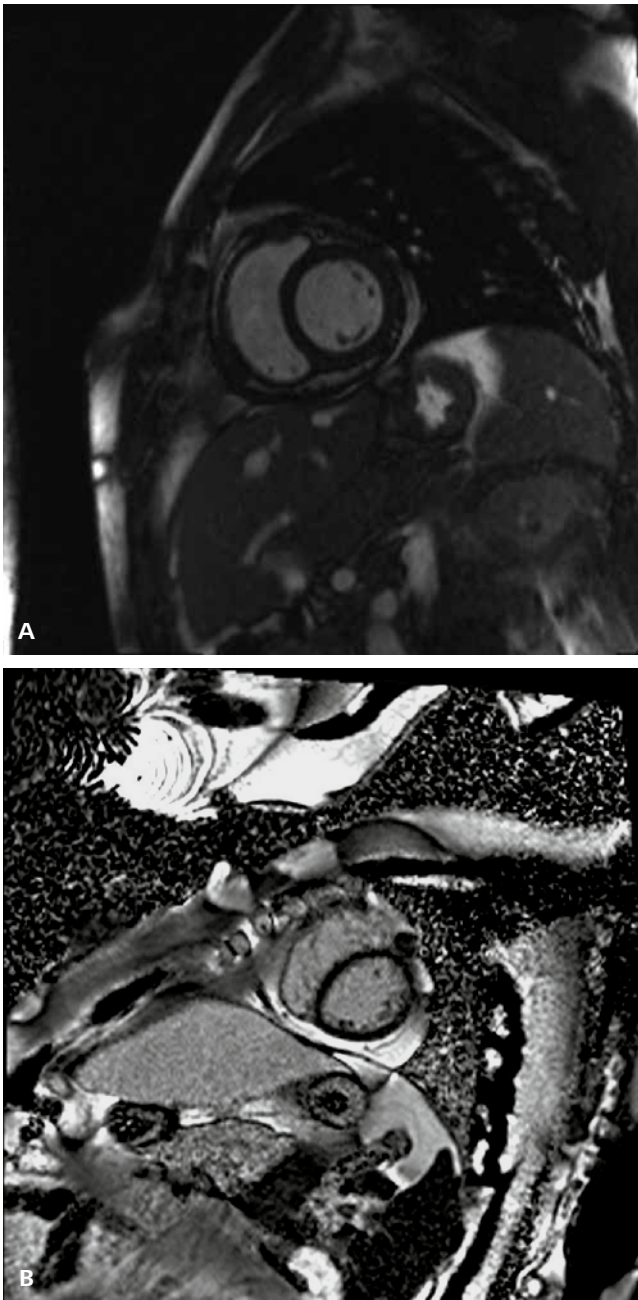


Figure 3. CMR imaging showing: A. 4-6mm thickened pericardium with no evidence of pericardial effusion. B, C. Delayed contrast enhanced imaging with gadolinium showing no area of myocardial hyper-enhancement to suggest myocardial fibrosis

a modified version of the serum (tube) agglutination test (SAT), to detect antibodies to *Brucella* species – *B. abortus*, *B. melitensis* or *B. suis* are also employed [2]. These serological tests are more practical but less specific than culture techniques and are affected by the presence of other infectious diseases in which case these test may show false-positive results [10]. The use of serological tests has been validated and these tests find wide spread application in the subcontinent because of their widespread availability and low cost [2]. In our case the diagnosis was suspected on the basis of history and positive *Brucella* serology. The blood cultures were negative likely because of a chronic course of the illness in our patient and prior use of antibiotics.

Echocardiography is the imaging modality of choice for evaluation of patients with suspected heart failure. In constrictive pericar-

ditis, certain 2D and Doppler parameters are classically seen. These include signs of ventricular interdependence i.e. septal bounce, an inspiratory septal shift, an increased E/A ratio, an inspiratory decrease in the early diastolic filling across the mitral valve, with the opposite occurring during expiration [11]. All these features were seen on echo of our patient.

These finding can be reproduced and confirmed with a cardiac CMR. In our case the CMR showed characteristic features suggestive of ventricular interdependence secondary to constrictive pericarditis, i.e thickening of the pericardium with septal bounce and ventricular septal shift towards left ventricle during inspiration.

All causes of diastolic dysfunction are included in the differential diagnosis of patients showing restrictive pattern of diastolic filling on 2D echocardiography. These include patients with advanced age, diabetes, coronary artery disease, restrictive cardiomyopathy, constrictive pericarditis and left ventricular hypertrophy. The clinical presentation, history, examination and echocardiography help in delineating the specific etiology.

It is essential in all cases of patients with restrictive pattern of diastolic filling to differentiate between restrictive cardiomyopathy and constrictive pericarditis, because restrictive cardiomyopathy has no specific therapy, whereas constrictive pericarditis is potentially curable with surgical pericardiectomy. Impaired myocardial relaxation in restrictive cardiomyopathy helps in differentiating it from constrictive pericarditis.

The treatment option in case of constrictive pericarditis of any origin is surgical pericardiectomy for relief of the pressure on the cardiac chambers [12]. The antibiotic regimen in case of *Brucella* with organ involvement is a combination of tetracycline with rifampicin for an extended period of six weeks [2]. Our patient was treated with the same regimen and responded well to treatment.

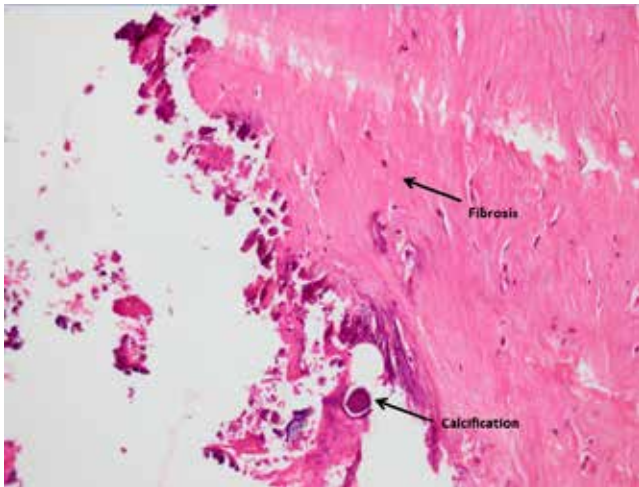


Figure 4. Hematoxylin and eosin staining of pericardium biopsy revealing multiple fragments of extensively fibrotic and calcified tissue

Patient management and follow up

The patient was referred to cardiothoracic surgery department. Pericardiectomy was performed without any complications. The biopsy of pericardium revealed multiple fragments of extensively fibrotic and calcified tissue (Figure 4). Tissue culture and nucleic acid amplification test for tuberculosis (GeneXpert) were negative. The patient did not report substantial dyspnea after the surgery, yet he continued to have low-grade fever and general weakness.

The patient was referred to an infectious diseases specialist for workup. A panel of investigations for chronic infection were ordered including erythrocyte sedimentation rate (ESR), C-reactive protein, interferon gamma response to tuberculosis antigen (IGRA), nucleic acid amplification test for tuberculosis (GeneXpert), hepatitis serology, Brucella serology and ACE levels.

Serum agglutination test for both *Brucella melitensis* and *Brucella abortus* were reported to be strongly positive with titres of 1:160. ESR was raised, while the rest of the tests were all negative.

On the basis of positive serology, treatment for brucellosis was initiated with doxycycline 100mg twice daily and rifampicin 600mg once a day for 6 weeks.

After six weeks of antibiotic therapy the patient was seen in the clinic. He was afebrile and his symptoms had improved. He did not report any symptoms on subsequent quarterly follow-up. His TEE after one year follow-up was normal.

Conclusion

In conclusion, *Brucella constrictive pericarditis* is an extremely rare clinical entity. The diagnosis can be established on the basis of symptoms, clinical examination and confirmed by cardiac imaging and positive serology for *Brucella*. In patients diagnosed with *Brucella constrictive pericarditis*, pericardiectomy along with antibiotic treatment for six weeks is required. The choice of antibiotics and duration of therapy are similar to the treatment

of brucellosis without pericardial involvement. Although rare, *Brucella constrictive pericarditis* should be considered in patients with chronic fever, a history of contact with animals or animal products presenting with signs and symptoms of right heart failure.

References

1. Madkour MM. Madkour's brucellosis. Springer Science & Business Media 2012.
2. Corbel MJ. Brucellosis in humans and animals. World Health Organization 2006.
3. Sasmazel A, Baysal A, Fedakar A, et al. Treatment of *Brucella endocarditis*: 15 years of clinical and surgical experience. *Ann Thorac Surg* 2010; 89(5):1432-1436.
4. Ugartemendia MC, Curós-Abadal A, Pujol-Rakosnik M, et al. *Brucella melitensis pericarditis*. *Am Heart J* 1985;109 (5):1108.
5. Gomez-Huelgas R, Demora M, Porras JJ, et al. *Brucella* and acute pericarditis: fortuitous or causal association? *J Infect Dis* 1986;154: 544.
6. Rivera JM, Garcia-Bragado F, Gomez FA, et al. Brucellar pericarditis. *Infection* 1988; 16(4): 254.
7. Gatselis NK, Makaritsis KP, Gabranis I, et al. Unusual cardiovascular complications of brucellosis presenting in two men: two case reports and a review of the literature. *J Med Case Rep* 201; 5(1): 22.
8. Karagiannis S, Mavrogiannaki A, Chrissos D, et al. Cardiac tamponade in *Brucella* infection. *Hell J Cardiol* 2003; 44: 222-225.
9. Kaya S, Eskazan AE, Elaldi N. Brucellar pericarditis: a report of four cases and review of the literature. *Int J Infect Dis* 2013;17(6): e428-432.
10. Hashemi SH, Alikhani MY, Naseri Z, et al. Diagnosis of human brucellosis by blood culture (BACTEC) and PCR method via whole blood and serum. *Jundishapur J Microbiol* 2013; 6(3): 248-251.
11. Napolitano G, Pressacco J, Paquet E. Imaging features of constrictive pericarditis: beyond pericardial thickening. *Can Assoc Radiol J* 2009; 60(1): 40-46.
12. Johnston DR. Surgical Management of Pericardial Diseases. *Prog Cardiovasc Dis* 2017; 59(4): 407-416.