Brucella endocarditis and its rare complications

Brucella endokarditi ve nadir komplikasyonları

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Background: Brucella endocarditis, which is a rare condition, is the most common cause of death in human brucellosis, leading to severe cardiac complications.

Methods: Ten patients were referred to our clinic with the diagnosis of Brucella endocarditis. The patients were given a medical treatment with triple antibiotherapy including doxycycline, rifampin and ceftriaxone. In the preoperative period, one of the patients had a sign of splenic infarction due to septic embolization. Echocardiographic evaluation revealed the development stages of the mitral valve injury due to Brucella endocarditis in another patient. All patients underwent open heart surgery immediately after reducing fever and relieving other symptoms.

Results: Six patients underwent aortic valve replacement (AVR), whereas three of them underwent both aortic and mitral valve replacement. In addition, AVR in combination with mitral ring annuloplasty were performed on one of the patients. Perforation of the aortic cusps was found in four patients. Perforation located in the commissure between the right and left coronary cusps was detected in one patient. Morbidity and mortality didn't developed in our patients. All patients were discharged with double antibiotherapy for a mean follow-up of four months (range, 2 to 6 months). None of the patients required re-hospitalization or re-surgery during the long-term follow-up period.

Conclusion: Our results show that surgical therapy must be combined with adequate preoperative antibiotherapy in cases with severe valve injury. Maintenance therapy with antibiotherapy should be optimized postoperatively on the basis of scheduled visits for successful definitive therapy and long-term quality of life.

Key words: Brucella; infective endocarditis; splenic infarction; valve rupture.

Amaç: Nadir rastlanan Brusella endokarditi, insanlarda brusellaya bağlı görülen ölümlerin başlıca nedeni olup, ciddi kardiyak komplikasyonlara yol açabilir.

Çalışma planı: On hasta Brusella endokarditi tanısıyla kliniğimize sevk edildi. Hastalar doksisiklin, rifampin ve seftriaksondan oluşan üçlü antibiyoterapi ile medikal olarak tedavi edildi. Ameliyat öncesi bir hastada dalak embolizasyonuna bağlı splenik infarktüs bulgusu tespit edildi. Başka bir hastada ise ekokadiyografik değerlendirmede Brusella endokarditinin mitral kapakta oluşturduğu hasarın gelişim evreleri gözlemlendi. Tüm hastalar ateşleri kontrol altına alınıp, diğer semptomları da baskılandıktan hemen sonra açık kalp ameliyatına alındı.

Bulgular: Altı hastaya sadece aort kapak replasmanı (AKR) uygulanırken, diğer üç hastaya da aortik ve mitral kapak replasmanı uygulandı. Buna ek olarak, bir olguya da mitral ring anüloplastisi ile AKR kombinasyonu gerçekleştirildi. Dört hastada aortik yaprakçıklarda perforasyon bulundu. Bir diğer hastada ise, sağ ve sol koroner yaprakçıklar arasındaki komissürde perforasyon saptandı. Hiçbir hastada mortalite ve morbidite gelişmedi. Tüm hastalar ortalama dört ay ikili antibiyoterapiyi sürdürmek koşuluyla taburcu edildi (dağılım, 2-6 ay). Geç dönemdeki izlemleri süresince hiçbir hastaya tekrar ameliyat ya da hospitalizasyon gerekmedi.

Sonuç: Çalışma bulgularımız, kapak harabiyetinin ağır seyrettiği olgularda cerrahi tedavinin, ameliyat öncesi antibiyoterapi kombinasyonu ile birlikte planlanması gerektiğini göstermektedir. Uzun dönem yaşam kalitesi ve başarılı kesin tedavi için, klinik izlem ile ameliyat sonrası antibiyoterapinin zamanlaması optimalize edilmelidir.

Anahtar sözcükler: Brusella; infektif endokardit; dalak infarktüsü; kapakçık yırtılması.

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Brucellosis shows various clinical signs and can affect different organs. Although rare, endocarditis can be fatal. Endocarditis due to the Brucella species can be seen more in the regions where rheumatic heart disease is widespread.[1] Brucellosis continues to be reported from Mediterranean and Middle Eastern countries.[1,2] Ten to 15% of patients have complicated brucellosis.[2] Although endocarditis is seen in less than 2% of the cases, it is responsible for half of the deaths due to brucellosis.[3] Brucella endocarditis was first reported in 1906, but a surgical approach as a treatment modality was only introduced in 1964.[2] Immediate surgery after medical treatment is very important because a delay may lead to complications that are difficult to repair.[1] In this study, we present 10 patients with Brucella endocarditis who were treated sequentially with a combination of medical and surgical therapy between September 2001 and September 2007.

PATIENTS AND METHODS

Ten patients (9 males, 1 female; mean age 41.2 years; range 29 to 60 years) were hospitalized at different times with symptoms of fever, weakness, dyspnea, fatigue, weight loss, and back pain. All of the patients had a history of intermittent fever reaching 40 ºC. Our patients inhabited rural areas and were working as farmers and livestock producers. All patients had been given different types of antibiotic therapies in various primary heathcare units. However, they were referred to our institution as their general status worsened. All of the patients were carefully examined, and routine laboratory studies were done on admission. Consecutive blood cultures were taken from the patients. Brucella standard tube agglutination tests were performed on the patients, and the results were 1/320 or higher. The data of our patients who were diagnosed with Brucella endocarditis after echocardiographic and laboratory examination is given in Table 1.

An echocardiographic evaluation of the second patient revealed mobile mass lesions compatible with vegetations on the left and noncoronary leaflets of the aortic valve and severe aortic and mitral regurgitations. Abdominal computed tomography (CT) also revealed a hypodense area as splenic infarction due to septic embolism (Figure 1).

Our ninth patient with severe rheumatic aortic valve stenosis, moderate aortic insufficiency, and mild mitral insufficiency was admitted to an institute in August 2005 but did not accept the recommended aortic valve replacement (AVR) operation (Figure 2). His job was animal husbandry, and he had been hospitalized for 15 days due to Brucellosis diagnosed in November 2005. Transthoracic echocardiography (TTE) performed in January 2006 showed that his mild mitral insufficiency had progressed and a 19.4x21.5 mm vegetation had developed in the anterior mitral leaflet. Also, the peak pressure gradient through the mitral valve secondary to mitral insufficiency had increased to 18.4 mmHg from 11.8 mmHg (Figure 3). Transesophageal echocardiography (TEE) showed a vegetation in the anterior mitral leaflet and increased mitral insufficiency (Figure 4).

Our 10th patient's job was also animal husbandry. The TTE performed on admission to our institution showed that his severe aortic insufficiency had progressed, and a 23x17 mm giant vegetation had developed on the right and left coronary leaflets. An image corresponding to right coronary leaflet perforation was suspected (Figure 5).

The Departments of Infectious Diseases, Cardiology and Cardiovascular Surgery observed all patients. All patients had a triple-antibiotic therapy regimen

Table 1. Data of our patients

Patient	Age (year)	Echocardiography	Vegetation	Brucella agglutination titration	Preoperative antibiotherapy (weeks)	Operation	Postoperative antibiotherapy (months)
1	44	AS,AR	+	>1/640	6	AVR	6
2	36	AR,MR	+	>1/320	4	AVR+MVR	4
3	29	AR	+	>1/640	5	AVR	3
4	33	AS,AR,MR	+	>1/640	5	AVR+MVR	2
5	41	AR	+	>1/640	6	AVR	3
6	31	AR,MR	+	>1/320	6	AVR+MRA	4
7	51	AR,AS	+	>1/640	5	AVR	3
8	60	AR,AS	+	>1/640	5	AVR	5
9	43	AS,AR,MR	+	>1/320	6	AVR+MVR	6
10	44	AR	+	>1/640	4	AVR	4

AS: Aortic stenosis; AR: Aortic regurgitation; MR: Mitral regurgitation; AVR: Aortic valve replacement; MVR: Mitral valve replacement; MRA: Mitral ring annuloplasty.

Figure 1. Septic embolic splenic infarction as viewed in the abdominal computed tomography of our second patient.

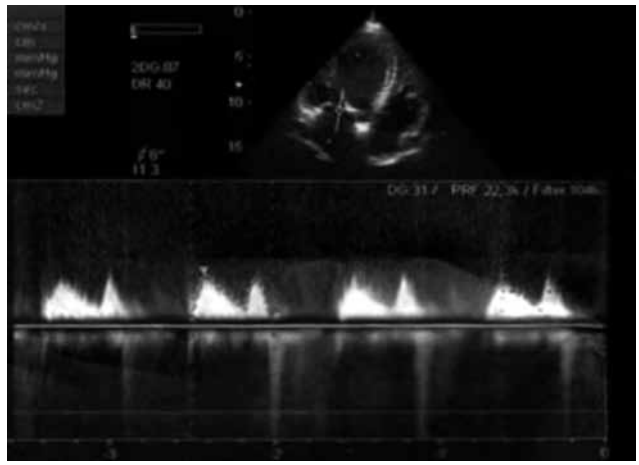

Figure 2. Image of mild mitral insufficiency in our ninth patient in August 2005.

(doxycycline 200 mg/d, rifampicin 600 mg/d, and ceftriaxone 2 g/d). Patients were taken for cardiac surgery without delay as the fever and other symptoms disappeared. The Department of Cardiology and Cardiovascular Surgery routinely observed the patients during their hospitalization in the Infectious Diseases Clinic for their medical treatment. Their echocardiographies were repeated weekly, and they underwent surgery after the antibiotic therapy.

Surgical technique

The patients were operated on under general anesthesia. All patients were approached via median sternotomy, and all surgeries were performed on cardiopulmonary bypass using ascending aortic and bicaval cannulation with caval snuggers and minimal manipulation. For myocardial protection, cardiac arrest was achieved with moderate hypothermia of 28 ºC and incompressive retrograde isothermic blood cardioplegia. After cross-clamping the aorta, tissue loss was detected in most of the affected leaflets. Vegetations were seen in all of the patients, and perforation of the aortic cusps was seen in four (Figure 6).

In our ninth patient, there was a high degree of calcification at the mitral valve, including all the anterolateral commissure which infiltrated the endocardium and myocardium. The subvalvular apparatus was normal. There were widespread, calcific, and vegetative images beginning from the anterolateral commissure and extending medially to both leaflets (Figure 7).

Following aortotomy in our 10th patient, exploration revealed that the left coronary leaflet had a highly

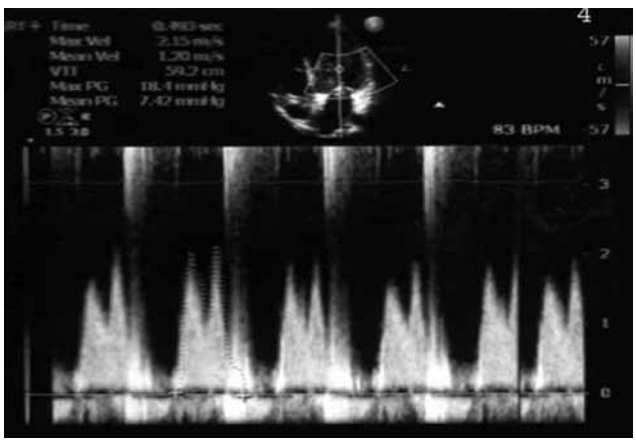

Figure 3. Doppler image when the peak gradient through the mitral valve increased to 18 mmHg confirming the increase in mitral insufficiency in January 2006.

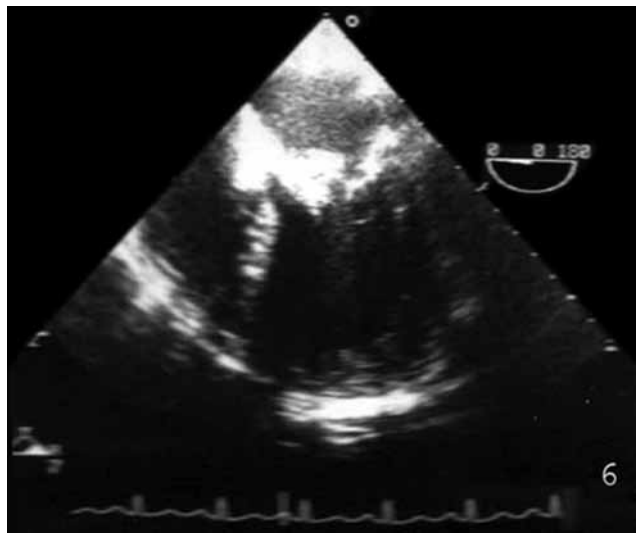

Figure 4. Image of mitral valve vegetation on transesophageal echocardiography.

Figure 5. Image of transthoracic echocardiography of our 10th patient at first admittance to our institute.

fragile vegetative mass of 3x3 cm in diameter on its side facing the ventricle. The right coronary leaflet also contained a vegetative mass of 2x2 cm in diameter on its ventricular face. The common commissure of these two leaflets was perforated, and the noncoronary leaflet remained intact (Figure 8).

The affected tissues beside the valves and the native valves were carefully excised before bileaflet mechanical valve replacement. Pledgetted sutures were used. The sewing rings of the valves were washed with rifampicin. All the surgical data is contained in Table 1.

RESULTS

There were no deaths or morbidity. The mean time to discharge was 13 days (range 10-19 days). The patients were discharged with doxycycline 200 mg/d and rifampin 600 mg/d. They were observed weekly in the first month and monthly in the following six-month

Figure 7. Calcific vegetation extensively invaded the anterolateral commissure at the mitral valve in our ninth patient.

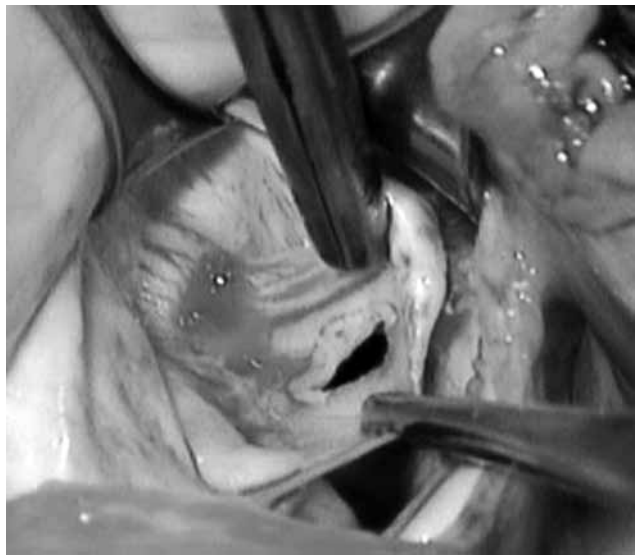

Figure 6. Leaflet perforation complication of our second patient.

period by the outpatient clinics of the Departments of Infectious Diseases and Cardiovascular Surgery. In every monthly visit, Brucella agglutination tests were examined. Double-antibiotic therapy was discontinued when it was decided that the infection had already been eradicated based on the decrease in agglutination titers and clinical evaluation of patients. Postoperative control echocardiography revealed no abnormalities. Our patients continued the postoperative double-antibiotic therapy for a mean of four months (range 2-6 months). The mean follow-up was 19.2 months (range 4-38 months). There were no related complications or need for hospitalization during follow-up.

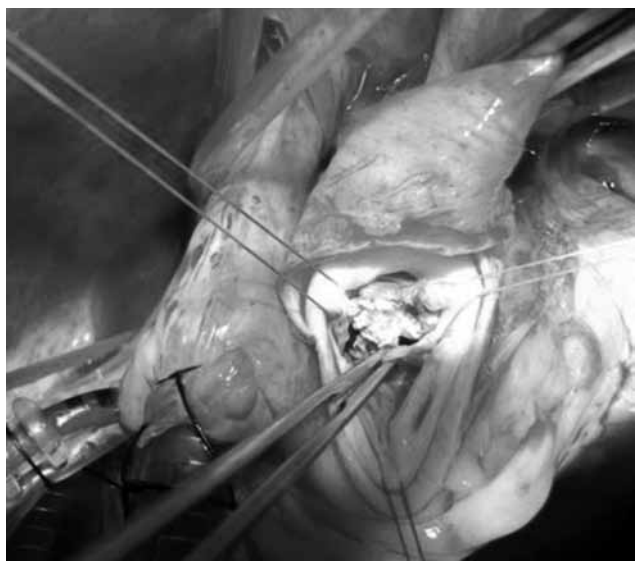

Figure 8. The complication of perforation located at the commissure between the right and left coronary leaflets.

DISCUSSION

Brucellosis is caused by Brucella organisms and acquired by direct contact with infected animals or indirectly by ingesting unpasteurized milk or milk products.[1,2] Our patients were infected directly because they were livestock producers.

Definitive diagnosis is based on recovery of the organism from the blood.[1] Wright's seroagglutination test is a very important serological test method for clinical diagnosis. Many cases have titers of 1:320 or higher.[4] Our cases were diagnosed by history, occupation, and positive serology along with echocardiography and showed big vegetations on the aortic and/or mitral valves.

Generally, aortic valve invasion is seen. Brucella endocarditis appears with a long-lasting subfebrile body temperature and a delayed (3 to 11 months afterwards) severe dysfunction occurring in the aortic valve.[5] Organisms such as *Staphylococcus aureus*, *Serratia species*, *Pseudomonas species*, *Candida species*, and *Brucella species* also injure the tissues.[2,6] Infective endocarditis injures the valve and causes insufficient flow.[7] Situations like leaflet perforation (ranging from small perforations to flail leaflets), rupture of paravalvular abscess, cardiac fistula, and leaflet prolapse due to rupture of commissure are responsible for acute valve insufficieny.[7,8]

Echocardiography is vital in determining the treatment protocol along with the morbidity and mortality rates in all infective endocarditis cases, including brucellosis.[1,6] It is a cheap, easy-to-use, noninvasive, and reproducible method. The most important point in echocardiographic evaluation is the combination of TTE and TEE. Most frequently, vegetations are examined in echocardiography and are usually found to cause insufficiency due to valve damage. If they're big enough and unstable, they can be easily determined by TTE. On native valves, the imaging rate is 25% for vegetations smaller than 5 mm and 70% for those larger than 6 mm.[9] The sensitivity and specificity for TEE are higher for small vegetations (<2 mm) and for the determination of the perivalvular extension of the infection.[10] Native valve endocarditis studies showed a sensitivity of 46% and specificity of 95% for TTE. These rates were 93% and 96% for TEE.[9,11] If there is important valve insufficiency, new flow records of severe aortic or mitral valve insufficiency are accepted as major endocardial symptoms, as in our ninth patient. Although definitive diagnoses of four of our patients as aortic valve pathology due to *Brucella endocarditis* were made by the cardiology clinic via TTE and/or TEE. Perforation of cusps could only be identified during operative exploration.

Embolization risk due to vegetation is in close relation with mortality and morbidity. Post-mortem studies have shown that splenic embolization rates can be as high as 44% and brain embolization rates as high as 40%.[12] Clinical symptom rates range from 10-50% for vegetations.[10] Native mitral valve infective endocarditis has a five times higher embolization risk than that for the aortic valve, so anterior mitral valve vegetations, particularly if larger than 15 mm, or recurrent embolisms are indications for surgery.[12] We determined a splenic infarction due to septic embolization in our second patient.

Medical treatment alone is unsuccessful for *Brucella endocarditis*, and surgery is necessary.[2,5] This microorganism, which adapts to the intracellular course, shows resistance to medication and shows recurrence that is actually not low.[1,13] Al Kasab et al.[14] reported recurrences in their study group that had only been treated medically. The most effective option is a combination of antibiotics and surgery. Our patients underwent triple-antibiotic therapy, and the infection was controlled in 4-6 weeks, at which time surgery was performed.

The two main goals of the surgery are controlling the infection by debriding the infected and necrotic tissue and reconstructing the cardiac morphology by repairing or replacing the damaged valves. Although homografts are ideal due to low infection risk, it is hard to produce them,[15] and they are not readily available in our center. The number of of centers in Turkey that perform valvular replacement with homografts is limited. The combination of antibiotic therapy and mechanical valve replacement has a satisfactory result. Early and late reinfection incidence of mechanical valve replacement can be compared with the results and survival expectations of homografts and tissue valves.[16] Mechanical valve replacement was used for *Brucella endocarditis* in a study with six cases, and there was no mortality or late recurrence during the 47 weeks of follow-up.[5] We used surgical debridement along with mechanical valve replacement and added doxycicline + rifampin for the postoperative period.

The bacteria in *Brucella endocarditis* survive because they are in the intracellular compartment.[1] For this reason, during the postoperative period, the use of antibiotics for at least a four-week period has a positive effect on survival. We used surgical debridement in conjunction with mechanical valve replacement and added double-antibiotic therapy for two to six months.

We did not see any recurrence in our patients, and this approach should prove to be helpful in the guidance of postoperative treatment.[1]

In conclusion, *Brucella endocarditis* is a rare form of infective endocarditis, and its diagnostic rate and surgical therapy practices have increased due to the availability of echocardiography. *Brucella endocarditis* does not show remission and has a high mortality if not treated. Control of the infection with preoperative antibiotic therapy and immediate surgery after improvement of the clinical status of the patient have gratifying outcomes.[1] Our study indicates that surgery increases the quality of life for a longer period of time in this type of endocarditis.[9]

Declaration of conflicting interests

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