

Cardiac manifestations in brucellosis

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SUMMARY Cardiac involvement in childhood brucellosis is rare and when present mimics findings usually noted in acute rheumatic fever with carditis. We report five children aged 6 to 11 years. Echocardiography showed mitral valve vegetations in one, functional mitral valve incompetence in two, and sluggish myocardial function in one. All the patients presented with fever, arthralgia, and malaise, four of them had leucopenia, and all five showed relative lymphocytosis. Blood cultures grew *Brucella melitensis*, biotype 1 in four cases and type 2 in one. Treatment with oral tetracyclines over three weeks together with streptomycin over the first two weeks was successful in all the patients, including one in whom oral trimethoprim/sulphamethoxazole was first tried but was unsuccessful as the patient developed a relapse after two months.

Endocarditis and myocarditis are rare but serious complications of infections with brucella microorganisms.¹⁻⁶ Patients presenting with a heart murmur and a history of ingestion of raw unpasteurised milk or its products from domestic animals known to harbour the brucella organisms should be suspected as having cardiac manifestations of brucellosis until otherwise proved.⁶

In this report we describe clinical and laboratory observations in five children with cardiac involvement due to infections with *Brucella melitensis*. Paediatric patients with this complication have not been described in detail before.

Case reports

Case 1. This boy was admitted to a neighbouring hospital at the age of 5 years with a history of arthralgia for two weeks, high fever for 10 days, and acute arthritis of both knees for one week before admission. On examination a pansystolic murmur grade 3/6 was heard over the apex propagating to the axilla. Radiological examination of the chest yielded normal results. An electrocardiogram (ECG) showed left ventricular hypertrophy, and a diagnosis of acute rheumatic fever with arthritis and carditis was made. The laboratory findings included a white cell count of 15 400/mm³, erythrocyte sedimentation rate 24 mm in the first hour, and antistreptolysin O titre 625 TU. Treatment with steroids and aspirin was given over a period of three weeks and three months, respectively, with no obvious cardiac improvement. One year later he was

admitted to our hospital with a history of high fever for one week and arthralgia, weakness, and malaise since being discharged one year before. A pansystolic murmur grade 3/6 propagating to the axilla was heard. Left ventricular enlargement was seen on chest x ray film. ECG showed left ventricular hypertrophy. The laboratory findings included a white cell count of 3400/mm³ with 63% lymphocytes, erythrocyte sedimentation rate 20 mm in the first hour, antistreptolysin O titre 625 TU, and raised concentrations of immunoglobulins G and M. The brucella agglutination titre was 1:1280, and *B. melitensis* biotype 1 was isolated from repeated blood cultures. Echocardiography showed vegetations over the mitral valve and rupture of the chordae tendineae. Treatment with streptomycin 15 mg/kg 12 hourly and tetracyclines 10 mg/kg six hourly was given over a period of two and three weeks, respectively. The patient's general condition improved dramatically within one week after the start of the treatment. During one year of follow up his general well being has been unremarkable, although the cardiac murmur has remained unchanged.

Case 2. This boy was admitted to our hospital at the age of 10 years with a history of high fever and arthritis of the left knee for two days. On examination a pansystolic apical murmur grade 3/6 propagating to the axilla was heard. Ectopic heart beats were recorded on ECG that also included a prolongation of the PR interval. Radiological examination of the chest yielded normal results. The

laboratory findings included a white cell count of 4000/mm³ with 65% lymphocytes, erythrocyte sedimentation rate 25 mm in the first hour, and antistreptolysin O titre 625 TU. He was diagnosed as a case of acute rheumatic fever and treated with steroids and aspirin as case 1 had been. After withdrawal of the treatment he presented with arthritis of the right knee and fever. On examination the cardiac findings were the same as before. Also the chest x ray film showed no change. Echocardiography showed normal valves but sluggish myocardial function. The laboratory findings included a white cell count of 3900/mm³ with 61% lymphocytes, erythrocyte sedimentation rate 40 mm in the first hour, and antistreptolysin O titre 1250 TU. The brucella agglutination titre was 1:1280, and *B. melitensis* biotype 2 was isolated from blood cultures. Treatment as in case 1 was started and a pronounced clinical improvement was noted after only four days. During three months of follow up the cardiac murmur was unchanged but did not propagate. The echocardiographic changes normalised subsequently.

Case 3. This girl presented at 11 years of age with high fever for two weeks and arthritis of the left hip and right ankle for one week. On examination a pansystolic murmur grade 3/6 propagating to the axilla was heard. Radiology of the chest yielded normal results. ECG showed left ventricular hypertrophy and echocardiography showed mitral incompetence but no vegetations. The laboratory findings included a white cell count of 3400/mm³ with 67% lymphocytes, erythrocyte sedimentation rate 50 mm in the first hour, antistreptolysin O titre 625 TU, and raised concentrations of immunoglobulins G and M. *B. melitensis* biotype 1 was isolated from repeated blood cultures, and the brucella agglutination titre was 1:1280. Oral treatment with trimethoprim/sulphamethoxazole 4/20 mg/kg 12 hourly was started and given over a period of one month. The brucella titre dropped to 1:640 and the left ventricular hypertrophy and mitral incompetence disappeared. The child, however, continued to consume raw goat's milk and two months after finishing the treatment she was again admitted to hospital with a history of fever for two weeks and arthritis of the left hip and right ankle for one week. The brucella agglutination titre was 1:2560. There was a reoccurrence of left ventricular hypertrophy and mitral incompetence, and repeated blood cultures grew *B. melitensis* biotype 1 again. Oral tetracyclines and intramuscular streptomycin as in case 1 were given and resulted in a considerable improvement during the first week of treatment. During two years of follow up no further relapses

Table Summary of important findings in five infants with brucella carditis

Case	Diagnosis	Age (yrs)	Intake of fresh milk	Duration of fever (wks)	White blood cell count (/mm ³)	Lymphocytosis (%)	Brucella titre	Blood culture	ECG	Echocardiography	Treatment
1	Endocarditis	6	+	1	3400	63	1:1280	<i>Brucella melitensis</i> type 1	Left ventricular hypertrophy	Mitral valve vegetations	Streptomycin + tetracyclines
2	Endocarditis	10	+	0-3	3900	65	1:1280	<i>B. melitensis</i> type 2	Left ventricular hypertrophy Increased PR interval	Normal	Streptomycin + tetracyclines
3	Myocarditis	11	+	2	3400	67	1:2560	<i>B. melitensis</i> type 1	Left ventricular hypertrophy	Mitral insufficiency	Streptomycin + tetracyclines
4	Myocarditis	10	+	1	4300	76	1:2560	<i>B. melitensis</i> type 1	Left ventricular hypertrophy Increased PR interval	Mitral insufficiency	Streptomycin + tetracyclines
5	Myocarditis	8	+	2	8400	66	1:640	<i>B. melitensis</i> type 1	Supraventricular ectopic beats Increased PR interval	Decreased myocardial function	Streptomycin + tetracyclines

have been noted. The ECG yields normal results, but an apical systolic murmur grade 1-2/6 without propagation is still heard.

Case 4. This 10 year old boy presented with a history of arthralgia, weakness, and malaise for one month and high fever for one week. Examination showed an apical systolic murmur grade 2-3/6 with propagation to the axilla. A chest x ray film yielded normal results. ECG showed left ventricular hypertrophy and prolongation of the PR interval. Echocardiography showed mitral incompetence but no vegetations. The laboratory findings included a white cell count of $4300/\text{mm}^3$ with 76% lymphocytes, erythrocyte sedimentation rate 26 mm in the first hour, and antistreptolysin O titre 625 TU. Concentrations of IgG and IgM immunoglobulins were raised. The brucella agglutination titre was 1:2560, and *B. melitensis* biotype 1 was isolated from blood cultures. Treatment with intramuscular streptomycin and oral tetracyclines as in case 1 was started. The patient was afebrile on the third day of treatment. The cardiac murmur disappeared after three months. The ECG and echocardiographic changes returned to normal. During 18 months of follow up no further attacks have been noted.

Case 5. This 8 year old boy was admitted with high fever and arthralgia of two weeks' duration. Examination of the heart showed normal findings. ECG showed prolongation of the PR interval with supraventricular ectopic beats. Echocardiography showed normal valves but sluggish myocardial function. A chest x ray film yielded normal results. The laboratory findings included a white cell count of $8400/\text{mm}^3$ with 66% lymphocytes, erythrocyte sedimentation rate 54 mm in the first hour, and antistreptolysin O titre 1250 TU. Concentrations of IgG and IgM immunoglobulins were both raised. The brucella agglutination titre was 1:640, and *B. melitensis* biotype 1 was isolated from blood cultures. Treatment as in case 1 was started. Pronounced clinical improvement was noted on the fifth day of treatment. The initial ECG and echocardiographic findings returned to normal subsequently.

The clinical and laboratory findings in all our patients are summarised in the Table. All the patients had ingested fresh, unpasteurised goat's milk. They were all treated with streptomycin and tetracycline.

Discussion

Cardiac involvement in brucellosis is rare.¹⁻⁹ According to O'Meara *et al*⁷ it is difficult to assess its

real incidence as reports vary. All the previously reported cases were adults in whom the endocarditis generally followed a fulminant course, either ending fatally or needing emergency valve replacement.^{8,9} Our five cases were collected during a five year period when altogether we had 300 cases of childhood brucellosis in our hospital. This gives an incidence of 1.7% for this complication in the paediatric age group.

We have been unable to find any previous report on cardiac brucellosis in children. Based on a comparison with adult patients, it seems from our patients that cardiac involvement in childhood brucellosis does not follow the fulminant course seen in adults. All our patients responded promptly to medical treatment.

It should be emphasised, however, that three of our patients probably had myocarditis, whereas two had mitral valve involvement. In most of the reported adult cases the aortic valves were affected.¹⁰

It is difficult to distinguish acute brucellosis from acute rheumatic fever, especially if cardiac involvement is noted. Both diseases may present with fever, arthralgia/arthritis, splenomegaly, and high erythrocyte sedimentation rate, but acute brucellosis only occasionally shows leucocytosis.¹¹ Our first patient did show leucocytosis on his first admission, which made rheumatic fever a more likely diagnosis. When he was admitted one year later the clinical and biochemical findings were in favour of a brucella infection of an already damaged valve during an initial septicaemic phase of the disease.

Two of our cases (Table) showed complete recovery of the valves rendered incompetent through the infection from a failing left ventricle. This speaks in favour of the diagnosis of myocarditis in these children. Though in case 3 a soft systolic murmur is still heard over the apex, we believe that this patient also had myocarditis giving rise to a functional and not an organic incompetence.

The electroencephalographic changes in brucella carditis mainly include affection of the conduction system as verified from postmortem studies, but atrioventricular or right bundle branch block has been seen in fulminant cases of brucella carditis.¹² A prolonged PR interval was seen in three of our patients and supraventricular ectopic beats in one.

Echocardiography is usually helpful in detecting valvular vegetations and may increase the ability to establish the diagnosis of infective endocarditis. We observed vegetations on the mitral valve in one patient, a picture of mitral incompetence in two, and sluggish myocardial function in one.

All our patients were treated with a combination of streptomycin and tetracycline, an effective combination recommended for the treatment of severely

ill patients with brucellosis.¹³ All our patients were asymptomatic within one week after the start of the treatment.

It seems from our experience that even if cardiac involvement is a severe complication brucellosis in children, it carries a good prognosis. The long term prognosis is, however, uncertain and must be the topic for future evaluation. This is especially necessary in countries where brucellosis is an endemic disease and the ingestion of raw, unpasteurised milk is a widely spread habit.

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