

## THREE CASES OF BRUCELLA PROSTHETIC VALVE ENDOCARDITIS CURED WITH MEDICAL TREATMENT

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### SUMMARY

*Brucella endocarditis is associated with high morbidity and mortality. The accepted treatment for Brucella endocarditis is a combination of surgical and medical approach. In this study, we report three cases of prosthetic valve endocarditis due to Brucella spp. treated successfully with antibiotic therapy alone between 2003-2007 years. This report describes that, in some instances, Brucella endocarditis could be managed by antibiotic therapy alone under careful observation.*

**Keywords:** *Brucella spp., endocarditis, prosthetic valve, treatment*

### ÖZET

#### Medikal Tedavi ile Düzelen Üç *Brucella* Protez Kapak Endokarditi Olgusu

*Brucella endokarditi yüksek mortalite ve morbiditeye sahiptir. Brucella endokarditinde kabul edilen tedavi protokolü cerrahi ve medikal tedavidir. Bu çalışmada Gaziantep Üniversitesi Tıp Fakültesinde 2003-2007 yılları arasında sadece medikal olarak başarılı şekilde tedavi edilmiş *Brucella spp.*'nin etken olduğu protez kapak endokarditli 3 hasta sunulmuş, bazı durumlarda *Brucella* endokarditinin dikkatli bir izlem altında sadece antibiyotik ile tedavi edilebileceği tartışılmıştır.*

**Anahtar sözcükler:** *Brucella spp., endokardit, protez kapak, tedavi*

### INTRODUCTION

Brucellosis is an endemic disease both in Turkey and many parts of the world. It is particularly seen in the region of the Mediterranean, the Middle East and Central and South American countries<sup>(1)</sup>.

Since brucellosis can affect all systems of body, clinical syndrome is ultimately diverse. Rare manifestation of brucellosis is a cardiovascular involvement, especially endocarditis, has high mortality rates and poor prognosis than other forms of the disease<sup>(1,5)</sup>. While the mortality rate for brucellosis is only 1 %, endocarditis accounts for 80 % of these deaths<sup>(4)</sup>. *Brucella*

endocarditis may develop not only on previously damaged valves by rheumatic fever or congenital malformed but also on normal valves<sup>(13)</sup>. The combination therapy of antibiotics and surgical valve replacement has been thought to be better compared to antibiotic therapy alone as treatment for *Brucella* prosthetic valve endocarditis<sup>(9)</sup>. But in recent studies, a few cases diagnosed with *Brucella* endocarditis successfully treated with antibiotic therapy alone were reported<sup>(9,11,12)</sup>.

In this study, we report three cases with infective endocarditis on prosthetic valve due to *Brucella melitensis* which were treated by antibiotic treatment alone.

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## CASES

### Case 1

The patient previously operated due to rheumatic fever on mitral valve was 42-year old female. She has lived in the endemic region and gave history of drunk raw milk. She had a history of headache, dyspnea and fever within a period of two weeks. On her physical examination the patient had fever of 39°C. On cardiac auscultation she had 2/6 systolic murmur and prosthetic valve sound. Her blood pressure was 130/60 mmHg and heart rate was 110 beats/min. The number of white blood cell count (WBC) and C-reactive protein (CRP) level were found 11,000/mm<sup>3</sup> and 80 mg/dl, respectively. In her cardiovascular examination, 0.8x0.9 cm sized mass on prosthetic mitral valve was detected by transesophageal echocardiography (TEE) (Figure A).

Empirical antibiotic regimen of vancomycin (2 g/day) and amikacin (1 g/day) was started. The serum tube agglutination test (STA) against *Brucella* spp. showed positive titer of 1/640 in this patient. *B.melitensis* was identified in blood culture on the eleventh day. Antimicrobial treatment was changed to the combination therapy of rifampicin (300 mg/day), doxycycline (200 mg/day) and amikacin (1 g/day). Since she had rejected surgical prosthetic valve replacement, the combination chemotherapy was kept going on. After 3 weeks, she was discharged with antibiotic and anticoa-

gulant therapy (warfarin). However, in the first month of the treatment, microembolization was occurred in central nervous system since she did not take anticoagulant therapy regularly. Surgical prosthetic valve replacement was reconsidered but she rejected. Medical treatment was continued with rifampicin, doxycycline and trimethoprim-sulfamethoxazole for 12 months until vegetation disappeared and *Brucella* titers was decreased to <1/160. She recovered with motor deficit due to embolic phenomenon on central nervous system. At follow-up 12 months, she had normal laboratory findings.

### Case 2

Patient 2 was 27 year old male, a sheep herder, admitted with symptoms of fever, dyspnea for 1 months. He had prosthetic aortic valve replacement in 1998 due to aortic stenosis. On his physical examination, 38.7°C fever was noted. He had murmur from the affected valve. The presence of endocarditis was considered due to dyspnea. In his cardiovascular examination, 1.4x0.6 sized vegetation on the atrial side of the prosthetic aortic valve was detected by TEE (Figure B). *Brucella* agglutination titer was positive at 1/640. *B.melitensis* was isolated from blood cultures in the tenth day. In his laboratory findings, CRP was 110 mg/dl, WBC was 7000/mm<sup>3</sup>. The antibiotic regimen was planned using doxycycline (200 mg/day), rifampicin (300 mg/day), ceftriaxone (2 g/day). Clinical picture recovered in the first month of antibrucellar treatment. After one month, he was discharged with combination of rifampicin and doxycycline. The treatment was continued for 6 months

until vegetation disappeared and *Brucella* titers was decreased to <1/160. This patient was cured without sequele. During 12 month follow-up his recent examination was found normal.

### Case 3

Patient 3 was 56 year-old male patient. He had a recent history of ingesting unpasteurized milk. He was admitted to our clinic with fever continuing for 2 weeks. 7 years ago, this patient underwent aortic valve replacement for rheumatic fever and coronary artery bypass grafting for coronary artery disease. On his physical examination 38.7°C of fever was detected. On his cardiac auscultation he had prosthetic heart sound. Periannular abcess (0.3x0.5 cm) surrounding prosthetic aortic valve was detected by TEE (Figure C). In his laboratory findings, WBC was 9000/mm<sup>3</sup>, CRP was 184 mg/dl. *Brucella* tube agglutination test of the patient was positive at 1/640 titer. Treatment was started for brucellosis including rifampicin and doxycycline. After first week of the treatment, the patient got apyretic and the laboratory findings were improved. *B.melitensis* was isolated from the first blood culture. At the end of the first month of the treatment, periannular abcess was disappeared and blood cultures were negative. Finally; the treatment was continued for 6 months. During 6 month follow-up without antibiotic therapy he showed normal both clinical and laboratory findings.

## DISCUSSION

Endocarditis is unfavorable complication of brucellosis<sup>(4,13)</sup>. It usually occurs on aortic valve and *Brucella* spp. as the pathogen of endocarditis is very rare, accounting for 0.3-0.6 % of cases<sup>(2,7)</sup>. In Turkey, Greece and countries in Arabic Peninsula where *B.melitensis* is endemic, it has been reported that *B.melitensis* is notable organism accounting for 4-9% in endocarditis<sup>(8,10)</sup>. In our study we reported three patients with endocarditis due to brucellosis. Definitive diagnosis of brucellosis is isolation of *Brucella* spp. from blood but this process is really difficult and can not be successful every time<sup>(8,12)</sup>. For this reason, antibiotic therapy must be started when *Brucella* agglutination test is found positive<sup>(14)</sup>, because the early treatment improves prognosis of this disease. In the endemic region, *Brucella* spp. should be considered as one of the etiologic agents of infective endocarditis.

*Brucella* spp. can cause destruction and ulceration in tissues slowly, the developing larger vegetation at the serious risk of embolization; for this reason, acceptable treatment of *Brucella* endocarditis for the sterilization of tissues is a combination of medical and surgical interventions<sup>(9)</sup>. Antibiotic treatment alone has not been recommended by most authors<sup>(9,15)</sup>. But, our patients with endocarditis on prosthetic valves due to *B.melitensis* were successfully treated with antibiotic therapy alone. Patient 3 had periannular abcess (0.3-0.5 cm) cured by antibiotic therapy within a short period. Murdaca et al.<sup>(12)</sup> reported remission of *Brucella* endocarditis in patient with prosthetic valve by antibiotic therapy. Mert et al.<sup>(11)</sup> reported a case with *Brucella* endocarditis cured by antibiotic therapy alone because of the patient's rejection of valve replacement. During 18 month follow up, the patient was free of the disease. Cohen et al.<sup>(3)</sup> described a patient with *Brucella* endocarditis and found another 12 similar cases, which were treated by antibiotic combination therapy alone. The indications for medical treatment are the absence of congestive heart failure or a prosthetic valve, relatively mild extravalvular cardiac involvement, and shorter disease period characteristic features of the patients with *Brucella* endocardi-

tis, who could be treated with antibiotic therapy alone<sup>(3)</sup>. The indications for surgery are failure of medical treatment, abscess, developing of vegetations while receiving antibiotics and *Brucella* prosthetic valve endocarditis<sup>(6,8)</sup>.

Several combinations of antibiotics have been used successfully in the treatment of *Brucella* endocarditis. The optimal combination therapy and duration of treatment are controversial. Medical treatment protocol was consisted of different combinations of antibiotic therapies in many reported studies<sup>(11-13)</sup>. Trimethoprim-sulfamethoxazole or aminoglycoside or ciprofloxacin must be added to rifampicin and doxycycline. The duration of treatment in these studies was between 6 weeks and 4 months<sup>(11-13)</sup>. In accordance with the related studies, aminoglycoside or ceftriaxone were added to the combination of doxycycline and rifampicin in the first month in patient 1 and 2, later the combination treatments of doxycycline and rifampicin or doxycycline, rifampicin and trimethoprim-sulfamethoxazole were continued until getting clinical improvement.

The decision to stop treatment could be individualized both improvement of clinical findings and progressive decrease in *Brucella* agglutination titer<sup>(8)</sup>. During the follow ups of our patients without antibiotic therapy, no blood cultures were obtained because of their clinical findings were normal and no increase was found in their *Brucella* tube agglutination titers. But obtaining blood culture may be important for determining relaps in these patients.

In conclusion, antibiotic therapy alone will provide an important advantage for decreasing the risks of cardiac surgery and the expensive costs of the treatment in developing countries. In some instances, antibiotic therapy alone could be acceptable just under careful observation.

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