ABSTRACT: A case of severe thrombocytopenic purpura as the sole manifestation of brucellosis in an eight-year-old boy is presented. Clinical examination revealed mucosal hemorrhages and splenomegaly. The initial diagnosis was immune thrombocytopenic purpura (ITP) and he received intravenous gamma globulins and steroids with good hematologic and clinical response. His brucella agglutination titer was positive and he received treatment with intravenous gentamicin and oral co-trimoxazole with good response. Although mild hematologic manifestations can be encountered in brucellosis, severe thrombocytopenia is rare. Prompt recognition of this association is essential for early therapy. A brief review of thrombo-cytopenic purpura associated with brucellosis is presented.

INTRODUCTION

Mild hematologic abnormalities can be encountered during the course of brucellosis. However, severe thrombocytopenic purpura associated with brucellosis has rarely been described in children [1-2].

Only in very rare cases, thrombocytopenia is severe enough to cause bleeding. Prompt recognition of this complication of brucellosis and aggressive therapy are essential, especially if there is suspicion of exposure to contaminated food products. We present the case of an eight-year-old boy with severe thrombocytopenia associated with brucella infection.

CASE PRESENTATION

The patient is an eight-year-old boy previously healthy, transferred to our institution from the Bekaa valley in Lebanon for severe thrombocytopenia.

One month earlier he reported having soft stool streaked with fresh blood without accompanying symptoms. Four days prior to admission, he developed a petechial rash over the lower and the upper limbs, face and trunk, sparing the palms and soles. Two days later, he developed oral mucosal bleeding and epistaxis.

Peripheral blood smear showed giant platelets and bone marrow aspiration showed increased megakaryocytes with no evidence of hemophagocytosis. Brucella serology was positive at 1/10240. Blood and bone marrow cultures remained negative for brucella.

Abdominal ultrasound confirmed the splenomegaly. He was started on steroids and intravenous immunoglobulins at a dose of 1 gm/kg/day for two consecutive days with a rise in the platelet count up to 57000/mm³ the second day and resolution of the mucosal bleeding.

By the third day of admission, treatment for brucel-
Brucellosis was started and consisted of intravenous gentamicin (5 mg/kg/day every 8 hours) and oral co-trimoxazole (160 mg/kg every 12 hours). The patient showed good progression under treatment and by the fifth admission day, his CBC showed a platelet count of 338,000/mm³.

He received a total of fourteen days of gentamicin and six weeks of oral co-trimoxazole.

The abdominal ultrasound was repeated after 14 days and showed regression of the splenomegaly.

He was discharged on weaning doses of prednisone which was stopped completely after four weeks. The platelet count continued to be normal for over six months. Repeat brucella serology two months later was negative. The patient, seen a year later, was still doing well.

DISCUSSION

Brucellosis is primarily a zoonotic infection found in both domestic and wild animals. Humans are accidental hosts. It is known by Mediterranean fever, Malta fever, gastric remittent fever, and undulant fever. It can be acquired via exposure to infected animals or infected food.

Brucella species are facultative intracellular pathogens that are capable of surviving and replicating within phagocytic cells of the host. They are small, fastidious, non-sporing, gram-negative coccobacilli. They lack flagella, endospores, capsules, and naturally occurring plasmids. Their metabolism is oxidative, and all strains are aerobic.

Four species are pathogenic to humans, namely, *Brucella abortus* (found in cattle), *Brucella melitensis* (goats and sheep), *Brucella suis* (swine, reindeer, rodents), and *Brucella canis* (dogs). After gaining the body, the organisms are ingested by polymorphonuclears (PMN). Those that are not killed by PMN are ingested by macrophages and become localized within the body organs where they multiply to give focalized brucellosis.

The host response to infection with *Brucella abortus* is characterized by the development of tissue granulomas [1-2]. In contrast, the infection with the more virulent species (*Brucella melitensis, B. suis*) more commonly results in visceral microabscesses.

Duration of symptoms for more than thirty days before diagnosis is the major risk factor for developing focal disease (osteoarticular, genitourinary tract, central nervous system, heart and liver) [3-4].

Diagnosis is made by cultures kept for three weeks or longer due to slow bacterial replication. Bone marrow cultures were found to be more sensitive than blood cultures (92% vs. 70%, respectively), with a shorter time to detection [18].

Some serologic titers can help in the diagnosis like the SAT titers of 1:160 or higher which indicates active infection. Brucella antibodies can possibly cross-react with other organisms, such as *Verrucomicrobium* serotype O9, *Francisella tularensis*, and *Vibrio cholerae*.

In children, brucellosis is a mild self-limiting illness and is less chronic than in adults. Symptoms are nonspecific, usually occurring within two to four weeks of inoculation including weakness, excessive sweating, lethargy, anorexia, weight loss, arthralgia, myalgia, abdominal pain, and headache.

In the chronic form, the patient can show symptoms for over one year. An afebrile pattern is typical, with a history of myalgia, fatigue, depression, and arthralgias. Hematological abnormalities, ranging from a fulminant state of disseminated intravascular coagulopathy to subtle hematological alterations have been reported in brucella infections.

Anemia is the most common finding and has been reported in 44 to 75% of the cases. Some patients can have evidence of hemolysis [15]. Leukopenia has been described in about 33% of the cases. Thrombocytopenia is the least common and depending on the series has been found in 5 to 40% of the cases [15, 17].

Pancytopenia has been described in 6 to 14% of the cases [2, 4, 7-8].

In these situations, a bone marrow aspiration should be done and a specimen should be sent to culture. It is of note that hematological manifestations of the disease in endemic areas seem to be more common [16].

Akdeniz et al. reported 8% of isolated thrombocytopenia in 233 patients with brucellosis, but clinically detectable bleeding (epistaxis, gross hematuria, cutaneous petechiae) was seen in only 3 (1%) of cases. All these bleeding episodes were considered mild [19].

Moreover, isolated thrombocytopenia was not encountered in El-Eissa’s study that reported 5% of thrombocytopenia in a total of 110 children with brucellosis [15].

Thrombocytopenic purpura associated with brucellosis has rarely been described in children [1, 3-4, 10-11, 16]. The platelet count in the reported cases increased with either treatment with IVIG or corticosteroids, but in other studies, the treatment of brucellosis with antibiotics only was able to recover a normal platelet count. Most of these cases presented with fever and other symptoms suggestive of brucella.

The majority of the cases of brucella reported, showed mild thrombocytopenia but no bleeding complications and responded to treatment with antibiotics only [10]. Two patients presented with severe epistaxis in brucellosis-induced ITP [6, 10].

Young et al. reviewed 41 cases of brucellosis complicated by thrombocytopenia severe enough to cause purpura and mucosal bleeding [4]. The principle sites of mucosal hemorrhage included epistaxis (69%), gingivorrhea (44%) and hematuria (64%).

There are only few reports describing severe thrombocytopenia as the only manifestation of brucellosis [6-7, 14].

The etiology of thrombocytopenia in brucellosis remains obscure. Multiple possible mechanisms have been suggested such as hypersplenism, bone marrow suppression, disseminated intravascular coagulation, direct damage to platelets by viruses and bacteria, hemophagocytosis, granulomas and immune-mediated [2, 15, 17].

Concerning treatment of acute brucellosis in children
older than eight years, the World Health Organization (WHO) guidelines recommend rifampin (600-900 mg) and doxycycline (200 mg) daily for a minimum of six weeks.

Treatment in children less than 8 years of age requires rifampin and cotrimoxazole. Treatment of meningoencephalitis or endocarditis requires combination therapy with rifampin, a tetracycline, and an aminoglycoside.

Use of corticosteroids as adjunctive therapy to antibiotics may be of benefit in culture-proven meningitis.

CONCLUSION

Brucellosis can present with hematological manifestations only. Although these are often mild, they can sometimes be severe and result in significant bleeding. It might be worth checking brucella titer in every patient with thrombocytopenia coming from an endemic area for brucella, if there is any suspicion of exposure to infected food products, or if any other atypical symptoms are seen in a thrombocytopenic child such as splenomegaly, fever, or arthralgia.

REFERENCES