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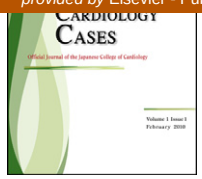

Case Report

Aortic valve endocarditis and cerebral mycotic aneurysm due to brucellosis

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KEYWORDS
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Summary Brucellosis is an infectious disease caused by Gram-negative coccobacilli. Direct contact with the infected tissue or blood, consumption of infected dairy products, and inhalation of infectious aeresol particles can transmit the disease. Brucella endocarditis is rare but the most fatal complication of brucellosis. The most commonly involved valve is aortic valve. Mycotic aneurysms result as an involvement of central nervous system and can lead to serious complications. Herein we present a case with mycotic aneurysmal rupture and aortic insufficiency and sinus valsalva fistula caused by brucella endocarditis. There were rare cases with brucella endocarditis and mycotic aneursymal rupture secondary to neurobrucellosis in the literature. Relevant complications are treated with aortic valve surgery and peripheral endovascular intervention.

Introduction

Brucellosis is an infectious disease and caused by Gram-negative coccobacilli. Direct contact with the infected tissue or blood, consumption of infected dairy products, and inhalation of infectious aerosol particles can transmit the disease. There are cases reported which were transmitted via sexual contact and breastfeeding [1]. Although fever, night sweats, weight loss, and myalgia are common symptoms, various symptoms can be seen according to the involved system [1]. Neurobrucellosis and brucella endocarditis are rare but fatal complications of the disease. Aortic valve involvement is common in endocarditis. Meningitis and meningoencephalitis are much more commonly seen in neurobrucellosis, but mycotic aneurysms can also be seen [2,3].

In our case there were aortic insufficiency and rupture of sinus valsalva due to brucella endocarditis and rupture of mycotic aneurysm as a result of neurobrucellosis. Those complications were successfully treated with medical

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therapy, surgery, and endovascular intervention. There were rare complications with brucella endocarditis and mycotic aneursymal rupture secondary to brucellosis.

Case report

A 29-year-old male patient was admitted to our hospital with symptoms of fever, night sweats, decreased functional capacity, weight loss of 8 kg over 5 months and headache, diplopia, and ataxia for one week. He had a history of consumption of raw dairy products, he was admitted to another hospital 4 months before with those symptoms and he was diagnosed as having brucellosis with brucella tube agglutination titers of 1/320 and positive Rose Bengal test. Doxycycline and rifampicin were prescribed, but he failed to continue treatment.

On physical examination, he was concious, well oriented and cooperative, blood pressure was 100/60 mmHg, pulse rate was 88 beats per minute, temperature was 38 °C and there was audible aortic diastolic murmur. There were no signs of Kernig and Brudzinski. Other physical examination findings were all normal. Hypochromic microcytic anemia, leukopenia, high erythrocyte sedimentation rate (ESR) and C-reactive protein levels were found on laboratory exams (Table 1). Brucella tube agglutination test titers were 1/640 positive and Brucella IgG (+). Lumbar puncture was performed and there were 130 leucocytes/mm^3 and dominancy of lymphocytes. On biochemical exams of cerebrospinal fluid (CSF), glucose was 39 mg/dl, protein 115 mg/dl, Cl 119 mEq/L, and lactate 2874 mmol/L (Table 1). CSF was negative for Brucella tube agglutination and there were no agents seen on Gram and Erlich—Ziehl—Nielsen stains. Blood, urine, and CSF cultures were collected and doxycyline, rifampicin, and ceftriaxone combination treatment was started with the prediagnosis of neurobrucellosis. Computerized tomography performed for the patient because of neurologic symptoms and a hyperdense image compatible with suspected arteriovenous malformation located at right thalamus extending to hypocampal area was detected. For differential diagnosis, a cranial magnetic resonance imaging scan with angiography was performed and aneurysm of right posterior cerebral artery and a subacute phase hemorhagic zone at right thalamus extending to parahypocampal and right cruris of mesencephalon were detected (Fig. 1).

Table 1 Patient's cerebrospinal fluid, blood biochemical, and hematological parameters.

	Value	Reference values
Complete blood count		
Hemoglobin (g/dl)	10.8	12.0—16.0
Hematocrit (%)	30.7	35.0—52.0
White blood cell ($10^3/mm^3$)	4.66	4.8—10.8
Mean corpuscular volume (fl)	76.9	80.0—102.0
Red cell distribution width (%)	13.2	11.5—15.5
Thrombocyte ($10^3/mm^3$)	183.0	150.0—450.0
Blood biochemistry		
Glucose (mg/dl)	128.00	70.0—105.0
Blood urea nitrogen (mg/dl)	24.00	6.0—20.0
Creatinine (mg/dl)	0.91	0.50—1.10
Alanine aminotransferase (U/L)	8.0	0.0—31.0
Aspartate aminotransferase (U/L)	13.0	0.0—32.00
Total bilirubin (mg/dl)	0.31	0.10—1.10
Direct bilirubin (mg/dl)	0.01	0.00—0.30
Na (mEq/L)	139.0	133.0—145.0
K (mEq/L)	4.88	3.30—5.10
Sedimentation (mm/h)	44	0.0—20.0
C-reactive protein (mg/dl)	2.18	0.0—0.5
Cerebrospinal fluid biochemistry		
Glucose (mg/dl)	39.0	40.0—70.0
Protein (mg/dl)	115.0	0.0—45.0
Chloride (mEq/L)	119	118.0—132.0
Lactate	2874	1100—2400

Selective cerebral angiography was performed and right posterior cerebral artery mid zone aneurysm was seen. Patient was referred to the neurosurgery clinic, but no operation was planned for the patient. Aneurysm development was assumed to be mycotic and because of a murmur heard on cardiac oscultation, echocardiography was performed for the patient to determine whether the mycotic aneurysm was secondary to infective endocarditis. Dilatation of left ventricular cavity with a preserved ejection fraction of 58%, bicuspid aortic valve, a mobile vegetation formation on right aortic cusp, severe aortic insufficiency, and a fistula between aorta and right atrium as a result of ruptured right sinus valsalva were detected on echocardiography (Fig. 2).

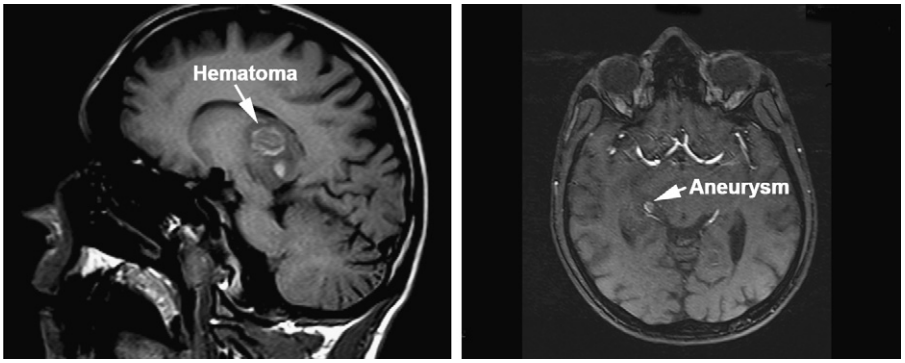

Figure 1 (Left panel) Magnetic resonance image of the subacute phase hemorhagic zone at right thalamus. (Right panel) Magnetic resonance angiographic image of aneurysm of right posterior cerebral artery.

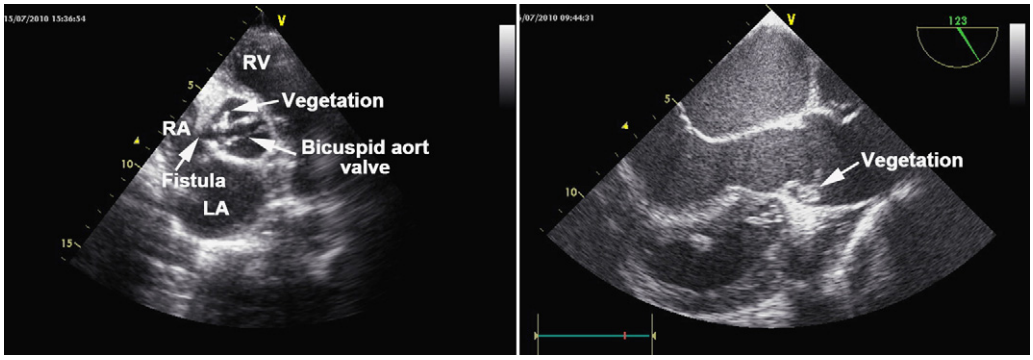

Figure 2 (Left panel) Echocardiographic image of bicuspid aortic valve, with a vegetation formation on aortic cusp and a fistula between aorta and right atrium as a result of ruptured right sinus valsalva. (Right panel) Transesophageal echocardiographic image of vegetation on aortic cusp. LA, left atrium; RA, right atrium; RV, right ventricle.

Ceftriaxone treatment was stopped and co-trimaxazole was initiated with a diagnosis of endocarditis. CSF cultures were sterile but *Brucella melitensis* was isolated in blood cultures. On the tenth day of treatment surgery was performed; aortic valve replacement (No: 21, St. Jude, St. Paul, MN, USA) and fistulous aortic segment was repaired with Goretex graft (Gore, Newark, DE, USA) and pericardium. The antibiotic regimen was continued after the operation and blood cultures after one month of operation were sterile. Because of cerebral aneurysm, the patient was discharged with enoxoparine instead of warfarin. The patient was followed up for two months with oral antibiotics and enoxoparine. A control angiography was performed for cerebral aneurysm and percutaneous embolization was perfomed for persisting aneurysm (Fig. 3). After the procedure warfarin was started. The patient is still being followed up in a healthy condition after the fifth month since diagnosis and treatment with oral antibiotics and warfarin.

Discussion

Brucella endocarditis is responsible for 3—4% of all endocarditis cases. In brucellosis prevelance of endocarditis varies between 0.4% and 2% [1,4,5]. Endocarditis is a rare complication of brucella infections but is responsible for 80% of mortality [1,5,6]. Mortality is usually caused by cardiac failure especially in patients with late diagnosis. In endocarditis cases, the most isolated forms are *B. abortus* and *B. melitensis*. *B. melitensis* causes more acute and serious clinical presentations. As in our case, the aortic valve is most commonly involved. Involvement of prosthetic valves and pathologic valves are commonly seen, but native valves are also seen [2,5,7,8]. Diagnosis of brucella endocarditis can be made with history, clinical findings, echocardiographic images confirming the diagnosis of infective endocarditis, isolation of the agent from tissue samples, positive agglutination test, and polymerase chain reaction tests [9]. The agent cannot be isolated in blood, because it is hard to produce in cultures and there is a long interval with antibiotic treatment between the symptom onset and diagnosis. Because of these reasons agglutination tests can be used in early diagnosis [2,3,5,9]. Titers of tube agglutination above 1/160 can help diagnosis [9]. Diagnosis in our case could be made by history of consumption of raw dairy products and previous brucellosis diagnosis, clinical and echocardiographic presentation, positive agglutination tests, and isolation of *B. melitensis* in blood samples.

Because of resistance of brucella to medical treatment, and persistence in tissue for up to eight weeks after

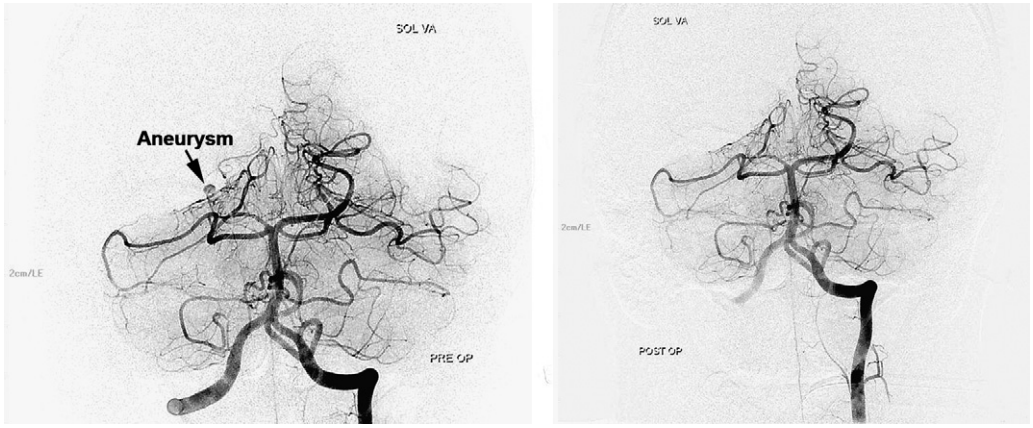

Figure 3 (Left panel) Angiographic image of right posterior cerebral artery aneurysm. (Right panel) Angiographic image of embolized posterior cerebral artery aneurysm.

treatment initiation despite effective antibiotic treatment, medical and surgical treatment combination approach is recommended. In selected cases without cardiac failure and with a short disease interval medical treatment can be sufficient alone but recurrence risk is high [10]. Vegetation, embolization, development of cardiac failure, valvular dysfunction, and hemodynamic instability necessitate surgical treatment [2].

Neurobrucellosis can be seen in 5% of cases [3]. Meningoencephalitis is the most commonly seen but polyradiculoneuropathy or diffuse involvement can also be seen. Direct involvement of the central nervous system with the agent and autoimmune mechanisms can be responsible for neurobrucelosis [3]. Diagnosis can be made by isolation of the agent in CSF and high antibody titers. Besides those, lymphocytosis, decreased glucose levels, and elevated protein concentration in CSF support the diagnosis [11]. Cerebrovascular involvement and mycotic aneurysm formation are rare in neurobrucellosis. Embolization of endocarditis or arteritis as a result of vascular inflammation can be responsible for cerebrovascular involvement. Lacunar infarcts, hemorrhages, and venous thrombosis may result in various clinical presentations [12]. In our case intraparencyhmal hematoma and right posterior cerebral artery aneurysm formation were seen. Vascular involvement in neurobrucellosis may lead to clinical presentations that necessitate urgent intervention and the mortality rate of neurobrucellosis is about 0.5—5% [3].

Long-term treatment is necessary for brucella infections, because it is an intracellular infection. Five months before his admission, our case was admitted to another hospital with symptoms of fever, night sweats, and weight loss, and he was diagnosed as having a brucella infection. Antibiotic therapy was given to the patient, but the patient stopped his treatment himself before the completion of the ideal treatment duration. And as a result of this, infection control could not be established. Progression of the untreated infection to the bicuspid aortic valve resulted in infective endocarditis. Septic embolisms as a result of infective endocarditis can have a role in the development of neurobrucellosis which accounts for the central nervous system manifestations. Besides these, mycotic aneuyrsm and intracranial bleeding resulting from vasculitic involvement of cerebral arteries, and CSF transmission of reactive proteins and inflammatory mediators also may have a role in the development of neurobrucellosis.

Doxycycline, rifampicin, streptomycin, co-trimoxazole, ceftriaxone, or ciprofloxacin can be used in the treatment of neurobrucellosis and brucella endocarditis. Because of intracellular involvement and antibiotic resistance, rifampicin, doxycycline and co-trimoxazole treatment is recommended for 6—12 months [2,3]. Bicuspid aortic valve and mechanical complications required surgical treatment with medical therapy in our case. Because of high complication risk and low success rate of endovascular treatment without infection control and the patient's neurological stability, intervention for the aneurysm was planned after infection control and aortic valve surgery. Endovascular treatment of mycotic aneuryms caused by neurobrucellosis can be achieved safely after the infection and vascular inflammation is taken under control. In case of fever of unknown origin and neurologic findings the diagnosis of neurobrucellosis should be kept in mind and it should not be forgotten that endocarditis could accompany neurobrucellosis.

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