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Brucella Endocarditis

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Introduction

Brucellosis is the most common bacterial anthropozoonosis in the world.[1] It is quite prevalent in developing countries like India with a predominant agrarian economy. Surveillance for brucellosis is not practiced regularly. It is underdiagnosed and under reported. The exact burden of this disease is not known in India because of paucity of reports.[2] The incidence of cardiovascular complications in brucellosis, such as endocarditis, myocarditis or pericarditis is reported to be as low as 1%[1,2] and usually <2% in most series.[2,3,4] In cases of endocarditis, the aortic valve is the most commonly affected. The mitral valve is affected much less commonly.[4,5]

Case Report

A 25-year old female from Edathua, presented to Govt. TD Medical College, Alappuzha with intermittent fever of one month duration associated with backache and multiple joint pains involving both elbow and knee joints. Fever was high grade, with chills, present towards the evening. She had been self medicating herself with paracetamol, and used to obtain relief for the fever which subsided, only to recur a day or two later. She also had headache, diffuse abdominal pain, watery non bloody diarrhea and vomiting of two weeks duration. There was history of loss of weight and appetite, myalgia and fatigue. Her urine output was adequate and there was no discoloration of urine. She was a staff nurse working in the intensive care unit of a private hospital in New Delhi and had returned to Kerala two days prior to admission. There was a history of rat bite four weeks before. She had no history of contact with any other animals. She had been evaluated for these symptoms in a private hospital and had received parenteral ceftriaxone 2g iv bd for 24 days, doxycycline 100 mg bd for 7 days and azithromycin 500 mg once daily for 5 days, but she continued to be febrile. There were no known comorbidities and the patient had been asymptomatic before the onset of fever.

On examination, the patient was found to be febrile with a temperature of 100.4F, blood pressure 130/80 mmHg, pulse rate 88 beats/min. She was mildly tachypnoeic, with a respiratory rate of 32/min. She was conscious, well oriented and cooperative. She was 1.64m tall, weighed 56kg, and was not pale. There was mild diffuse abdominal tenderness. There were no masses palpable per abdomen and no free fluid. There were no cutaneous markers of infective endocarditis. She was not in congestive cardiac failure. There were no audible murmurs and the chest was clear. There was no neck stiffness.

On admission, the total white blood cell count was 4860/cmm with 69.5% polymorphs, hemoglobin was 12.8 g/dL, platelet count was 2,52,000/cmm. Renal and liver function tests were normal.

All antibiotics were stopped. The patient was put on oral rehydration solution for diarrhea and supportive management with intravenous fluids were given. Temperature monitoring was meticulously done.

On the second day, the temperature recorded was 101.6 F and the patient continued to have headache and loose stools. Tests for malaria, typhoid, autoimmune disorders, sputum AFB, viral markers, Mantoux, thyroid function tests, ESR, CRP, stool and blood cultures, stool clostridium difficile toxin, serology for leptospirosis, dengue, brucellosis, scrub typhus and urine AFB were performed as part of routine workup for pyrexia of unknown origin.

On day 3, a temperature of 102F was recorded, loose stools were persisting and the patient was started on ciprofloxacin and metronidazole. Oral rehydration and symptomatic and supportive management was continued.

A blood culture sent was sterile after 48H. Repeat blood cultures and peripheral smear for malaria were sent during fever spikes. Tests for malaria and typhoid were repeatedly negative. Serology for leptospirosis and dengue, ANA and dsDNA were negative. Peripheral smear showed a normocytic normochromic blood picture. Ultrasound abdomen showed mild hepatosplenomegaly and a few sub centrimetric lymphnodes and mild free fluid in the right iliac fossa. Cardiology consultation and an echocardiogram were scheduled as part of routine workup for pyrexia as other investigations were not yielding positive results.

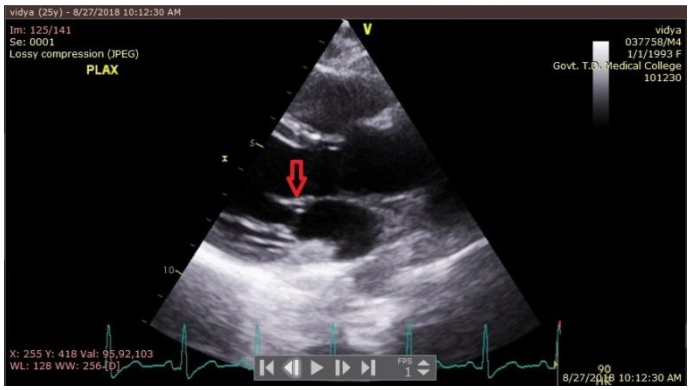
On day 4, temperature recorded was 104.7F and there was headache with a single episode of vomiting. There was no neck stiffness or focal neurological deficit and the patient was mentally alert. A CT brain was performed which was normal, and a lumbar puncture was planned.

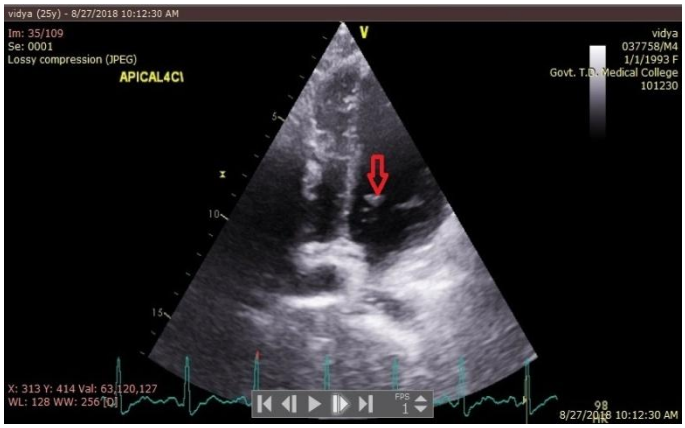
Brucella antibodies were detected by the IgM Brucella ELISA kit (1.99, Normal <0.9, sensitivity 70%, specificity 99%). On further probing, the patient admitted to consumption of milk beverages multiple times from roadside shops, which could have been unpasteurised. Antibiotics were changed to doxycycline 100 mg 12 hourly and rifampicin 600 mg daily.

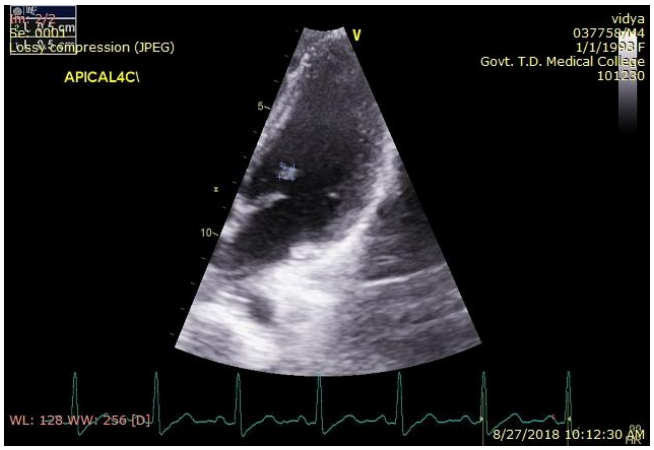
On day 5, temperature recorded was 101F. The routinely scheduled transthoracic echocardiogram showed the presence of a mobile vegetation on the anterior mitral leaflet measuring 6 x 5 mm. Intravenous streptomycin 1g daily was started. Adequate hydration and daily renal function monitoring was done.

Over the next few days, temperatures recorded were steadily lower. The patient became completely afebrile by day 9. Her abdominal pain, headache and loose stools resolved, and her general condition and appetite improved. Repeat IgM Brucella showed rise in titre (3.99). Three more blood cultures were sent and were sterile even after 7 days of incubation with subcultures.

On days 10 and 15, repeat echocardiograms were performed which showed no increase in the size of the vegetations. The patient continued to remain afebrile. She was advised to continue all antibiotics for 3 weeks and review with a repeat echocardiogram. Doxycyline and rifampicin were advised for a total of six weeks.







Discussion

In the retrospective study conducted by Vishwanath Sathyanarayanan et al[6] of 68 confirmed cases of brucellosis in Southern India, diagnosis of brucellosis was made by testing the sera for Brucella agglutinins. 32% patients were female. 64.7% had history of contact with unpasteurized dairy products. Fever was the most common presenting complaint and was present in 100% of patients, of which 63% had fever of > 4 weeks duration. 31% had myalgia, 34% had musculoskeletal symptoms such as arthralgia and backache, 24% had headache, 28% had gastrointestinal symptoms such as nausea, vomiting, diarrhea and abdominal pain, 6% had hepatosplenomegaly and 14.7% had leucopenia. Endocarditis was present in 1 patient, a 45 year old female, which occurred on a bicuspid aortic valve and responded well to medical therapy.

In the study by Kokuglu et al[7] in 138 patients, 78.3% had fever, 77.5% had arthralgia, 26.85% had hepatomegaly and 36.2% had splenomegaly.

In the study by Mantur et al[8] in 495 patients, 84.2% had fever, 23.6% had arthralgia.

The constitutional and gastrointestinal symptoms of our patient were similar to those of patients in the above studies.

Diagnosis of brucellosis depends upon isolation and identification of *Brucellae* from clinical samples, detection of antigen, genome, and antibodies.

Serological testing such as serum agglutination test and immunoenzymatic assays for detection of antibody against *Brucella* are important laboratory diagnostic tests for brucellosis[9] and are said to be the most useful.[10] Antibodies usually begin to appear in the blood at the end of the first week of the disease, IgM

appearing first followed by IgG.[10] In comparison with the serum agglutination tests, ELISA yielded higher sensitivity and specificity.[10,11] Studies have given a specificity of 100% for the detection of IgM by ELISA for the diagnosis of acute brucellosis,[18,19,20] a sensitivity of 96%,[20] a positive predictive value of 100%,[20] and a negative predictive value of 94%.[20] The Brucella ELISA is a reliable, sensitive and specific test in the diagnosis of brucellosis.[20]

The diagnosis of brucellosis in our patient was done by detecting antibody by IgM ELISA, which had a high specificity of 99%. On repeated estimation, there was a rise in titre, which showed that the disease was acute, and that seropositivity was not due to preexisting disease.

In the study by Kochar et al,[13] out of 175 cases, only 1 had endocarditis. In most studies, the incidence of cardiovascular complications in brucellosis is <2%. [2,3,4,12]

Approximately 50% of patients with Brucella endocarditis have underlying valvular diseases.[14] When predisposing cardiac condition were evaluated in 233 patients, no underlying condition was found in 32.6%.[15] Aortic was the most commonly involved valve, in 75-85% of cases.[16] Mitral valve is less frequently involved.[15] The infection of a previously healthy valve most often involves the aortic valve, whereas secondary

infection of pre-damaged valve prefers the mitral valve.[16] Jeroudi et al[16] from Saudi Arabia reported 4 adult patients with normal hearts who developed severe aortic regurgitation after infection with *Brucella*, and in one of them mitral valve was also affected.

Our patient was not known to have previous valvular disease and there were no cardiac symptoms or physical signs on examination.

There are several reasons for low incidence of positive blood culture in Brucella endocarditis such as intracellular location and fastidious nature of organism,

previous treatment with antibiotics, and long duration between beginnings of symptoms and the diagnosis.[16]

Our patient had received doxycycline 100mg bd for 7 days prior to admission which could have affected her blood cultures adversely.

Brucella endocarditis is usually treated with a combination of medical and surgical approaches.[16] Medical treatment alone can be used for mild cardiac involvement and within a short duration of symptoms onset.[17]

In our patient, the vegetation was not large and medical management was initiated early. She had a good clinical response to medical treatment alone, and therefore surgical management was not considered.

Conclusion

This case is of special interest due to several reasons. Brucellosis presenting as endocarditis is rare, occurring in only 1-2% of cases.[2,3,4,12,13] Our patient did not have an agricultural background and did not initially have a definite history suggesting brucellosis. There were no cardiac symptoms or signs of endocarditis. But Brucella serology and echocardiography identified the disease. Endocarditis has been usually documented on the aortic valve,[4,5] whereas vegetations were present on the mitral valve in our patient. Timely diagnosis and appropriate medical management alone yielded a good clinical response.

In an agrarian economy like India, brucellosis is endemic. It is a neglected tropical disease which can mimic any other disease. It can present as prolonged fever of unknown cause. History of contact with unpasteurized milk products, if obtained, is a useful pointer to diagnosis. A high index of suspicion is necessary. Brucella titre and echocardiography should be part of the routine diagnostic workup of patients presenting with prolonged fever of unknown cause. A cardiac evaluation should be performed even if the predominant symptoms are not cardiac, especially when other investigations are negative. Diagnosis is challenging because of negative blood cultures. Clinical or echocardiographic evidence of endocarditis especially when culture negative, should always prompt testing for brucellosis. Serological testing for brucella antibodies is sensitive and highly specific. If appropriately and timely treated, a good clinical response may be obtained in brucella endocarditis. Prevention should be attempted in general population by advising consumption of only pasteurized dairy products.

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