

Thrombocytopenic purpura as only manifestation of brucellosis in a child

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SUMMARY: Yalaz M, Arslan MT, Kurugöl Z. Thrombocytopenic purpura as only manifestation of brucellosis in a child. Turk J Pediatr 2004; 46: 265-267.

Thrombocytopenic purpura associated with brucellosis has been rarely reported in the world literature. Thrombocytopenic purpura is generally part of the array of manifestations of brucellosis such as fever, arthritis, malaise and hepatosplenomegaly. We describe a nine-year-old girl who presented with thrombocytopenic purpura as the sole manifestation of brucellosis, which resolved with anti-Brucella chemotherapy. Her physical examination was remarkable for hepatomegaly of 3 cm and splenomegaly of 2 cm palpable below the costal margin. Initial laboratory investigations revealed isolated thrombocytopenia with platelet count of 11,300/mm³ and positive serology for Brucella. Thrombocytopenia resolved promptly with proper antibiotics on 7th day of treatment. Brucellosis should be included in the differential diagnosis of thrombocytopenic purpura in Brucella-endemic areas.

Key words: brucellosis, thrombocytopenic purpura.

Brucellosis continues to be a major public health problem in Turkey. Brucellosis may be the cause of many hematological abnormalities, including leukopenia and anemia during childhood^{1,2}. Thrombocytopenia is less common and is rarely severe enough to cause purpura and mucosal bleeding³. Thrombocytopenic purpura is usually part of the array of manifestations of brucellosis, such as fever, arthritis and hepatosplenomegaly. We report a nine-year-old girl in whom thrombocytopenic purpura was the only manifestation of brucellosis and which resolved after antibiotic therapy.

Case Report

A nine-year-old girl admitted with a two-day history of rash covering the body and mouth bleeding. On physical examination, her weight and height were at the 75th percentile (33 kg and 135 cm, respectively). Body temperature was 36.7°C, heart rate 112/min, and respiratory rate 20/min. Petechial-purpuric skin rash covered her body, more strikingly over the lower extremities and groin. Her liver was 3 cm and her spleen 2 cm palpable below the costal margins. Laboratory tests were as follows: hemoglobin, 12.1 g/dl; white blood cells, 7930/mm³ with 78%

neutrophils and 22% lymphocytes; platelets, 11.300/mm³; erythrocyte sedimentation rate, 13 mm/h; prothrombin time, 14.5 sec: international normalized ratio, 1.19; and partial thromboplastin time, 24.6 s. The fibrinogen level was 241.3 mg/dl (N: 125-300). Renal and liver function tests were within normal limits. Antinuclear antibodies and Coombs' test were negative. Adenosine deaminase level was 93.5 U/L (n<17 U/L). Bone marrow aspiration showed increased number of megakaryocytes but no evidence of hemophagocytosis. The diagnosis of acute idiopathic thrombocytopenic purpura was considered. For mucosal bleeding, local tranexamic acid (3 times daily for 3 days) was applied. Serological tests for Salmonella, Epstein-Barr virus (EBV) and cytomegalovirus (CMV) were negative. Brucella agglutinin titer was positive at 1: 640 and did not change after treatment with 2-mercaptoethanol. Blood cultures for brucella melitensis were sterile. Diagnosis of brucellosis was considered, and treatment was begun with doxycycline (200 mg/day) and rifampin (600 mg/dy). After seven days, the patient improved dramatically and thrombocytopenia resolved completely. After 10 days, she was discharged to complete therapy with

doxycycline and rifampin. In the 3rd week of follow up, hepatosplenomegaly disappeared. Adenosine deaminase levels, which were high at the diagnosis, returned to normal limits. A history of ingesting unpasteurized goat's milk cheese was defined, and family screening for brucellosis also revealed her sister to have brucellosis.

Discussion

Thrombocytopenia has been reported to occur in 1%-8% of patients with brucellosis and is generally mild³⁻⁵. In rare cases, thrombocytopenia can be severe and may cause purpura and mucosal bleeding^{3,6-8}. In these patients, thrombocytopenic purpura is part of the array of manifestations of brucellosis such as fever, malaise, arthritis, hepatosplenomegaly and lymphadenopathy⁹. We describe here a girl in whom severe thrombocytopenic purpura was the sole manifestation of brucellosis and which resolved promptly with specific anti-Brucella chemotherapy.

The mechanisms responsible for thrombocytopenia in brucellosis is not clear, but some mechanisms have been proposed, such as hypersplenism, disseminated intravascular coagulation (DIC), bone marrow suppression, hemophagocytosis, and immune destruction of platelets. Splenomegaly is reported to occur in 46% of cases with complicated thrombocytopenia, which is higher than the 15% incidence reported for uncomplicated brucellosis^{3,10}. Platelet sequestration may be responsible for thrombocytopenia. In addition, the hypertrophied spleen can be a site for the production of cytotoxic antibodies¹¹, and occasionally it is a site of hemophagocytic histiocytes¹².

Disseminated intravascular coagulation is common in patients with bacterial septicemia. Bacterial products such as meningococcal endotoxin are implicated in the etiology of endothelial damage as inducing the dermal Schwartzman reaction. However, DIC seems to be rare in patients with brucellosis, because Brucella endotoxin is less toxic than lipopolysaccharides from other Gram-negative bacteria and does not induce the Schwartzman reaction³.

Bone marrow failure is considered to be responsible for thrombocytopenia in brucellosis. However, the majority of the patients presenting with thrombocytopenia have hypercellular bone

marrows with abundant megakaryocytes. The finding of hemophagocytic histiocytes in the marrow of patients with brucellosis has been reported by some authors^{3,4,7,13,14} and reactive hemophagocytosis has also been considered to be responsible for thrombocytopenia.

Another possible immune mechanism is the immune destruction of platelets^{3,15}. The presence of antiplatelet antibodies has been demonstrated in some patients with brucellosis associated with thrombocytopenic purpura. However, antiplatelet antibodies are difficult to detect by usual tests, and when present, there is often little correlation between their titer and the degree of thrombocytopenia. Therefore, evidence for an immune mechanism includes the apparent response to corticosteroids by the majority of patients and positive Coombs' tests³. We did not find any evidence of DIC, hypersplenism, hemophagocytosis or bone marrow suppression in our patient with thrombocytopenic purpura associated with brucellosis. She had hypercellular marrows with abundant megakaryocytes. Immune destruction of platelets was considered to be responsible for thrombocytopenia in our patient.

In conclusion, thrombocytopenic purpura may be the only manifestation of brucellosis, without other manifestations such as fever, malaise, arthralgia and lymphadenopathy. Brucellosis should be included in the differential diagnosis of thrombocytopenic purpura in areas endemic for brucellosis especially when there is a history of exposure to infected foods.

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