Correspondence

Brucellosis and thrombocytopenia

Dear Sir,

We have read the article by Hussain et al published in the Saudi Medical Journal regarding Brucellosis and thrombocytopenia.[1] It was very interesting and the authors deserve congratulations for managing the patient so well. Our comments regarding this article are as follows. Brucellosis is endemic in Saudi Arabia and any patient presenting with fever, arthralgia and low backache should be screened for brucellosis. Brucellosis is the most common diagnosis made in expatriate farm workers in our practice. Symptoms are non-specific, as are the clinical signs. Splenomegaly is found in 25% of our patients and the most common laboratory findings are thrombocytopenia, leucopenia, and rise in serum glutamic-oxaloacetic transaminase (SGOT) / serum glutamic-pyruvic transaminase (SGPT) without clinical hepatitis and anemia in that order of frequency. In fact, the most common cause of thrombocytopenia, with or without leucopenia, is brucellosis followed by viral fever in our practice. Chronic liver disease and hypersplenism come next. Although a 2-drug treatment is widely recommended for brucellosis, we have found a very high relapse rate with this regime. We use a 3-drug regime consisting of streptomycin 1 gm intramuscularly daily for an initial 3 weeks and doxycycline 100 mg BD and septrin one and a half tablet (Trimethaprim: sulphamethaxazole 240:1200 mg) BD for 6 weeks (starting all together) with excellent results. Rifampicin is reserved for pregnant females only, according to a Ministry of Health circular and also in view of a possible resistance which might develop to this drug. Rifampicin also forms the corner stone of anti-tubercular drug therapy and its widespread use might lead to resistant strains of tubercle bacilli in the community. Both thrombocytopenia and hemolytic anemia in brucellosis are well reported in the literature.[2] Postulated mechanisms for thrombocytopenia are hypersplenism, reactive cytophagocytosis, release defect from marrow and immune destruction of platelets.[3] In a series of brucellosis patients Garcia et al[4] found that bone marrow was hypercellular in 70% of patients and normocellular in 28% of patients. Direct correlation was found in patients showing cytophagocytosis and peripheral hematological abnormalities. Although this is considered to be the most important mechanism for thrombocytopenia in brucellosis, immune mediated destruction as well as megakaryocytic aplasia are also well known. The mechanism of thrombocytopenia in brucellosis as reported by the authors is indirect. Disseminated intravascular coagulation (DIC) was not seen in the patient, although fibrinogen degredation products (FDP) and fibrinogen levels are not reported in the case report. Rise in platelet associated immunoglobulin, as reported in septicemia patients, cannot be automatically applied to this patient. In fact, anti-platelet antibodies should have been carried out to prove the point. Hyergammaglobulinema is not the evidence, as, hypergammaglobulinema occurs in brucellosis as a response to the invading organism like in any other infection. Brucella agglutination test or 2-Mercapto-Ethanol test (2ME-test) in fact measures immunoglobin levels of the patient. Rise in total immunoglobulin levels does not prove that accelerating destruction of platelets is immune mediated. Although, splenomegaly can occur in immune mediated thrombocytopenia, it is difficult to prove that it is due to autoimmune thrombocytopenia in view of acute brucellosis itself causing splenomegaly. The patient also had anemia, a drop of Hemoglobin from 12.4 gm/dl to 8.3 gm/dl, so much so that the patient required 2 units of packed cells. There was no obvious significant cause of bleeding, so thrombocytopenia was not the only presentation. Coombs test was not carried out; peripheral blood film was not mentioned in the report; and bone marrow showed a normal cellular pattern. Though it rules out secondary invasion and primary bone marrow disorder (megakaryocytic aplasia or hypoplasia), it does not confirm the autoimmune nature of thrombocytopenia.

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Reply from the Author

Dear Sir,

We thank Dr. Khan and Dr. Hateeti for their interest and comments on our publication Brucellosis associated with thrombocytopenia.[1] We entirely agree with regards to the endemic nature of the disease in Saudi Arabia and the need for screening for brucellosis in any patient presenting with fever, arthralgia and low backache. The association of thrombocytopenia with brucellosis is often encountered in practice as mentioned by them and this fact has been referred to by us.[5] However, brucellosis associated with symptomatic thrombocytopenia is comparatively rare and this is the reason for publishing this case report. Although for the past 10 years we have investigated, diagnosed and managed a number of cases of brucellosis, as

mentioned in our report this was the first such case presenting with bleeding tendencies.[1] We agree with Dr. Khan and Dr. Al-Hateeti regarding reservation of Rifampicin as an anti-tubercular drug therapy. However, the treatment regime differs and depends upon the choice of the attending physician. Furthermore, Rifampicin has been included as one of the drugs that can be used in cases of brucellosis according to the Ministry of Health policy on treatment of brucellosis. The emergence of resistant tubercle bacilli is more of a problem where tuberculosis is endemic and rampant in developing countries such as India, Pakistan, Bangladesh etc. Such endemicity and rampant spread of tuberculosis is not found in the Kingdom. The mechanism of thrombocytopenia as has been mentioned is indirect. Since DIC was not suspected in our patient and FDP levels were within normal limits, we did not think it necessary to mention it. Yes, we agree that the rise in immunoglobulin levels is not direct evidence, but only a pointer towards the destruction of platelets, since we did not have the facilities to look for anti-platelet antibodies. Indeed, there was a drop in the level of hemoglobin as the patient presented with extensive bleeding without any obvious cause except thrombocytopenia. Many patients with brucellosis and thrombocytopenia do not present with bleeding. Peripheral blood film was normal and was not mentioned as bone marrow also showed a normal picture. Moreover, it is not necessary to mention all the investigations carried out which are within normal limits. Since the patient responded to antibrucella, steroid and immunoglobulin therapy, and as there was no other obvious cause for thrombocytopenia, it was postulated that thrombocytopenia was immune mediated secondary to brucellosis and causing splenomegaly as mentioned in our discussion.

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