

## Successful Medical Treatment of Prosthetic Mitral Valve Endocarditis Caused by *Brucella abortus*

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Although *Brucella* endocarditis is a rare complication of human brucellosis, it is the main cause of the mortality in this disease. Traditionally, the therapeutic approach to endocarditis caused by *Brucella* species requires a combination of antimicrobial therapy and valve replacement surgery. In the literature, only a few cases of mitral prosthetic valve endocarditis caused by *Brucella* species have been successfully treated without reoperation. We present a case of a 42-year-old man with a prosthetic mitral valve infected by *Brucella abortus* who was cured solely by medical treatment. (**Korean Circ J 2014;44(6):441-443**)

**KEY WORDS:** Infective endocarditis; Cardiac valve prosthesis; *Brucella abortus*.

### Introduction

Human brucellosis is an acute or sub-acute febrile illness usually marked by intermittent or remittent fever accompanied by malaise, loss of appetite, myalgia, headache and chills. In untreated patients, the symptoms of human brucellosis show an undulating pattern that persists for weeks or months. Thus, the diagnosis may be delayed for many years. Although the incidence of *Brucella* endocarditis (BE) as a focal complication of human brucellosis is reported in only about 0.3-0.7% of cases,<sup>1,2)</sup> BE has a high fatality rate (80%) and is the most common cause of death in this disease.<sup>3)</sup> Traditionally, the therapeutic approach to BE requires a combination of antimicrobial therapy and valve replacement surgery.<sup>1,4-10)</sup> However, rare cases of prosthetic valve BE cured solely with medical treatment have been reported.<sup>2,11)</sup> Here, we present a case of a 42-year-old

man with a prosthetic mitral valve infected by *Brucella abortus* (*B. abortus*) who was cured solely by medical treatment.

### Case

A 42-year-old male was hospitalized in July 2008 with dizziness and mild dyspnea lasting two months. He also complained of intermittent febrile sensations and night sweats. His medical history revealed three open heart surgeries before admission. The patient underwent open mitral commissurotomy with mitral valve stenosis in 1986. After five years, he underwent mitral valve replacement with a Carbomedics prosthetic valve (CarboMedics, Inc.; Austin, TX, USA) in 1991. In 2005, his tricuspid valve was also replaced with a St. Jude Medical prosthesis (St. Jude Medical Inc.; Minneapolis, MN, USA) due to severe tricuspid regurgitation. He also had a history of atrial fibrillation and cardiac liver cirrhosis. The patient was a stock farmer and had buried cattle afflicted by brucellosis one year before this admission.

Upon admission, his vital signs showed a blood pressure of 130/70 mm Hg, pulse rate of 106 beats/min, respiratory rate of 22 breaths/min and body temperature of 37.5°C. Irregular heartbeats without murmurs were heard on auscultation and his electrocardiogram showed atrial fibrillation with a rapid ventricular response rate of 112 beats per minute. Laboratory studies revealed anemia and leukopenia with a hemoglobin level of 6.9 g/dL, a total white cell count of 2600/mm<sup>3</sup> (66% neutrophils, 22% lymphocytes, 11% monocytes) and a platelet count of 191000/mm<sup>3</sup>. The C-reactive protein level of

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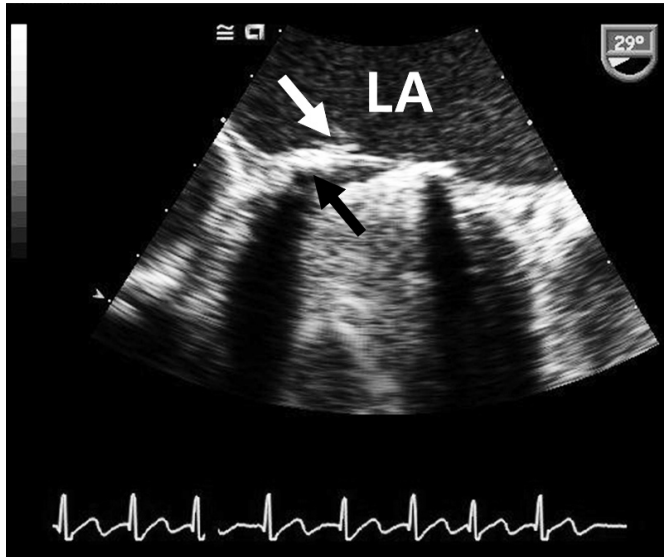
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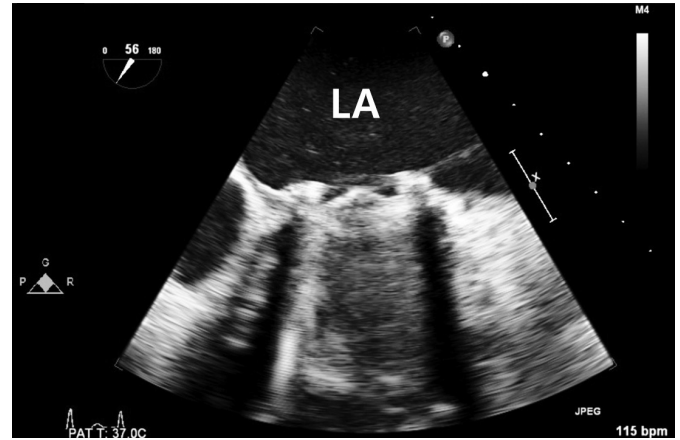


**Fig. 1.** Transesophageal echocardiography at admission demonstrated a small vegetation (3×8 mm; white arrow) attached at the inferomedial portion of the mitral prosthetic valve annulus (black arrow). LA: left atrium.

5.76 mg/dL was elevated. The peripheral blood smears showed normocytic hypochromic erythrocytes with some fragmented cells.

Transesophageal echocardiography (TEE) demonstrated a very small echogenic mass (3×8 mm) attached to the inferomedial portion of the prosthetic mitral valve annulus (Fig. 1; Video in the online-only Data Supplement) which was not seen on the last TEE. The function of the prosthetic mitral valve and tricuspid prosthetic valve was normal. Under suspicion of infective endocarditis, six blood cultures were drawn for the first 48 hours and inoculated into an automated system (BACTEC; Becton Dickinson, Sparks, MD, USA). Because gram-negative coccobacilli were isolated from the initial blood culture after two days of incubation, an empirical antibiotic regimen of ceftriaxone (2 g/day) and gentamicin 3 mg/kg/day was started. The serum (tube) agglutination test against *Brucella* species showed a positive titer of 1:1280. The isolates of the automated hemoculture system were identified as *Brucella* species after six days and further identification of *Brucella* strains revealed *B. abortus*.

A diagnosis of BE on the prosthetic mitral valve was considered in this patient and specific antibiotics were started. The patient was given a triple combination therapy consisting of oral doxycycline 100 mg twice a day, oral rifampin 600 mg once daily and an intramuscular injection of streptomycin 1000 mg once daily. After 12 days of treatment, his fever recurred and streptomycin was switched to intravenous gentamycin (5 mg/kg/day). Although surgery was initially planned, the patient refused reoperation at that time. Therefore, he was treated with antibiotics alone under close follow-up. After 12 days of treatment, the blood cultures were negative. Three weeks after treatment, the follow-up echocardiography demon-



**Fig. 2.** Transesophageal echocardiography after 16 days of treatment revealed the complete resolution of the mitral vegetation. LA: left atrium.

strated no vegetations in the prosthetic mitral valve (Fig. 2). After seven weeks of hospitalization, he was discharged with oral doxycycline 200 mg/day. Doxycycline was maintained for one year and his *Brucella* titers decreased to <1:160. The patient has been regularly followed in the outpatient clinic. At present, five years after discharge, the patient remains free of symptoms.

## Discussion

Although BE is a rare complication of human brucellosis accounting for only 0.3–0.7% of cases,<sup>12)</sup> it has a high fatality rate and is the most common cause of death. By postmortem examination, endocarditis was responsible for 80% of deaths.<sup>13)</sup> *B. abortus* and *B. melitensis* are reported to be the most frequently isolated species.<sup>3)9)</sup> *B. melitensis* tends to be associated with a more acute and aggressive presentation, while *B. abortus* infections may be more insidious in onset and more likely to become chronic.<sup>9)</sup>

Because the clinical picture of brucellosis is not distinctive, the diagnosis of BE cannot be made solely on clinical grounds and it is essential to perform bacteriological and serological testing. The isolation of brucellae from blood, although highly specific, presents quite a low sensitivity (15–20%).<sup>10)</sup> Thus, serology is the most useful diagnostic approach. Confirmation of endocarditis is required through echocardiography. TEE offers improved diagnosis capabilities over transthoracic echocardiography (TTE) because TEE can pick up very small vegetations that would be overlooked by TTE. TEE also provides more information on the degree of valvular destruction, the existence of rings or myocardial abscess and the formation of aneurysms. In the current guidelines for infective endocarditis,<sup>12)</sup> TEE rather than TTE is recommended as the initial diagnostic tool in patients with prosthetic valves and those who have prolonged symptoms before infective endocarditis is suspected. In this case, TEE was essential for diagnosis and in accordance with the very high

risk of mortality and morbidity. The early detection of vegetations and the accurate diagnosis using TEE resulted in the patient achieving a good clinical outcome.

In most of the literature, the combination of antimicrobial therapy and early valve replacement is recommended as the most effective therapy of BE.<sup>14-10</sup> However, some cases of native or prosthetic BE cured with medical treatment alone have been reported.<sup>27,9,11,12</sup> Only a few cases of prosthetic mitral valve endocarditis due to *B. melitensis* have been treated successfully without reoperation.<sup>11</sup> In these cases, doxycycline (200 mg/day), trimethoprim-sulfamethoxazole (2700 mg/day) and rifampin (600 mg/day) were administered, and vegetations completely disappeared with the patient showing no signs of relapse during a twelve-month follow-up. Our patient was given a triple combination of doxycycline (200 mg/day), rifampin (600 mg/day) and gentamycin (5 mg/kg/day) for six weeks and a maintenance therapy of doxycycline for 12 months. Vegetations completely disappeared and his recent examination was normal at the five-year follow-up period.

Although the antibiotic regimen and optimal duration of treatment are not yet established, the combination of doxycycline and streptomycin has produced the best results in the treatment of human brucellosis.<sup>19,13</sup> In cases of endocarditis, the addition of rifampin has been advocated because of its excellent tissue distribution and high penetration in valvular vegetations. Clinical, serological and biological findings may help the physician decide whether antimicrobial treatment should be continued. The normalization of anti-*Brucella* titers is occasionally suggested to be the end-point of therapy.<sup>11,14</sup> Relapse occurs in up to 30% of poorly compliant patients. Thus, patients should be followed clinically for up to two years to detect relapse. In this case, the patient showed no signs of relapse in a five-year follow-up period; therefore, we concluded that he was completely cured with antimicrobial therapy only. We believed that the key to the successful management of this patient's BE was early and accurate diagnosis, the presence of small vegetations without other valvular complications and the insidious property of *B. abortus*; only then could a good outcome be expected.

In conclusion, a high degree of suspicion with careful history-taking and early diagnosis are fundamental in order to ameliorate the course of BE. TEE can play a key role in the early diagnosis of prosthetic valve infective endocarditis. Even in patients with BE of their prosthetic valves, antimicrobial therapy alone can be considered in case of small vegetations without any other valvular complications. More patients and longer follow-up periods are necessary to obtain guidelines for this complex disease.

## Supplementary Materials

The online-only Data Supplement is available with this article at <http://dx.doi.org/10.4070/kcj.2014.44.6.441>.

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