



Severe Thrombocytopenia Associated with Brucellosis

Bruselloz ilişkili Ciddi Trombositopeni

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Abstract

Brucellosis is a zoonotic infection transmitted to humans by contact with fluids from infected animals or derived food products such as unpasteurized milk and cheese. This article describes a case of a 12-year-old patient who presented with a 15-day history of fever and pain in both legs and ankles, and was subsequently diagnosed with brucellosis. During follow-up, severe thrombocytopenia was detected along with widespread petechiae on the body, with no other clinical findings. The patient was conscious, and had normal vital signs. The patient, who was undergoing antibiotic treatment for brucellosis, developed uncontrollable epistaxis. Intravenous immunoglobulin and subsequently intravenous methylprednisolone were administered as the patient's bleeding remained uncontrollable. Mucosal bleeding was controlled after four days of methylprednisolone, nine days of doxycycline and rifampicin treatments, and six days of gentamicin treatment. Severe thrombocytopenia associated with brucellosis is a rare condition; therefore, we believe that our case can contribute to the medical literature.

Keywords: Brucellosis, thrombocytopenia, child

Öz

Bruselloz, insanlara enfekte hayvanların sekresyonları veya pastörize edilmemiş süt ve peynir gibi üretilmiş gıda ürünlerinden bulaşan zoonotik bir enfeksiyondur. Bu yazıda, 12 yaşında, 15 gündür devam eden ateş, her iki bacak ve ayak bileğinde ağrı nedeniyle başvuran ve bruselloz tanısı konulan, takibi esnasında vücutta yaygın peteşi gelişmesi üzerine ciddi trombositopeni saptanan bir olgu sunulmuştur. Hastanın başvurusunda bilinci açık, vital bulguları normaldi. Yaygın peteşi dışında bir klinik bulgu yoktu. Bruselloza yönelik antibiyotik tedavileri almakta olan hastanın takibinde durdurulamayan epistaksisi olması üzerine intravenöz immünoglobulin verildi ve ardından intravenöz metilprednizolon tedavisi başlandı. Metilprednizolon tedavisinin dördüncü, doksisisiklin, rifampisin tedavilerinin dokuzuncu, gentamisin tedavisinin altıncı gününde mukozal kanaması kontrol altına alındı. Bruselloz ile ilişkili kanamaya yol açabilecek ciddi trombositopeni nadir bildirilen bir durumdur, bu nedenle olgumuzun literatüre katkı sağlayacağını düşünmekteyiz.

Anahtar Kelimeler: Bruselloz, trombositopeni, çocuk

Introduction

Brucellosis is a chronic granulomatous infection caused by intracellular bacteria, which can lead to mortality and morbidity (1). Brucellosis can be transmitted to humans from secretions of infected animals (such as sheep, cattle, goats, pigs, and others) or through unpasteurized dairy products like milk

and cheese (2). Various hematological findings have been reported, including thrombocytopenia, anemia, leukopenia, pancytopenia and leukocytosis at the time of diagnosis or during the course disease (3).

This presentation focuses on a pediatric patient with brucellosis who had severe thrombocytopenia during their follow-up.

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Case Report

A 12-year-old male patient with a 15-day history of fever and pain in both legs and ankles, with no previously known illnesses, presented to another hospital. The *Brucella* standard tube agglutination test conducted at the hospital returned positive with a titer of 1/640. Subsequently, the patient started on doxycycline and rifampicin treatment. In the patient's medical history, he had a history of consuming cheese made from raw milk. Additionally, his family history indicated that his father had a *Brucella* infection five years ago. Upon follow-up, the patient was referred to our hospital due to the development of widespread petechiae across the entire body, and further investigations revealed thrombocytopenia.

The patient presented with a good general condition and was conscious upon admission. The recorded vital signs were a body temperature of 36.8 °C, a respiratory rate of 22 breaths per minute, a pulse rate of 104 beats per minute, and blood pressure of 110/60 mmHg measured from the left arm. During the physical examination, widespread petechial rashes, especially on the lower extremities, were noted. There were no signs of hepatosplenomegaly or lymphadenopathy. Examinations of other systems appeared normal.

The laboratory examination revealed the following results: Total white blood cell count was= 8350/mm³, hemoglobin was= 11.6 g/dL, platelet count was= 4000/mm³, alanine aminotransferase (ALT) was= 24 U/L, aspartate aminotransferase (AST) was= 28 U/L, blood urea nitrogen (BUN) was= 21 mg/dL, creatinine was= 0.45 mg/dL, activated partial thromboplastin time (aPTT) was= 29 seconds, international normalized ratio (INR) was= 1.17, direct Coombs test was negative, ferritin level was= 140 ug/L (Normal range: 13-150 ug/L), triglycerides were 112 mg/dL (Normal range: 0-150 mg/dL), and fibrinogen was= 280 mg/dL (Normal range: 200-400 mg/dL). Upon peripheral blood smear examination, no platelets were observed. Bone marrow aspiration was performed, revealing normoblastic erythropoiesis, adequate numbers of megakaryocytes, an increase in young megakaryocytes in some areas, and no blast formation or hemophagocytosis was observed. The bone marrow findings were consistent with immune thrombocytopenic purpura, although antiplatelet antibody testing could not be conducted. *Brucella* spp. was isolated in the blood culture taken from the patient.

The patient, who developed severe thrombocytopenia associated with brucellosis, had intravenous gentamicin added to the ongoing doxycycline and rifampicin treatment on the third day. Due to widespread petechiae and uncontrollable epistaxis along with tamponade application on the first day of gentamicin treatment, the patient received a single dose of 1 g/kg intravenous immunoglobulin (IVIG). Twenty-four hours after IVIG treatment, a follow-up complete

blood count was conducted, resulting in a platelet count of 1000/mm³. As the patient's mucosal bleeding persisted and the platelet count did not rise during follow-up, intravenous methylprednisolone at a dose of 30 mg/kg/day was initiated on the fourth day. On the fourth day of methylprednisolone treatment, and on the ninth day of doxycycline and rifampicin treatments, and the sixth day of gentamicin treatment, mucosal bleeding was completely controlled. On the eighth day of methylprednisolone treatment, the patient's complete blood count showed a platelet count of 78,000/mm³, and platelets were observed in clusters in the peripheral blood smear. As the platelet count increased and there were no active bleeding episodes, the clinically stable patient was discharged with a plan for continued treatment. Ten days after discharge, during a follow-up, the patient's platelet count was 267,000/mm³. The patient completed six weeks of doxycycline-rifampicin treatment without developing complications during follow-up.

Discussion

Brucellosis is a disease seen endemically in Türkiye, transmitted from animals to humans. It can manifest as acute, localized, or chronic. Acute brucellosis typically presents with fever, night sweats, joint pains, muscle aches, back pain, weakness, headache, dizziness, depression, and anorexia (1,4,5). In our case, the patient had fever and pain in both legs and ankles. Chronic brucellosis refers to patients with clinical symptoms persisting for over a year after the diagnosis (4, 6). Localized infection occurs in approximately 30% of cases, and brucellosis can affect any organ system (7-10).

In the literature, hematological abnormalities associated with brucellosis have been reported (11). A study conducted with 223 patients diagnosed with brucellosis revealed isolated thrombocytopenia in 8% of patients, with clinically detectable bleeding (such as epistaxis, gross hematuria, petechiae) observed in only three cases (1% of all cases) (12). Thrombocytopenia seen in brucellosis is usually in an isolated form, clinically and laboratory-wise mimicking idiopathic thrombocytopenic purpura. In most cases, it follows a clinically mild course (11). Severe isolated thrombocytopenia or severe pancytopenia is quite rare (13). Hemophagocytosis might be considered in patients with pancytopenia or bicytopenia (14). The pathogenesis of thrombocytopenia in brucellosis remains unclear; however, various mechanisms such as hypersplenism, hemophagocytosis, increased platelet clearance due to damage caused by endotoxins and exotoxins, platelet adhesion to vascular surfaces, and bone marrow suppression are thought to play a role (11).

While antiplatelet antibodies can cause peripheral immune destruction of platelets, detecting these antibodies through routine tests is quite challenging. Bone marrow aspiration and biopsy in thrombocytopenic patients with

brucellosis typically reveal hypercellularity along with megakaryocytic hyperplasia and rarely megakaryocytic aplasia. The clinical symptoms and signs of brucellosis patients presenting with thrombocytopenia are similar to those without thrombocytopenia. Findings such as petechiae, ecchymosis, and bleeding are often associated with the severity of thrombocytopenia. In rare cases presenting with bleeding despite mild thrombocytopenia, it has been suggested that this might be related to either platelet dysfunction or vasculitis, which is also rarely found in the etiopathogenesis of brucellosis (11). Here, we present a case of severe thrombocytopenia developing on the fourth day of brucellosis treatment, with signs of bleeding, leading to advanced treatment planning. The absence of splenomegaly, normal fibrinogen and triglyceride levels, and the lack of hemophagocytosis in the bone marrow examination led to the exclusion of macrophage activation syndrome.

Brucellosis treatment aims to control the disease and prevent complications, relapses, and sequelae (12). For children aged eight and above, combination therapy with tetracycline or, for those under eight, trimethoprim-sulfamethoxazole combined with at least one other agent (such as rifampicin, gentamicin, or streptomycin) is recommended (15). There is no specific recommended regimen for treating brucellosis with hematological manifestations. Generally, hematological laboratory abnormalities tend to improve with brucellosis treatment. In cases of thrombocytopenia accompanied by bleeding, short-term high-dose steroid and IVIG treatments may be considered (15). In the case presented, consecutive IVIG and high-dose steroid treatments were administered due to severe thrombocytopenia and bleeding.

Conclusion

Patients diagnosed with brucellosis and presenting with petechial rashes should prompt consideration of secondary hematological involvement related to brucellosis, and the potential for severe thrombocytopenia caused by the disease should not be overlooked. In this case, a patient with severe thrombocytopenia and serious mucosal bleeding while under treatment is presented and demonstrates successful management and resolution of the condition.

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