

# THE EVALUATION OF CASES WITH BRUCELLA ENDOCARDİTİS. REPORT OF FOUR CASES

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*Endocarditis is a rare but severe complication of brucellosis. In this case report we evaluated the clinical data and therapeutic approach of our four cases diagnosed as brucella endocarditis. For three of them the diagnosis of endocarditis was suspected in the early period but Brucella spp. was ascertained as the responsible pathogen just after the positivity of serology and blood cultures. The diagnose and the treatment of these patients was delayed due to the fact that epidemiological data for brucellosis was not examined carefully. It is important to evaluate the epidemiological data for brucellosis in patients with cardiac symptoms in our country where brucellosis is seen endemically.*

**Key Words:** Brucellosis, Endocarditis

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## INTRODUCTION

**B**rucella infection is a zoonotic disease, endemically seen in the Mediterranean, the Arabian Gulf, Latin America, Asia, parts of Mexico and the Indian sub continent. Brucellosis is still of great health importance and economic significance in our country. Acute and chronic brucellosis results with multisystemic severe complications (1,2). Endocarditis is a rare but highly mortal complication (1,3,4). In several studies the incidence of brucella endocarditis is reported as less than 2% of the cases (1,2).

However, as the clinical features of brucella endocarditis are indistinguishable from those caused by other organisms, it is very difficult to prove that endocarditis is due to brucellosis. The epidemiological data is the cornerstone of diagnosis (1,2,5). Definitive diagnosis is based on the isolation of Brucella spp. from the blood cultures, though the isolation rate is low. Additionally, serological confirmation of the microorganism is an important step in the diagnosis (6). High degree of suspicion is important for early diagnosis of this infrequent disease.

The aim of the present study was to evaluate the clinical data of our cases with brucella endocarditis.



## CASE 1

A 47-year-old male with rheumatologic valvular heart disease, was admitted to our hospital with complaints of fever, fatigue, dyspnea, and pretibial oedema. His past medical history comprised of cardiomyopathy and mitral stenosis.

On his physical examination, he had fever of 39°C, his blood pressure was 100/60 mmHg, with a heart rate of 95 bpm and breath rate of 24/min. His pulse was irregular. On cardiac auscultation 3/6 diastolic murmur was heard at apex. He also had hepatosplenomegaly. On echocardiographic examination, a systolic motion of vegetation on the mitral valve through left ventricle was detected and severe mitral stenosis was diagnosed.

In the laboratory tests, the leucocyte count was 7600/mm<sup>3</sup> (65% neutrophil, 35% lymphomonocyte), erythrocyte sedimentation rate (ESR) was 48 mm/h and C reactive protein (CRP) was 2.8 mg/dl. His liver functional tests (AST:95 IU/L, ALT: 65 IU/L) were elevated. Other biochemical tests were within normal limits.

The patient was diagnosed as infective endocarditis and was hospitalized in the cardiology unit. Serial blood cultures were taken and Penicilin G (20 million units /24 h with continuous infusion) and gentamycine (40 mg/ every 8h) was started empirically. On the second day of the treatment Brucella slide agglutination test was defined as positive. Additionally, Brucella tube agglutination test was positive at 1/20480 titers. The patient was evaluated by a specialist in infectious diseases and it was learned that he was diagnosed as brucellosis eight months before and had received doxycycline and rifampicin for six weeks. He was diagnosed as brucella endocarditis and ceftriaxone (2 gr/day), rifampicin (600 mg/day), and doxycycline (200 mg/day) was started. Four days later Brucella species were isolated from the blood cultures taken at the first three days on admission. As the fever persisted and the hemodynamic condition deteriorated, a mitral valve replacement was performed on the fifteenth day of the brucella endo-

carditis therapy. The fever and chills disappeared and his hemodynamic state stabilized following the surgical intervention. Operative mitral valve specimen and vegetation specimen cultures were found to be negative. He had uncomplicated postoperative course and was discharged on antibiotic therapy consisted of rifampicin, doxycycline and cotrimaxazole for 9 months. He had no signs or symptoms of cardiovascular disease during follow up.

## CASE 2

A 17 year-old male with rheumatologic valvular heart disease presented with complaints of chills, fever, weakness, sweating, palpitations, and dyspnea. Symptoms were present for four days before his admission. On physical examination the patient's fever, blood pressure, heart and breath rates were as follows: 38°C, 146/64 mmHg, 100 bpm, and 22 /min, respectively. Cardiac auscultation revealed arrhythmia and 4/6 diastolic murmur in the aortic and mesocardiac area. On echocardiographic examination, nodular thickening of aortic valve, severe aortic valvular and intermediate mitral valvular failure was detected.

On admission the leucocyte count was 3300/mm<sup>3</sup> (65% neutrophil, % 35 lymphomonocyte), haemoglobin was 10 mg/dl, platelet count was 116000/mm<sup>3</sup>, ESR was 50 mm/h and CRP was 13 mg/dl. The other biochemical tests were within normal limits.

Rheumatologic cardiac valvular disease, infective endocarditis, and heart failure were the possible diagnosis and the patient was hospitalized in the cardiology clinics in our hospital. An empirical antibiotic regimen of penicilin G (20 million units /day with continuous infusion) and gentamycine (40 mg/8 h ) was started for the treatment of possible infective endocarditis. Serial blood cultures were taken before the beginning of the antibiotic treatment.

During his clinical follow up period, intense abdominal pain and acute abdominal clinics developed. An urgent surgical intervention was



performed and mesenteric lymphadenitis was diagnosed as the source of this clinical table.

A week after the hospitalization, fever still continued and gram negative coccobacillus was detected in all of three blood cultures. Infectious disease consultation was performed for the first time. The patient gave a recent history of stockbreeding. His past medical history did not comprise of brucellosis or a period consisted of complaints considering brucellosis. Brucella slide agglutination test was positive. Brucella tube agglutination test was positive at 1/1280 titers. Brucella melitensis was isolated in all three blood samples. The antibiotic regimen was changed to ceftriaxone (2 gr/day), rifampicin (600 mg/day), and doxycycline (200 mg/day) for the diagnosis of brucella endocarditis. The fever was discontinued at the fifth date of the treatment, his general condition improved and he preferred to go to another hospital for surgery owing to his personal reasons.

### CASE 3

A 33-year-old woman was admitted to our hospital with the chief complaints of chills and fever up to 38°C, fatigue, nausea and vomiting. Symptoms were present for two months before her admission. On physical examination she had fever of 38.6°C. Her blood pressure was 123/61 mmHg with a heart rate of 119/bpm. Her breath rate was 30/min. On cardiac auscultation, an arrhythmia was revealed. Additionally, 2/6 diastolic murmur was heard at apex. Her physical examination was normal except for splenomegaly.

An abdominal ultrasonography was performed for the presence of abdominal pain and multiple infarct foci on spleen were detected. On echocardiographic examination, aortic and mitral valvular failure and vegetation on the aortic valve was revealed. The patient was hospitalized in the cardiology unit with a diagnosis of infective endocarditis, and an empirical treatment with penicillin G (20 million units /day with continuous infusion) and gentamycine (40 mg/8h) was start-

ed. At the second day hemiplegia and confusion developed and she was transferred to the intensive care unit. At that time Brucella spp. was isolated in her blood cultures taken before the beginning of the antibiotic treatment. A specialist in infectious disease examined the patient for the first time. She was found to have a recent history of consuming dairy products with unpasteurized milk. Brucella slide agglutination test was positive and Brucella tube agglutination test was positive at 1/640 titers. On the admission, the laboratory evaluation showed that the leucocyte count was 13300/mm<sup>3</sup>, platelet count was 114000/mm<sup>3</sup>, CRP was 17.4 mg/dl and ESR was 76 mm/h. Her liver functional tests (AST:289 IU/L, ALT: 479 IU/L) and bilirubin (1.8mg/dl) were elevated. Her other biochemical test were within normal limits.

The patient was diagnosed as brucella endocarditis and the antibiotic treatment was changed to ceftriaxone (2 gr/day), rifampicin (600 mg/day), and doxycycline (200 mg/day). She was planned to undergo a cardiac surgery after the improvement of her clinical status. Unfortunately, she died due to brucella endocarditis and its complication on the eighth day of the treatment.

### CASE 4

A 32-years old male was hospitalized in the infectious diseases clinics in our hospital with the symptoms of oedema in his joints, fatigue, palpitation and chest pain for 3 weeks. The patient gave a recent history of stockbreeding and consuming dairy products with unpasteurized milk. Additionally, cases with brucellosis were present in his family. On his physical examination, he had fever of 38.6°C, his blood pressure was 130/80 mmHg with a heart rate of 119/bpm and breath rate of 24/min. The systemic evaluation was normal except for hepatosplenomegaly. On the laboratory evaluation, the leucocyte count was 13100/mm<sup>3</sup>, ESR was 31 mm/h and CRP was 14.2 mg/dl. The other routine biochemical and hematological tests were within normal limits. Brucella slide



agglutination test was positive and Brucella tube agglutination test was positive at 1/320 titers. He was diagnosed as brucellosis and rifampicin (600 mg/day) and doxycycline (200 mg/day) therapy was started.

At the second day of admission oedema was detected in his scrotum. Scrotal doppler ultrasonography revealed orchitis and hydrocele. The patient has complaints of migratory arthritis and chest pain. On echocardiographic examination, rupture on the chordae tendinae of anterior mitral valve secondary to endocarditis was detected and ceftriaxone (2 gr/day) was added to the antibiotic therapy. The patient was evaluated by a specialist in cardiovascular surgery and medical therapy was suggested to be continued. His parenteral treatment was continued 21 days. Thereafter, the patient treatment was continued with trimetoprim / sulfamethoxazole (320 / 1600 mg/day), rifampicin (600 mg/day) and doxycycline (200 mg/day). The patient's complaints disappeared except palpitation and chest pain. In his control echocardiography, an appearance of endocarditis sequel was revealed and control echocardiography was planned to be done every 6 month. He was discharged on antibiotic therapy for 9 months. He did not determine any signs or symptoms of cardiovascular disease, or abnormality on echocardiography needing surgical operation during follow up.

## DISCUSSION

Brucellosis is a zoonosis caused by gram (-) coccobacilli. Brucella infections can develop with different clinic symptoms. Endocarditis is the most destructive, therapy resistant, and fatal complication of the disease (1-4). Endocarditis due to Brucella spp. may occur on previously damaged valves, as by rheumatic fever or may also develop on previously normal valves (7). Two of our patients had a medical history of rheumatologic valvular heart disease. The most frequent symptom among our cases was fever. Aygen et al. (2) found that the rate of brucella endocarditis was 0.4% in 480 cases and the most

frequent symptom was fever.

Acute and chronic brucellosis results with multi-systemic severe complications (1,2). In our four cases; endocarditis, mesenteric lymphadenitis, arthritis and orchitis were found as the multisystemic complications of brucellosis. Aygen et al (2) reported that endocarditis, orchitis and peritonitis were rare complications of brucellosis.

Brucella endocarditis causes predisposition to ulceration, development of vegetation and embolisation (3). These factors destroys the tissues and organs slowly. The most frequent affected cardiac valve is the aortic one (1,4). However, in two of our patients both mitral and aortic valves, in the other two of them only mitral valves were affected.

The diagnosis of brucella endocarditis is based upon epidemiological evidence and positive culture or serology. Serology plays a significant role in the diagnosis of brucellosis as it is easy to be performed and is associated with good specificity and sensitivity (8). In all of our patients serology was positive indicating the presence of acute brucellosis. The specificity of blood culture is high but sensitivity is low (5,6). In our cases, three of them were positive for blood cultures and only in one case endocarditis was diagnosed by serological tests and epidemiological data.

The treatment of brucella endocarditis is still a controversial subject. Usually combination of medical and surgical interventions are the preferred regimen (9). On the other hand, other studies report that antibiotic regimen is enough for the treatment, especially if an extravalvular involvement of the disease is not present (10,11). In our patients a combination of doxycycline, rifampicin, and ceftriaxone or cotrimaxazole was used which was showed to be effective in the treatment of Brucella endocarditis (9,12) A medical and surgical treatment was applied for our fourth case. Operation materials were culture negative and the medical treatment was continued for the patient who was stable. If a congestive cardiac failure not able to be treated medically develops, an emergency cardiac surgery



has to be done (5,13). Endocarditis due to brucella is associated with a high mortality rate (1,3,4). The second case died due to endocarditis and its complication before the cardiac surgery was possible to be done.

For the first three cases the diagnosis of endocarditis was suspected in the early period but *Brucella* spp. came was ascertained as the responsible pathogen just after the positivity of serology and blood cultures. The diagnose and the treatment of these patients was delayed due to the fact that epidemiological data was not examined carefully and the infectiouse disease specialist did not consultate them at the admission.

In conclusion, brucella endocarditis is a rare complication but it is very important to evaluate the epidemiological data for brucellosis in patients with cardiac symptoms in our country where brucellosis is seen endemically. While investigating the etiology of endocarditis, *Brucella* must be suspected as a responsible pathogen, especially in patients with a history of stockbreeding and consuming dairy products with unpasteurized milk, or merely living in rural regions.

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