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BRUCELLA ENDOCARDITIS: A CASE STUDY

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Abstract

Endocarditis is a rare and serious complication of brucellosis and is the main cause of death in this pathology. Diagnosis requires a high level of attention, and is based on the association of epidemiological, clinical and serological elements. Echocardiography plays a crucial role in early diagnosis, as well as in identifying a predisposition to heart disease and local complications typical of this pathology. This case study follows a case of *Brucella* endocarditis involving the aortic valve, in a 39-year-old male, diagnosed in October 2010. Despite being given complete pharmaceutical treatment, in this instance emergency heart surgery was necessary, due to an inability to control the infection and subsequent changes in the patient's condition, which were leading to congestive heart failure. Aggressive treatment, with surgery performed during a period of active infection, produced good results in the eradication of infection, and in preventing fatal complications. The patient is now fully recovered, and was given triple therapy for brucellosis according to existing recommendations.

Key words: endocarditis, brucellosis, echocardiography

Introduction

Brucellosis is still a frequently occurring major infectious disease, particularly in the Mediterranean, the Middle East, and Central and South America.(1, 2) Although typical brucellosis is easily diagnosed in endemic areas, in other regions where the incidence of brucella is very low, definitive diagnosis of the infection is quite difficult. A patient presenting with a heart murmur, who has a history of exposure to infected animals or animal products, and ingesting unpasteurised milk, should be considered to have cardiac manifestations of brucellosis until it is proven otherwise. In *Brucella* infective endocarditis, the most frequently isolated species are *Brucella melitensis* and *B abortus*. Despite having an incidence of less than 2%, these two species are the aetiological factor in most mortal infections.(3) *B suis* and *B canis* are rare causative species.(4) Endocarditis and myocarditis are rare, but constitute the most serious complications of brucellosis.(5) *Brucella* appears to be a slowly destructive organism, with a marked tendency towards: tissue ulceration; the development of

large vegetations carrying significant risk of embolisation; and difficulty to eradicate with medical therapy alone. A case of *Brucella* endocarditis (BE), as well as a brief review, is presented below.

Case presentation

A previously healthy 39-year-old male was hospitalised for the first time at the Clinic for Infectious Diseases, University Clinical Center Tuzla, on June 10, 2010. His symptoms included fever, sweating, weakness, loss of appetite and loss of body mass. These problems began one month before he was admitted, before which he had been healthy. From local epidemiological history we discovered that he was farmer, and was involved in cattle breeding. One month before his health problems occurred, he had been in contact with diseased sheep. During the physical examination the patient was conscious, oriented, communicative, without fever, eupnoic, hydrated, and mobile. He had normal skin colour and turgor with no hives present, whitish sclera, smooth pharynx, and carious teeth. His lymph nodes in accessible regions were not palpable, and his lungs had presented normal findings. A cardiac examination revealed a rhythmic heart action, clear tones, and an audible systolic murmur at the ictus and Erb. His vital signs were RR 110/70, PR 90/min. His abdomen was soft, without pain, and the liver and spleen were not palpable. His meningeal signs were negative.

Initial laboratory work revealed: WTC 11,400/ul; RBC 5.070/ul; Hb 140 g/l; HCT 43.3%; platelets 319,000 u/l; C-reactive protein 69.3 mg/l; erythrocyte sedimentation rate 40/60 mm/h; serum creatinine 58 μ mol/l; alanin-aminotranspherase ALT 17 u/l; aspartat aminotranspherase 23 u/l; total serum protein 76 g/l; serum albumins 34 g/l; serum globulins 42 g/l; TSH 1.56 mIU/l; T3 1.66 pmol/l; T4 114.8 pmol/l; and urine normal.

Blood cultures were positive for *Brucella* species. The indirect Rose Bengal micro-agglutination test for *Brucella* was positive. The ELISA test for *Brucella* was: IgM positive (67 U/ml); IgG positive (272 U/ml); and IgA positive (230 U/ml).

Echocardiographic findings prepared in June show attributed hyperkineticism with an intergrown commissure between the right and left lobes of the velum, and a practically bivelar aortic valve with subsequent mild AR. No visible vegetation. The other valve was competent, and the Pericardium normal. The first conclusion was a bivelar aortic valve. The ECG shows sinus rhythm, with a PQ interval of 0.20 sec., and an intermediate node, with no visible ischemia.

The patient was discharged from the hospital on June 22, 2010, with a diagnosis of brucellosis of the bivelar aortic valve. Medications administered to him during his hospitalisation were: gentamicin; doxycycline; vitamin B complex; atenolol; and ASA. It was recommended that he reduce physical activity until his next check-up, and in order to prevent bacterial endocarditis, he was instructed to repair his dentures, and prescribed: Doxycycline 2x100 mg cps for 4 weeks; vitamin B complex

tablets 3x1; atenolol tablets 25 mg; and ASA tablets 100 1x1. It was recommended that he was checked by the doctor for infectious diseases after 14 days, with laboratory tests for CBC, ESR, and CRP, and that he had a controlled echocardiographic examination within 6-12 months.

When presenting for his follow-up examination on October 18, 2010, the patient reported no particular symptoms.

Laboratory work conducted at that time revealed: WTC 10,910/u/l; RBC 4,480/u/l; Hb 127 g/l; HCT 37.0%; platelets 337,000 u/l; C-reactive protein 25.1 mg/l; erythrocyte sedimentation rate 48/63 mm/h; alanin-aminotransferase ALT 9 u/l; aspartat aminotransferase 19 u/l; total serum protein 78 g/l; serum albumins 38 g/l; serum globulins 40 g/l; serum iron 9.0 umol/l; RF 132; fibrinogen 4.45 g/l; and urine normal.

The patient was referred for a cardiac ultrasound (echocardiogram) on October 22, 2010, at the Clinic for Internal Diseases, University Clinical Center Tuzla. Echocardiographic findings on the doppler echocardiography show dilatation of the left heart cavities (LA 4.53 cm, LVDD 6.53 cm) (Fig.1), the initial spherical shape of the left ventricle, estimated EF 50%, and no segmental failure.

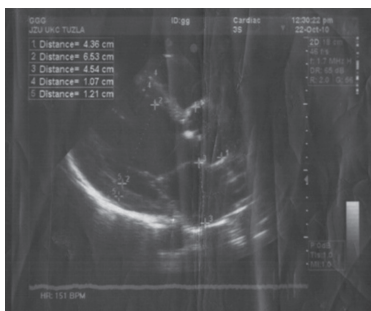


Figure 1. Dilatation of the left heart cavities and vegetations on the aortic valve in the parasternal long axis view

The aortic valve was three-foil (Fig. 2), with vegetation present (Fig. 3a, 3b).

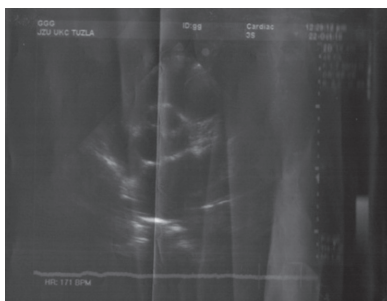


Figure 2. Three-foil aortic valve in the parasternal short axis view

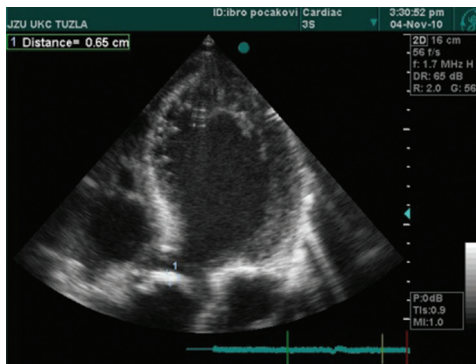


Figure 3a. Vegetations on the aortic valve in the apical four-chamber view

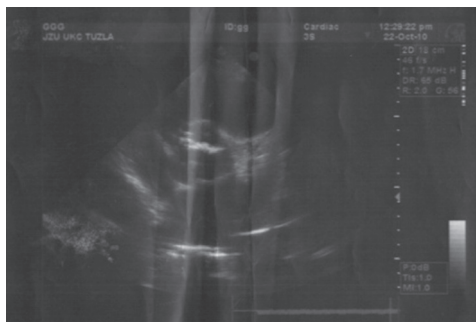


Figure 3b. Vegetations on the aortic valve in the parasternal short axis view

The registered transaortic regurgitation jet had an average velocity flow of about 200 m/sec, and accelerated systolic flow with V max 1.85 m/sec, with dilated root and ascending aorta (root area measured 4.41 cm, ascending aorta measured 3.48 cm) (Fig. 4, 5, 6).

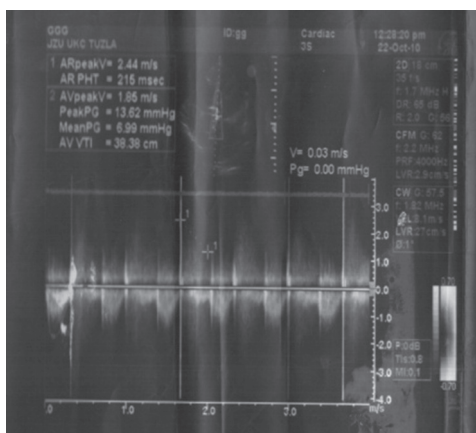


Figure 4. Transaortic regurgitation jet and accelerated systolic flow

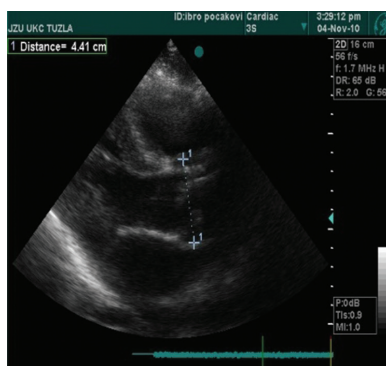


Figure 5. Dilated root of aorta in the parasternal long axis view



Figure 6. Dilated ascending aorta in the suprasternal long axis view.

The conclusion of these findings was a diagnosis of aortic valve endocarditis, with the development of severe aortic regurgitation. This indicated that surgery (the Benthal procedure) would be required. The patient was examined on November 4, 2010 in the Clinic for Cardiovascular Diseases, University Clinical Center Tuzla. From the results of subsequent transoesophageal echocardiography, a diagnosis of Brucella endocarditis with the involvement of a trivelar aortic valve and severe aortic regurgitation was reached. Surgery was recommended, with the previous preoperative treatment. The patient underwent surgery on December 17, 2010 in the Clinic for Cardiovascular Diseases, University Clinical Center Tuzla. He is now fully recovered, and was administered triple therapy for brucellosis according to existing recommendations.

Discussion

Endocarditis is an uncommon but devastating complication of brucellosis. The rate of BE has been accepted as lower than other causes of infective endocarditis (3), but its incidence was reported to be 10.9% by Al-Kasab and colleagues.(6) A review of 66 cases of native valve infective endocarditis at Istanbul's Kosuyolu Heart and Research Hospital revealed a BE incidence of 9.1%. BE is a destructive process of

the native valve that commonly leads to heart failure occurring within 3 to 11 months after the onset of symptoms.(4) The aortic valve is the most commonly affected cardiac valve, reported in 75% of cases, and a particularly feared complication is the formation of aortic root abscesses.(7,8) The involvement rate of prosthetic valves was found to be 8%.(7) Myocarditis is another rare complication of adult brucellosis, which is initially associated with a prolonged PR interval and T segment changes.(5) Gross abscesses of myocardium or their consequent aneurysm are apparently more frequent in *Brucella* endocarditis than in endocarditis caused by any other bacteria. (8) Peery and Belter found endocarditis in 80% and myocardial abscess in 43% of cases in a study including 44 necropsies on cases of fatal brucellosis.(9) The diagnosis of brucellosis is based on epidemiological evidence and positive culture or serology. The manifestations of the disease, especially in its chronic stage, make diagnosis difficult, and most conventional diagnostic methods have their limitations. Blood culture is the only specific test; its sensitivity ranges from 17% to 85% depending on culture conditions, antibiotic therapy, and the length of the interval between the onset of symptoms and diagnosis. Thus, diagnosis from the culture of *Brucella* species from body specimens is often unsuccessful.(2,4,10) Laboratory diagnosis is usually established by a positive blood culture and/or fourfold increase in *Brucella* titres. It can also be identified by a single serum agglutination test titre $<1:320$, or by an ELISA titre of IgM $<1:800$, either alone or with IgG $<1:1600$ and IgA $<1:200$.(5) It can often be difficult to differentiate acute brucellosis from acute rheumatic fever, especially if cardiac involvement is prominent. Both diseases may present with fever, arthralgia, splenomegaly, and a high erythrocyte sedimentation rate, but acute brucellosis only occasionally shows leucocytosis.(7) Echocardiography is usually helpful in detecting valvular vegetations, and may increase the ability to establish a diagnosis of infective endocarditis. The accepted treatment for BE is a combination of medical and surgical interventions.(6,8,11,12) Although conservative antibiotic treatment alone is considered ineffective, and has not been recommended by most authors for this reason, a complete cure has been reported in a few cases of BE (13,14) using this method. Patients who may be suitable for this kind of treatment are those with congestive heart failure, relatively mild extravalvular involvement and a short symptomatic period before antibiotic therapy begins. In most other cases, surgery should be considered for patients with endocarditis and/or prosthetic heart valves, or abscesses that are antibiotic resistant.(15) The treatment of BE still raises the problem of selecting the correct antibiotic, and the duration of its use. Brucellosis treatments must effectively control the acute illness, and prevent complications and relapse. The choice of regimen and duration of antimicrobial therapy should be based on the presence of focal disease and underlying conditions that contraindicate certain specific antibiotics.(15) Indeed, requirements may be complex because one must select antibiotics that are active in vitro and that diffuse readily into tissues and cells without developing bacterial resistance. The microorganism's intracellular localisation makes it refractory to the activity of various antibiotics.(1) Combinations of doxycycline and rifampicin or doxycycline and streptomycin have

been used with variable success rates.(15-17) Tetracycline and gentamicin as well as intravenous cotrimoxazole have been found to be effective.(1) The timing of surgical intervention and the duration of subsequent medical therapy remains controversial in the treatment of BE. There is no indication in published reports on how long antibiotic treatment should continue after surgery, but 6 months seems to be adequate if *Brucella* titres are decreasing. Optimal treatment of prosthetic valve endocarditis due to BE should achieve the sterilisation of infected cardiac tissue, and extensive surgical debridement without delay to control acute illness and prevent complications and relapse.

Conclusion

The diagnosis of *Brucella* endocarditis requires a high amount of attention, as the symptoms of brucellosis may mimic many other diseases. In areas where this disease is endemic, incorporating *Brucella* agglutination titres in the work of patients presenting with prolonged fever increases the chance of diagnosis. When endocarditis complicates *Brucella*, mortality is high. Therefore, Doppler echocardiography should be performed in patients early in the course of the disease, to identify vegetations. Early treatment with the appropriate antibiotics results in a more favourable clinical response, and reduces the need for emergency surgical intervention. For an optimal outcome and prognosis, surgery should be performed after adequate sterilisation has been achieved. The recommended antibiotic treatment consists of doxycycline, rifampin and aminoglycoside for 3-6 months. Even if symptoms improve with antibiotics, surgery is still necessary due to the embolic potential of residual vegetations, or valvular obstruction. The timing of surgery is critical. In haemodynamically stable patients, administration of antibiotics for 6 weeks preoperatively is indicated in order to achieve sterilisation. However, the presence of vegetations and congestive heart failure are indications for early surgical intervention.

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