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INTERNAL MEDICINE

□ CASE REPORT □

# An Uncommon Case of Acute Brucellosis Presenting with Severe Thrombocytopenia

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## Abstract

A 49-year-old man was admitted to the hospital with complaints of fatigue, epistaxis and a skin rash. The whole blood count revealed isolated thrombocytopenia (4,000/mL), and the patient was admitted to the hematology department with a diagnosis of immune thrombocytopenia. He did not respond to steroid treatment for 15 days, and a subfebrile fever developed during this period. A diagnosis of acute brucellosis was considered due to positive serological tests and a blood culture positive for *Brucella* spp. After starting doxycycline and rifampicin therapy, the patient's thrombocyte count increased to 15,000/mL on the third day, to 41,000/mL on the sixth day and was normal on the 21st day of treatment. A diagnosis of brucellosis must be considered in patients presenting with severe and isolated thrombocytopenia in countries where brucellosis is endemic.

**Key words:** thrombocytopenia, brucellosis, immune

**(Intern Med 51: ***-***, 2012)**
**(DOI: 10.2169/internalmedicine.51.7365)**

## Introduction

Brucellosis is a common bacterial zoonosis in our country and worldwide. In 2004, the reported morbidity rate was 26 per 100,000 and the mortality rate was 0.03 per million in our country (1). The seropositivity rate is 1.8% in the normal population and 6% in at-risk groups (2). In another study from Malatya, the seropositivity rate was found to be 5.1% in populations at risk (3). Brucellosis is one of the great imitators in the world of infectious diseases. It can mimic various multisystem diseases, showing wide clinical polymorphism, which frequently leads to misdiagnosis and treatment delay and further increases complication rates (4). This disease can involve many systems, including the reticuloendothelial system, musculoskeletal system, gastrointestinal system, cardiovascular system, lymphoreticular system and central nervous system, and can therefore present with a wide variety of clinical pictures and complications. Brucella infection can show many hematological signs such as anemia, thrombocytopenia, leucopenia and pancytopenia (5, 6). We herein present a case of isolated and severe thrombocytopenia diagnosed as immune thrombocytopenia due to the presence of bleeding signs.

## Case Report

A 49-year-old man who was employed in the farming and animal husbandry sector presented at the emergency service with listlessness, epistaxis, leg bruising and a rash inside the mouth and on the back. His symptoms had begun 10 days previously with weakness, weight loss and mild fever. His temperature had not been measured. The leg bruising and epistaxis had begun two days previously. A rash had appeared inside the mouth the day before admission. There was no history of arthralgia or sweating. A physical examination performed in the emergency unit revealed common ecchymotic lesions on the legs and petechiae on the back and inside the mouth. The general condition of the patient appeared good; however, he was cachectic. His vital signs were normal and his body temperature was 36.6℃. No hepatomegaly or splenomegaly was detected on the physical

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examination; however, ultrasonography of the abdomen demonstrated minimal splenomegaly (14.5 cm) with a few calcific foci in the spleen secondary to a past infection. There were no other pathologic findings. The laboratory results obtained on presentation were as follows: hemoglobin: 13.4 g/dL, leukocytes: 6,000/mL and thrombocytes: 4,000/mL. The C-reactive protein level was 35 mg/L on admission. The erythrocyte sedimentation rate was not evaluated. The patient was therefore admitted to the hematology department in order to investigate the etiology of thrombocytopenia. Treatment with prednisolone at a dose of 1 mg/kg/day was started based on a preliminary diagnosis of immune thrombocytopenia (ITP). A bone marrow biopsy performed on the 6th day of prednisolone treatment showed normal erythroid and myeloid cell maturation, the presence of megakaryocytes and no nonhematopoietic cells. The patient's thrombocyte count did not go over 5,000/mL despite 15 days of 64 mg of prednisolone tablet od treatment. Hematology department follow-up visits revealed a subfebrile temperature, brucella agglutination tests were positive for Rose Bengal and the patient exhibited a Wright test value of 1/320. The patient was therefore transferred to our department with a diagnosis of brucellosis. He was placed on treatment with doxycycline at a dose of 100 mg bid and rifampicin at a dose of 600 mg od, and the thrombocyte count increased to 15,000/mL on the second day of treatment. The blood culture obtained before the administration of the anti-brucellosis treatment grew *Brucella* spp. The thrombocyte count was 41,000/mL on the sixth day of doxycycline and rifampicin treatment. The patient's general condition improved and the fever resolved. He was discharged and instructed to come to the outpatient department for follow-up. Tests performed on the 21st day of treatment showed a normal (150,000/mL) thrombocyte count. The brucellosis treatment was discontinued after eight weeks. The thrombocyte count was 256,000/mL on the 56th day of treatment. No recurrence was observed within one year.

## Discussion

Thrombocytopenia is a hematological sign that occurs in patients with brucellosis at a reported rate of 5-14% (7, 8). However, severe thrombocytopenia occurring in patients with brucellosis has been reported only rarely (9, 10). The presence of severe and isolated thrombocytopenia, intraoral petechiae, epistaxis and a purpuric rash on the trunk and legs led to a preliminary diagnosis of ITP in our patient. The patient did not respond to steroid treatment, and the severe thrombocytopenia continued. Brucellosis treatment led to a rapid increase in the thrombocyte count.

Immune-mediated thrombocytopenia is a clinically important mechanism that may be encountered during the course of brucellosis (11, 12). Brucella-associated thrombocytopenia can be associated with hypersplenism, autoimmune destruction due to the development of antithrombocyte antibodies, DIC, hemophagocytosis and granulomas in bone marrow (6, 9, 11, 13, 14). Sevinc et al. (12) presented the case of a patient who presented with thrombocytopenia of 9,000/mL and received a diagnosis of transient ITP. However, that case differs from ours, as the patient responded to steroid treatment. Gürkan et al. (11) presented the case of a patient with a thrombocyte count of 3,600/mL and severe epistaxis who responded to high-dose steroid treatment with 30 mg/kg of methylprednisolone. Our patient did not respond to 1 mg/kg/day of prednisolone administered for 15 days. Although the lack of response may be related to the steroid dose, a response within 48 hours to specific brucellosis treatment shows the importance of treating the cause directly. Thrombocytopenia that is induced directly by infection should obviously be treated by treating the infectious agent itself. The rapid response to antibiotic treatment observed in our case supports this notion. Young et al. (14) reported two cases of patients with high fevers, peripheral pain and thrombocyte counts of 3,000/mL and 5,000/mL. Both patients were found to have *Brucella melitensis*. The treatment for these two patients was reported to include platelet transfusion, fresh-frozen plasma, steroids and antibacterial drugs. However, one patient died due to intracranial bleeding.

ITP can only be diagnosed after excluding all other possible causes of thrombocytopenia. Our patient did not have a fever or any other signs indicating brucellosis on admission and was admitted to the hematology department with a preliminary diagnosis of ITP. The subfebrile fever observed during the clinical follow-up and the patient's occupation as a farmer (occupational exposure) indicated a diagnosis of brucellosis. The diagnosis was made according to the growth of the bacterial agent and serology. Although bacteria were grown in our case, we were not able to identify the species. Thrombocytopenia cases caused by both *B. melitensis* and *B. abortus* infections have been reported in the literature (14). Our patient had severe thrombocytopenia and symptoms that were similar to ITP. Our case also differed from other cases in that the patient did not respond to steroid therapy. Cases of steroid-refractory ITP have been reported, and treatment should be changed to intravenous immunoglobulin administration or splenectomy in life-threatening situations (15). Several authors have reported good responses to steroid treatment in patients with thrombocytopenia induced by *Brucella* spp. Plasma exchange, intravenous gamma globulin administration or antibacterial treatment only have also been used successfully in some patients (6, 11, 12, 14, 16). We found no brucellosis cases of steroid-refractory thrombocytopenia reported in the literature. It may be a good idea to evaluate steroid-refractory ITP patients for brucellosis. The lack of a response to steroid therapy by a patient with thrombocytopenia may be explained by the suppression of bone marrow by *Brucella* spp. The bacteria may also possibly cause destruction of thrombocytes in the periphery. In this case, the patient's response to antibacterial treatment showed that the thrombocytopenia was secondary to brucellosis.

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A diagnosis of brucellosis was suspected, and blood cultures and a serology test were performed in our case due to the patient's low-grade fever and occupational exposure. The patient was a farmer, and cheese is traditionally produced from raw milk in our region. Drinking raw milk is not a problem, while eating cheese produced from raw milk is an important risk. A diagnosis of brucellosis should therefore be kept in mind when encountering patients with either fever or relevant symptoms in patients from our region.

In conclusion, patients presenting with isolated thrombocytopenia that does not respond to steroid treatment should not immediately be considered to have refractory ITP. Brucellosis should also be considered in the differential diagnosis, especially in endemic regions. Starting brucellosis treatment promptly is of critical importance in controlling thrombocytopenia.

**The authors state that they have no Conflict of Interest (COI).**

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