

Intravenous Gamma Globulin is Effective as an Urgent Treatment in *Brucella*-Induced Severe Thrombocytopenic Purpura

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Severe thrombocytopenia is a rare hematologic manifestation of brucellosis, which can occasionally be associated with bleeding into the skin and from mucosal sites. Prompt recognition of this brucellosis complication and aggressive therapy is vital because the mortality rate associated with bleeding into the central nervous system is high. We report a case of a patient infected with *Brucella melitensis* who was admitted with a severe case of thrombocytopenic purpura. The patient responded well to intravenous gamma globulin (IVIg) treatment with platelet recovery within 2–3 days. For cases of *Brucella*-induced thrombocytopenic purpura, IVIg may be administered as an urgent therapy until the microbial therapy takes effect. *Am. J. Hematol.* 80:204–206, 2005. © 2005 Wiley-Liss, Inc.

Key words: brucellosis; thrombocytopenia; intravenous gamma globulin; treatment

INTRODUCTION

Brucella infection rarely causes hematological complications. Anemia and leukopenia are the most frequently observed hematological abnormalities in brucellosis [1,2]. Thrombocytopenia, reported in 1–26% of cases, can cause bleeding in only very rare cases [1–3]. Thrombocytopenia related to systemic infections may be due to a variety of causes: hypersplenism, bone marrow suppression, disseminated intravascular coagulation, increased clearance, immune-mediated destruction, hemophagocytosis, and adherence to damaged vascular surfaces [4–10]. The data is presently insufficient regarding the management of *Brucella*-associated bleeding and the time for antimicrobial therapy to take effect [10,11]. In this report, we discuss the management of a Turkish patient with brucellosis who presented with bleeding as the first manifestation of illness due to severe thrombocytopenia. Brucellosis is a common disorder in Turkey, especially in rural settings.

CASE REPORT

A 26-year-old female was admitted to the hospital with fever, purpura, and petechiae. Her previous

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history revealed the presence of fever, weakness, headache, and lumbago over a period of 3 weeks. She had a significant pallor, fever (39°C), tachycardia (100/min), petechiae, and ecchymoses on the lower extremities. There was no evidence of splenomegaly, hepatomegaly, and lymphadenopathy. A complete blood count revealed anemia (hemoglobin, 10.4 g/dL) and thrombocytopenia ($4 \times 10^9/L$). The reticulocyte index was 1.3%. A direct antiglobulin test was negative. Transferrin saturation and ferritin levels were 21% (normal range, 20–40%) and 15 ng/L (normal range, 22–322 ng/mL), respectively. Serum biochemistry, coagulation parameters (prothrombin time, activated partial thromboplastin time and fibrinogen level), vitamin B₁₂, and folic acid levels were in the normal range. Serological studies for hepatitis A, B, and C were negative. Test for anti-nuclear antibody, antineutrophil cytoplasmic antibody, Anti-ds-DNA, and rheumatoid factor were negative.

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A peripheral blood smear revealed hypochromia and microcytosis in the red blood cells with inadequate platelets. A bone marrow examination was normal except for an increased number of megakaryocytes. Because she was symptomatic and had severe thrombocytopenia ($4 \times 10^9/L$) with giant platelets in the peripheral smear, increased megakaryocytes in the bone marrow, the patient was placed on intravenous gamma globulin (IVIg) at 800 mg/kg/day for 3 days. On day 5, the platelet count increased ($55 \times 10^9/L$). While the etiology of the fever was being investigated, a positive agglutination test for brucellosis was documented at a titer of 1:1280. *Brucella* spp. was isolated from the blood cultures taken on the day the fever was present. The patient was removed from steroid therapy, and appropriate treatment for brucellosis of rifampicin (600 mg/day) and doxycycline (200 mg/day) was initiated; this brucellosis treatment was maintained for 6 weeks. During follow-up visits at month 1 and month 3, the platelet counts were $108 \times 10^9/L$ and $405 \times 10^9/L$, respectively (Fig. 1). Repeated cultures of blood and bone marrow as well as agglutination tests were negative.

DISCUSSION

Brucellosis is a disease leading to changes in hematological parameters [1,2,12]; its diagnosis is based on positive blood or bone marrow cultures. The most frequently observed hematological abnormalities in brucellosis are anemia and neutropenia [1,2], and thrombocytopenia is reported in 1–26% of cases [1–3]. Hemorrhages have been reported in 3–19% of patients with brucellosis, which is more frequently associated with *B. melitensis* than with other *Brucella* spp. The mortality rate, however, is as high as 9.3% [11].

It is well documented that appropriate antimicrobial therapy improves the clinical and hematological status of brucellosis patients. Platelet recovery usually occurs within 2–3 weeks of initiation of appropriate antimicrobial therapy [3,13]. IVIg may be used primarily when clinical situations require a transient

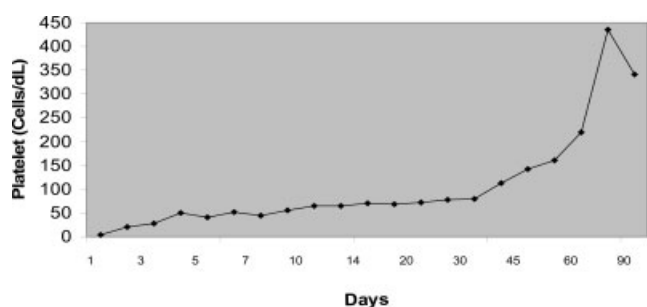


Fig. 1. Change of platelet count with IVIg and antibiotic therapy.

increase of the platelet count or when the use of glucocorticoids is contraindicated [14]. Our patient presented with severe bleeding symptoms (e.g., petechiae and ecchymoses) and displayed symptoms of idiopathic thrombocytopenic purpura (ITP), e.g., severe thrombocytopenia, inadequate platelets in the peripheral blood smear, and increased number of megakaryocytes in the bone marrow. Tsirka et al. reported a prompt hematological response to IVIg in a patient with *Brucella*-induced thrombocytopenia [15]. Therefore, we started IVIg as an urgent treatment and the patient responded well. Due to the high mortality rate, a short-term trial of IVIg treatment may be recommended in emergent cases to increase platelet count and control bleeding in these patients.

In conclusion, differential diagnosis of ITP should include brucellosis in patients presenting with thrombocytopenic purpura, especially in regions where brucellosis is endemic. IVIg treatment may be instituted as an emergent treatment which appears to result in improved clinical and hematological status pending anticipated effects of antimicrobial therapy.

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