Thrombotic Thrombocytopenic Purpura in a Patient with Brucella Infection Is Highly Responsive to Combined Plasma Infusion and Antimicrobial Therapy

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Key Words
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Introduction
Thrombotic thrombocytopenic purpura (TTP) is a syndrome characterized by thrombocytopenia as well as microangiopathic hemolytic anemia and often accompanied by fever, renal failure and neurologic abnormalities. In adults, TTP is idiopathic in about one third of cases. However, in the rest, TTP is encountered in a variety of clinical situations such as viral, bacterial and mycobacterial infections, drug reactions, connective tissue disease, solid tumors, bone marrow transplantation and pregnancy \[1\]. Brucella infection as a causative agent of microangiopathic hemolytic anemia has been reported \[2\]. A case of TTP in a patient with brucellosis is reported here.

Case Report
A 51-year-old man was admitted to the hospital, complaining of a 2-day history of moderate confusion, low mood and dysarthria. Four months before admission, he had consulted a local practitioner for back pain, generalized weakness, anorexia, fever, jaundice, hematuria, dark urine, urinary tract symptoms, nausea and vomiting. Gentamycin (80 mg twice daily, 14 days) and a non-steroidal anti-inflammatory drug were administered. However, the symptoms persisted. On examination, the patient appeared...
A pentad of signs and symptoms has been associated with TTP: thrombocytopenia, microangiopathic hemolytic anemia, neurological abnormalities, renal failure and fever, as was the case with this patient.

Brucellosis is an important zoonotic disease, since it remains a worldwide public health problem. The use of a rifampicin-containing regimen is generally avoided in our region due to concerns regarding induction of rifampicin resistance, which may be problematic as in endemic tuberculosis [3–6]. Humans acquire the infection through the consumption of raw milk products, cheese and raw meat or direct animal exposure [7]. In Turkey, about 18,000 new cases of brucellosis are diagnosed each year. The prevalence of seropositivity in the Turkish population varies from 2.6 to 14.4%, depending upon the geographical location [8]. Thus, this patient, being from an area with a high incidence of brucellosis, displayed a high level of seropositivity. In patients with brucellosis pancytopenia, incidence is found in 3–21% of cases. Brucella infection as a causative agent of microangiopathic hemolytic anemia has been reported [2]. Microangiopathic hemolytic anemia caused by bacterial agents may occur due to release of circulating endotoxins and/or immune complexes in the circulation, which may result in alterations in the function of several organs [2].

The patient in this study showed hemolytic anemia, thrombocytopenia, schistocytes in the blood smear, reticulocytosis, increased serum LDH, fever, neurological abnormalities and renal impairment. The diagnosis of acute brucellosis was based on the presence of clinical signs and symptoms with \( >1:160 \) tube agglutination test [9].

Plasma infusion and exchange are usually employed with the rationale of restoring a component that is missing in the patient’s plasma, possibly an enzyme, that by modulating protease activity of Willebrand factor in handling may prevent abnormal fragmentation of that molecule during the acute phase of the disease [10]. It has
been suggested that fresh-frozen plasma infusions may have an effect similar to plasma exchange, provided that patients can tolerate the volume load [11]. In this patient, a rapid improvement in platelet count, LDH level, hemolytic anemia and neurologic symptoms was observed with treatment of fresh-frozen plasma infusions combined with specific antimicrobial therapy. Therefore, in this case, it was thought that TTP was due to brucella infection. Therapies (i.e. plasma exchange or infusion) aimed at stopping the microangiopathic process and TTP should always be tried. However, this approach is seldom effective in secondary forms, where the outcome mainly depends on the prognosis of the underlying condition [12]. Therefore, specific therapy should be started as soon as the diagnosis of the predisposing condition has been established in order to effect disease recovery and minimize the risk of sequelae. The treatment recommendation is to continue therapy until complete disease remission is achieved. Although short-term plasmapheresis may be applied as an urgent therapy, in addition to antimicrobial therapy, in infection-induced thrombotic microangiopathy, the therapy of underlying infection together with plasma was successful in this case of brucellosis-induced TTP.

**Conclusion**

This report shows that therapy of underlying infection together with plasma infusion may be a successful treatment option for brucellosis-induced TTP.

**References**