A Case of Mitral Stenosis Complicated With Seronegative Brucella Endocarditis

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SUMMARY

Brucellosis is a multisystemic disease. The most common cause of death from the disease is endocarditis. The aortic valve is most commonly affected. The disease rarely involves the mitral valve.

A 30 year-old woman presented with complaints of chills and fever up to 38°C at night, fatigue, palpitations, and dyspnea for the previous 3 weeks. Cardiac auscultation revealed a diastolic murmur in the mitral area. Her temperature was 38.3°C. On echocardiographic examination, the mitral valve area was 0.62 cm² and an isoechoic mass thought to be a vegetation was detected on the anterior mitral leaflet. A diagnosis of infective endocarditis was made and vancomycin administration was commenced.

Brucella melitensis was isolated in all three blood samples, however, the patient remained seronegative with Brucella agglutination titers of up to 1/160. The antibiotic therapy was then shifted to doxycycline (200 mg/day), rifampicin (600 mg/day), and ciprofloxacin (1000 mg/day). After 30 days of treatment, surgery was performed for the severely stenotic mitral valve and to remove the vegetation.

The operation was successful. The postoperative period was uneventful. On the follow-up she had no complaints.

In cases with Brucella endocarditis, after diagnosis, antibiotic therapy must be started immediately and when the clinical condition improves, surgical intervention should be performed when indicated. (Jpn Heart J 2004; 45: 353-358)

Key words: Brucellosis, Endocarditis, Mitral valve, Seronegativity

BRUCELLOSIS is a frequently seen zoonotic disease in some regions of the world, such as the Mediterranean, Middle Eastern, Asian, and Central and South American countries.1) Although it is a multisystemic disease, the most common cause of death is endocarditis.2) The aortic valve is the most commonly affected cardiac valve, which may lead to abscess formation in the aortic root.3) The mitral
valve is less frequently affected. Prosthetic valve endocarditis due to Brucellosis has also been reported in the literature. Although treatment is controversial, the most widely accepted is the combination of medical and surgical therapy. A case of seronegative Brucella melitensis that had affected the mitral valve and subsequent treatment by the combined therapy is discussed in this report.

CASE REPORT

A 30-year-old woman come to our clinic with the complaints of chills and fever up to 38°C at night, fatigue, palpitations, and dyspnea for the previous 3 weeks. She had rheumatic fever when she was 10 years old, and was put on benzathine penicillin prophylaxis monthly thereafter.

On physical examination she had a fever of 38.3°C. Her blood pressure was 110/60 mmHg with a heart rate of 110/bpm. Her pulse was irregular. She also had dyspnea, hepatomegaly, and pretibial edema. A diastolic murmur was heard at the apex on auscultation. Electrocardiography showed rapid atrial fibrillation. Chest x-rays revealed cardiomegaly.

On echocardiographic examination, the mitral valve area was 0.62 cm² and an isoechoic mass which was thought to be a vegetation was detected on the anterior mitral leaflet (Figure 1).

Her routine biochemical and hematological tests were within normal limits except an elevated erythrocyte sedimentation rate (ESR). Its level on admission was 65 mm/h. It decreased to 20 mm/h before the operation and 18 mm/h six weeks after the operation.

Figure 1. Transthoracic echocardiography showing a mobile isoechoic mass on the anterior mitral leaflet.
White blood cells (WBC) were measured four times. The measured values were 8900/mm$^3$ on admission, 7800/mm$^3$ after two weeks of treatment, 8550/mm$^3$ before the operation, and 7900/mm$^3$ one week after the operation.

A diagnosis of acute infective endocarditis was made. After serial blood cultures were taken at 1 hour intervals, an empiric antibiotic regimen of vancomycin was started.

Brucella melitensis was isolated in all three blood samples, but the patient remained seronegative with Brucella agglutination titers of up to 1/160. The antibiotic therapy was then shifted to doxycycline (200 mg/day), rifampicin (600 mg/day), and ciprofloxacin (1000 mg/day).

The fever and chills disappeared and her hemodynamic state stabilized. Also, the vegetation decreased in size on echocardiographic examination.

Surgery was performed on the severely stenotic mitral valve and to remove the vegetation.

**Surgical technique:** A median sternotomy was performed after intravenous administration of 0.1 mg/kg midazolam and 10 µg/kg fentanyl. Cardiopulmonary bypass with moderate systemic hypothermia (28°C) was initiated through aortic and bicaval cannulation. Myocardial protection was provided by combined cold potassium cardioplegic arrest (St.Thomas Cardioplegic solution number 2) with topical hypothermia (with cold saline at an approximate temperature of 4°C). A membrane oxygenator was used in the operation (Dideco, Mirandola, Italy).

After left atrial incision, an atrial retractor provided exposure of the mitral valve. A 0.8 × 0.7 cm vegetation was seen on anterior mitral leaflet (Figure 2). Fibrocalcific degeneration and commissural fusion was observed on both leaflets. The valve was excised and replaced with a number 25 Carbomedics bileaflet mitral mechanical valve.

*Figure 2.* Huge vegetation on mitral anterior leaflet is shown after left atriotomy.
No microorganism was isolated in the cultures taken intraoperatively. No complications were observed. She was discharged on the 8th postoperative day. Antibiotic therapy was continued for one month after surgery (combination of ciprofloxacin, doxycycline, and rifampicin).

Neither vegetation nor paravalvular leak was observed in control echocardiography performed at the first and third month postoperatively.

**DISCUSSION**

Brucellosis is a zoonosis caused by aerobic gram (-) coccobacilli. It can affect multiple organ systems, and endocarditis is the most destructive, therapy resistant, and fatal complication of the disease. Although it is rare in nonendemic regions, Brucella endocarditis may reach up to 10.9% in endemic regions. A high level of clinical suspicion is the first step for diagnosis, especially in endemic areas.

In most patients no difficulty is encountered in a diagnosis. The sedimentation rate is generally elevated. It is known that C-reactive protein (CRP) and ESR, which are recognized as traditional inflammation markers, increase in acute brucellosis cases and decrease to normal levels after treatment. Therefore, we measured sedimentation as an inflammation marker, however, we did not measure CRP. After a 30 day treatment, the sedimentation rate returned to a normal range.

Group agglutination antibody titres are frequently over 1/320. In large series, 96% of the cases are seropositive but may be seronegative as in our case. The exact diagnostic method is the isolation of Brucella melitensis or Brucella abortus, which are the etiologic factor in 98% of Brucella endocarditis, in blood cultures. It should be emphasized that seronegativity does not exclude the diagnosis and positive blood cultures with echocardiographic findings are the most important criteria for the diagnosis of Brucella endocarditis.

It is widely accepted that a combination of medical and surgical methods is generally necessary for successful treatment. Medical treatment consists of combined administration of streptomycin, tetracycline, rifampicin, doxycycline, or ciprofloxacin for at least 6 weeks, although medical therapy alone is not effective in most cases. Ciprofloxacin is the most effective antibiotic against Brucella melitensis. We used the combination of ciprofloxacin, doxycycline and rifampicin for 4 weeks before and 4 weeks after surgery.

Generally antibiotic therapy for the treatment of Brucella is recommended for at least 6 weeks. However, the presence of vegetation and congestive heart failure are indications for early surgical intervention. Hadjinikolaou, et al and Al-Kasab, et al have operated on patients within one week after the commencement of the antibiotic therapy. Our patient had vegetation on the mitral
valve and congestive heart failure. Therefore, as soon as she stabilized, which was after one month of antibiotic therapy, surgical intervention was undertaken.

Medical therapy can be used for patients with mild cardiac involvement and with symptoms of short duration. Surgical therapy is mandatory in the presence of congestive heart failure, abscess formation, and involvement of prosthetic valves.10)

Even if the symptoms last a short time and disappear with antibiotic therapy, surgery is necessary due to the embolic potential of residual vegetation or to relieve the stenotic valves. Although the symptoms of our case were new onset and disappeared within 1 month with antibiotics, severe mitral stenosis and a large residual vegetation on the mitral valve led us to perform surgical intervention.

In cases with chills, fever, night sweats, dyspnea, and signs and symptoms of cardiac involvement, Brucella endocarditis must be highly suspected, especially in the endemic areas of the world. After diagnosis, antibiotic therapy must be started immediately and surgical intervention should be performed, when indicated, when the clinical condition has improved.

REFERENCES