

Treatment of Brucella Endocarditis: Our Surgical Experience with 6 Patients

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ABSTRACT

Background: Endocarditis is a rare but life-threatening complication of brucellosis. Its mortality rate has recently been reduced with the use of combined medical and surgical treatment.

Methods: Between March 2002 and April 2004, 6 patients with Brucella endocarditis underwent surgery at the Siyami Ersek Cardiovascular Center in Istanbul, Turkey. The diagnosis of Brucellosis was based on the presence of clinical signs and symptoms compatible with brucellosis, serology and/or a positive blood culture. All patients with suspected Brucella endocarditis were studied by echocardiography. The diagnosis of Brucella endocarditis was made in accordance with Duke's criteria.

Results: The most commonly affected valve was the aortic valve (4 patients). Four patients had prosthetic valves because of a previous history of rheumatic fever. In 5 patients, elective surgery was performed. Five patients underwent valve replacement with prosthetic valves, but 1 patient underwent excision of the abscess cavity without valve replacement. There was no operative mortality. All patients continued antibiotic treatment for at least 3 months postoperatively. The median duration of follow-up after surgery was 12 months. During the follow-up period, 1 patient died, while the others remained alive with no recurrences.

Conclusion: Prosthetic valve replacement is a safe procedure in patients with Brucella endocarditis. Surgical interventions combined with triple antibiotic therapy yield good results with no recurrence in the long-term follow-up.

INTRODUCTION

Brucellosis is a zoonotic infection disease; according to the WHO 500,000 new cases, mainly caused by *Brucella melitensis*, are reported annually [Report of the WHO 1992].

Received December 27, 2004; received in revised form April 15, 2005; accepted April 26, 2005.

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Humans usually become infected by indirect contact with unpasteurized milk or dairy products or direct contact with infected sheep, goats and cattle. Brucellosis is a multisystemic disease which is characterized by fever, generalized malaise, chills, profuse sweating, anorexia and arthralgia. In Turkey, approximately 15,000 cases of brucellosis were reported in 2001 according to data from the Ministry of Health; however, it is thought that the real number of cases is 50,000-100,000 per year, when the unreported and subclinical cases are taken into account [Karabay 2004]. Therefore, brucellosis remains a serious health problem in Turkey and developing countries.

Cardiac involvement occurs in about 1.0% to 10.9% of all types of Brucella infection [Al-Kasab 1988, Jacobs 1990]. Endocarditis is a rare but life-threatening complication of brucellosis, and its mortality rate has recently been reduced with the use of combined medical and surgical treatment.

We report our experience with 6 surgically treated patients with BE in order to better evaluate, the clinical and laboratory findings, and the combined medical and surgical approach.

MATERIALS AND METHODS

Between March 2002 and April 2004, 6 patients with BE underwent surgery at the Siyami Ersek Cardiovascular Center in Istanbul, Turkey. The diagnosis of brucellosis was based on the presence of clinical signs and symptoms compatible with brucellosis such as fever of unidentified source, arthralgia, malaise, sweating, weight loss, serology and/or a positive blood culture [Ariza 1996, Aygen 2002].

The serological criteria were positive Rose Bengal test and Wright seroagglutination assay titers. All sera obtained from the patients were examined by serial dilution (from 1:10 to 1:1280) using a bacterial antigen. The antigen was obtained from the Ministry of Agriculture (Veterinary Research Institute, Pendik, Istanbul).

All patients with suspected BE were studied by echocardiography. The diagnosis of BE was made in accordance with Duke's criteria [Duract 1994]. Characteristic valvular changes were confirmed visually during surgery and confirmed histopathologically after the operation.

All patients were invited back to the hospital, where the clinical examination and repeat echocardiography were performed by a cardiologist 1 month after the operation. The

Table 1. Patients' Clinical and Laboratory Findings*

Case No.	Age/ Gender	Symptoms/Duration, months	Laboratory	Physical Examination	Serologic Test	Blood Culture	Rose Bengal	NYHA
1	32/M	Fever, malaise, weight loss/2 mo	ESR:30/h, Hb:10.7, WBC:7600	SM	1/320 Wright	+	+	II
2	36/F	Sweat, night fever, weight loss/9 mo	ESR:84/h, Hb:11, WBC:7000		1/160 Wright	-	+	IV
3	35/M	Sweat, night fever, weight loss/2 mo	ESR:5/h, Hb:11.3, WBC:3600		1/640 Wright	+	+	III
4	43/M	Fever, malaise, weight loss/5 mo	ESR:80/h, Hb:9.4, WBC:7600	HSM	1/320 Wright	-	+	IV
5	66/M	Fever, malaise, weight loss/3 mo	ESR:56/h, Hb:9.2, WBC:3600		1/640 Wright	+	+	III
6	44/M	Sweat, night fever, weight loss/1 mo	ESR:20/h, Hb:10.1, WBC:8600		1/1280 Wright	-	+	IV

*NYHA indicates New York Heart Association; M, male; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; WBC, white blood cell count; SM, splenomegaly; F, female; HSM, hepatosplenomegaly.

demographic characteristics, as well as the clinical and laboratory findings, are summarized in Table 1.

RESULTS

From March 2002 to April 2004, 29 patients with infective endocarditis were operated on at our institution. Of these, 6 had BE: 1 woman and 5 men. Their average age was 42.6 years (range 35 to 66 years). All patients with BE had a history of exposure to unpasteurized goat's milk or contact with sheep. All of the patients were admitted with fever, sweating, weight loss, malaise and arthralgia. The median duration of symptoms and signs before admission was 3.5 months (range 1 to 9 months). Four patients had prosthetic valves because of a previous history of rheumatic fever. Among the routine blood tests, WBC counts were within normal limits or low and Hb was low in all patients, and the ESR was elevated in 5 patients. Despite at least 3 blood culture samples being obtained from each patient, *Brucella* species were isolated from blood cultures in only 3 patients. The Rose Bengal and Wright agglutination tests were positive (titer > 1/160) in all patients.

The aortic valve was affected in 4 patients. Of these, 2 had a prosthetic valve; the other 2 had a prosthetic mitral valve. Echocardiography showed vegetations in 5 patients, accompanied by severe valvular dysfunction in 3 patients, and perivalvular destruction with a minimal abscess cavity between the prosthetic valve and left atrium wall in 1 patient. Cardiac catheterization was performed in 2 patients (cases 4 and 5).

All patients were treated with oral doxycycline, 100 mg every 12 hours, oral rifampicin 900 mg every 24 hours, and co-trimoxazole 160/800 mg every 12 hours.

Indications for surgery included valve dysfunction and progressive heart failure in 4 patients, and persistent and mobile vegetations despite medical therapy longer than 6 weeks in 2 patients.

In 5 patients, elective surgery was performed after 6 weeks of antibiotic treatment. Another patient required urgent surgical treatment before the antibiotic therapy was complete because of hemodynamic compromise. Five patients underwent valve replacement with prosthetic valves (3 AVR, 2 MVR), but 1 patient (patient number 3) with a prosthetic aortic valve had perivalvular destruction with a minimal

abscess cavity and underwent excision of the abscess cavity without valve replacement.

There was no operative mortality. All patients continued antibiotic treatment for at least 3 months postoperatively.

The median duration of follow-up after surgery was 12 months (range, 2 to 27 months). During the follow-up period, 1 patient (patient number 6) who underwent AVR because of native valve endocarditis suddenly died unexplainably 6 months after the operation.

All other patients remained alive with no recurrences. (Demographic findings of echocardiography, operations, and outcome are presented in Table 2).

DISCUSSION

In a large series of patients with brucellosis, endocarditis was reported in only 0.5% of cases [Saadeh 1996]. BE is associated with a high mortality rate, accounting for 80% of deaths from brucellosis [Leandro 1998, Peery 1960]. Halim et al reported that BE was seen in 8.5% of patients treated for endocarditis [Halim 1986]. The patients operated on for BE represent a major proportion of our patients operated on for endocarditis during this period (6 of 29 patients with endocarditis, 20.7%). This high frequency of BE may be related to the high prevalence of brucellosis in Turkey and the fact that our center is a referral hospital.

Brucella spp. were reported to be isolated from blood samples in about 15% to 70% of cases [Renzulli 1999]. Therefore, the demonstration of high or rising antibody titers of *Brucella* agglutination tests establishes the presumptive diagnosis of brucellosis [Memish 2002]. The isolation rate of brucellosis in our series was 50%, which may be attributed to the fact that these patients were admitted during the subacute or chronic period, and they had received antibiotics before admission to our clinic. The diagnosis of brucellosis in 3 culture-negative patients was based on the clinical and serological findings.

Echocardiography is useful for the detection of vegetation and the evaluation of valve function. TTE may be inadequate in up to 20% of adult patients because of acoustic shadowing [Bayer 1998]. TEE has a substantially higher sensitivity and specificity than TTE for perivalvular extension of infection, and IE vegetations of prosthetic valves [Daniel 1991, Karalis 1992, Pedersen 1991, Rohmann 1991]. All the patients in our

Table 2. Findings, Operations, and Outcome*

Case No.	Previous Valve Disease	Echocardiography	Medical Treatment, Duration, week	Indication for Operation	Surgery	Follow-up Month/Outcome
1	Rheumatic fever-(MI) 1998 MVR	TEE: .5 × 1.5 cm mobile vegetation on the mitral valve	D+R+Co-tri, 6 wk	Persistent sepsis, large mobile vegetation	Redo-MVR (23 St Jude)	11 mo/well
2	No	TTE: 5 × 10 mm vegetation at least 3 different particle, on the aortic valve, +4 aortic valvular insufficiency	Relapse after therapy with R+D for 45 days, and D+R+Co-tri for 6 wk	LV failure due to severe AI	AVR (19 St Jude) + Mitral Ring annuloplasty (27 No)	11 mo/well
3	Rheumatic fever-(AI) AVR-1999	TEE: abscess cavity between prosthetic aortic valve and LA wall (1.5 × 1 cm)	D+R+Co-tri, 6 wk	Persistent sepsis, risk of emboli	Excision of abscesses	13 mo/well
4	Rheumatic fever AVR+MVR 1993	TTE: vegetation and + 3/4 paravalvular leakage on the mitral valve	D+R+Co-tri, 6 wk	Risk of emboli and LV failure due to severe MI	Redo MVR	28 mo/well (27 St Jude)
5	Rheumatic fever AVR-1977	TEE: Mean aortic valve gradient of 100 mm Hg with vegetation	D+R+Co-tri, 6 wk	Congestive heart failure due to severe AS, risk of emboli	Redo AVR (23 St Jude) + RCA safen Bypass + Mitral commissurotomy	3 mo/well
6	No	TTE: Aortic vegetation, +4 aortic valvular insufficiency	D+R+Co-tri, 2 wk	Pulmonary edema and LV failure, risk of emboli	AVR (25 St Jude)	6 mo/exitus

*MI indicates mitral insufficiency; MVR, mitral valve replacement; TEE, transesophageal echocardiography; D, doxycycline; R, rifampicin; Co-tri, co-trimoxazole; TTE, transthoracic echocardiography; LV, left ventricle; AI, aortic insufficiency; AVR, aortic valve replacement; AS, aortic stenosis; RCA, right coronary artery.

series were examined with TTE. In addition, TEE was performed in 3 patients because of inadequate TTE views to detect small vegetations.

The aortic valve is the most commonly affected cardiac valve, reported in 82% of BE cases [Reguera 2003]. Brucellosis affects mainly damaged valves, and prosthetic valves were found to be involved in 8% of patients [Al-Harhi 1989, Lubani 1986]. In our series, 4 patients (67%) had prosthetic valves because of acute rheumatic fever, and the aortic valve was the most commonly involved valve (in 4 of 6 cases, 67%).

In endemic areas, BE should be considered in the differential diagnosis of patients with prosthetic valves with persistent fever, normal or low WBC counts and a history of unpasteurized dairy product consumption. Keles et al reported that a normal WBC count was the most significant predictor for acute brucellosis, allowing differentiation from acute rheumatic fever [Keles 2001]. Solera et al reported that the WBC count remains normal or low and the ESR may be normal or elevated in brucellosis [Solera 1997]. In our patients with BE, WBC counts were within normal ranges or low, and ESRs were elevated (in 5 of 6 patients).

Many authors suggest that a combination of medical and surgical treatment is the only therapeutic option for BE

[Al-Kasab 1988, Quiroga 1996, Report of the WHO 1992, Uddin 1998]. There are no specific data for the ideal regimen or the duration of medical therapy. A single agent and a short duration of treatment for brucellosis were not acceptable because of the high rate of relapse [Food and Agricultural Organization-World Health Organization 1986, Hall 1990]. Although a combination of streptomycin and tetracycline was recommended by the WHO, co-trimoxazole and rifampin have been used because of the low rate of relapse [Ariza 1985, Food and Agricultural Organization-World Health Organization 1986]. In endemic areas the trend is to use a combination of 3 antibiotics [Shamelian 2000]. Triple antimicrobial therapy has proved effective and very well tolerated [Reguera 2003]. Doxycycline plus co-trimoxazole, or rifampin has been recommended for a duration of 8 weeks, up to 10 months after valve replacement [Guerrero 1993]. We used the combination of co-trimoxazole, doxycycline and rifampin for 6 weeks before and at least 3 months after surgery.

Although the best results were achieved with homografts in cases of endocarditis [Haydock 1992, McGiffin 1992], we preferred valve replacement with prosthetic valves in 5 patients in our series because of the limited availability of homograft tissue. In the present study, prosthetic valve

replacement for BE was not associated with increased hospital mortality and we did not observe recurrence of endocarditis with mechanical valves.

Duran et al recommended vegetectomy in selected patients with a well-preserved aortic valve and single vegetation that was easily excised [Duran 2001]. We preferred simple excision of abscesses pouch in a patient with an aortic prosthesis that had perivalvular destruction with a minimal abscess cavity between the prosthetic valve and left atrium wall. There was no evidence of recurrence of infection in the 13-month follow-up.

We conclude from the current study that prosthetic valve replacement is a safe procedure in patients with BE. Surgical interventions combined with triple antibiotic therapy yield good results with no recurrence in the long-term follow-up.

ACKNOWLEDGMENT

We would like to thank Professor Dr. Mustafa Bakir for reviewing the manuscript.

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