Case Report

Epistaxis as the initial manifestation of brucellosis

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Abstract

Brucellosis is a multisystem disease with a broad spectrum of clinical manifestations. Hematologic complications in the form of mild pancytopenia are occasionally reported in the course of acute brucellosis. Rarely, thrombocytopenia is severe and can be associated with purpura and mucosal bleeding. Epistaxis as the initial manifestation of brucellosis is a rarely reported phenomenon. A case of young adult is being reported who presented with epistaxis due to brucellosis-induced thrombocytopenia.

Key words: brucellosis; epistaxis; immune; thrombocytopenia

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Introduction

Brucellosis remains a major health problem in many parts of the developing world including Saudi Arabia. It is a multisystem disease with a broad spectrum of clinical manifestations. Like many viral and bacterial infections, brucellosis can cause hematological abnormalities e.g., anaemia, leucopoenia, thrombocytopenia, pancytopenia, and disseminated intravascular coagulation (DIC). Some cases of brucellosis with predominant hematologic changes may mimic a primary hematological disease.[1,2] Cases of brucella-induced isolated thrombocytopenia has been reported with an incidence varying from 1% to 8%.[2,3] The pathogenesis of thrombocytopenia in brucellosis includes several possible mechanisms such as hypersplenism, intravascular coagulation, bone marrow depression, hemophagocytosis and granulomas.[4-6]

Patients with severe thrombocytopenia can present with purpura and mucosal bleeding. Epistaxis due to reduction of platelets as the first manifestation of brucellosis is extremely rare and only few cases are reported in the literature.[4-9]

This case report describes a patient with thrombocytopenia who presented with epistaxis as his initial symptom but on investigation was finally diagnosed as having brucellosis.

Case Scenario

A 23-year-old man presented to the emergency department complaining of nose bleeding and malaise for two days. Two weeks before admission, he had consulted a private clinic for fever, sweats, fatigue and back pain. The symptoms had begun suddenly, but he admitted to weight loss of 10 kg over the previous 5 months. The patient stated that he had been in good health prior to the present illness. He denied headache, stiff neck, nausea, vomiting, diarrhea, cough, chest pain, abdominal pain, dysuria, petechiae, purpura, or rash. There was no history of contact with a sick patient. The risk factors for HIV were absent. He denied the use of unpasteurized milk or cheese but he was employed as a farmer frequently coming in contact with animals. The patient's past medical history was insignificant. His family history was noncontributory. He denied using alcohol, tobacco, and illicit drugs.

On physical examination, the patient appeared well developed and well nourished. His body temperature was 38 C, pulse 87 beats/min, respirations 18 breaths/min, and blood pressure 135/80 mm Hg. The pupils were equally round and reactive and extraocular movements were intact. The oral and nasal mucosae were dry but without inflammation .The neck was supple without masses or bruits. Examination of the heart and lungs was normal. The abdomen was nontender and there were no masses or hepatosplenomegaly. The examination of the extremities revealed no deformity, tenderness, or joint effusion. The skin and scalp were free of rash .The neurological examination was normal.

On laboratory testing, routine urine analysis (UA) was normal. Erythrocyte sedimentation rate measured 30 mm/h. His hemoglobin was 14.6 gm/dL and the hematocrit was 43.8%. The white blood cell (WBC) count was 4100 cells/mm^3. The WBC differential was neutrophils 70%, bands 2%, lymphocytes 17%, monocytes 5% and eosinophils 5%. The platelet count was 37,000/mL. The fibrinogen levels, prothrombin time, and activated partial thromboplastin time were all normal. The peripheral blood smear revealed normal morphology of RBCs and platelets with no circulating blast cells or leukoerythroblastic picture.

Serum bilirubin levels were normal but some liver enzymes were elevated alanine aminotransferase (ALT) 127 U/L, aspartate aminotransferase (AST) 141 U/L, and alkaline phosphatase 280 U/L. Serum electrolytes, BUN, creatinine, and glucose were normal. Coombs test, antinuclear antibody, serological tests for HbsAg, anti-HCV, HIV, Rubella and cytomegalovirus were all negative. Abdominal ultrasonography was unremarkable. The chest radiograph was negative for masses, infiltrates, hilar adenopathy, and cardiomegaly. A 12-lead electrocardiogram was normal.

Because of the patient's fever, malaise and being from a rural community Brucella agglutination test was ordered and blood cultures were drawn. The blood culture revealed no growth. While hematology aspects were being debated and bone marrow examination was planed, the result for brucella was received and the agglutinin titer for brucella melitensis was positive at 1:5120. A diagnosis of brucellosis with thrombocytopenia was established, and treatment was begun with doxycycline 100 mg PO twice daily for six weeks plus streptomycin 1 gram IM daily for 21 days.

After six weeks of initiation of treatment, the platelets and leukocytes counts had returned to normal and agglutination titers were progressively declined to 1:640.

Discussion

Brucellosis is an important enzootic infection because it remains endemic worldwide with a predominance of rural population.[10] The patients of brucellosis are still seen in Saudi Arabia especially in the Qassim area. The humans acquire this infection through the consumption of contaminated milk, cheese, yoghurt and butter; while exposure to raw meat and direct animal contact may be responsible in some cases.[11,12] The consumption of untreated milk product is a common practice in rural areas.[13]

Most hematologic abnormalities that occur in patients with brucellosis are mild and resolve promptly with antimicrobial therapy.[14] In the course of human brucellosis, commonly seen hematologic abnormalities are mild anemia, leukopenia and thrombocytopenia. In a large series of almost 1,000 brucellosis cases, mild thrombocytopenia was present in almost 10% of patients on presentation.[15] However severe thrombocytopenia resulting in bleeding and even misdiagnosed as idiopathic thrombocytopenic purpura (ITP) has been rarely reported in patients with brucellosis.[16-18] About 3–19% of patients with brucellosis-induced thrombocytopenia may present with bleeding manifestations and it is more frequently associated with B. melitensis than with other Brucella species.[9] The severe thrombocytopenia with hemorrhages can result in serious consequences especially in case of cerebral hemorrhage. A mortality rate of 9.3% is reported by Young et al.[14]

The pathogenesis of thrombocytopenia in brucellosis has been widely debated in the literature and there appears to be a consensus that etiology may be multifactorial.[2] Theoretically, any bacterial or protozoal infection can be associated with thrombocytopenia that is caused by mechanisms such as increased clearance of damaged platelets with endotoxins, exotoxins, or platelet-activating factor or direct platelet toxicity caused by the microorganism, immune-mediated destruction of the platelets, and platelet adherence to damaged vascular surfaces.[19] Hematologic changes in the course of acute brucellosis usually take the form of mild pancytopenia, which is attributed to bone marrow suppression because brucella species express an affinity for reticuloendothelial tissue. Hypersplenism, in the same pathophysiological context, could in part be implicated in cases of brucella-related pancytopenia.[15] The predominant role of hypersplenism however can only be established in patients who present with pancytopenia, splenomegaly, and a normal bone marrow aspirate. There are reports of brucella-induced massive thrombocytopenia that responded to splenectomy.[14]

Other mechanisms implicated in platelet depletion in the course of brucellosis include hemophagocytosis [20] and disseminated intravascular coagulation (DIC).[21,22] In certain cases, brucellosis induces a severe immune reaction sometimes even with the presence of platelet antibodies. This autoimmune stimulation results in autoimmune hemolysis and platelet destruction, and such cases tend to present dramatically, with sever hemolytic anemia and hemorrhagic purpura.[7,16,17,23] Another mechanism that could be implicated in brucella-related

thrombocytopenia is granulomatous infiltration of the bone marrow in the chronic form of the disease.[15]

The mechanism of thrombocytopenia in the reported patient remains obscure because normal mean platelet volume (MPV) with absence of megakaryocytes and normal sized spleen rules out the brucellosis induced peripheral destruction of platelets.

It is well known that the most important therapy for infection-related thrombocytopenia is that directed at the underlying infection. The platelet recovery usually occurs within 2–3 weeks of initiating appropriate antimicrobial therapy.[3,9,14] The thrombocytopenia in this reported case quickly responded to a course of doxycycline plus streptomycin. In a review of literature on the subject, Young et al. reported an apparent response to corticosteroids by the majority of patients with brucella induced immune-mediated thrombocytopenia.[14] Corticosteroids are generally undesirable as a treatment for thrombocytopenia for patients with severe infection because of their potential for suppressing immune response. However, due to the high mortality rate, some authorities have proposed institution of high-dose parenteral glucocorticoids as an urgent treatment, which may result in increased platelet count and can be used to control bleeding until the microbial therapy takes effect.[9]

In conclusion, brucellosis should always be kept in mind in the differential diagnosis of isolated thrombocytopenia particularly when the disease is epidemiologically suspected. Patients from endemic areas presenting with fever and family history should be tested for brucellosis to avoid misdiagnosis of ITP.

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