Severe Thrombocytopenia and Hemorrhagic Diathesis due to Brucellosis

Hasan Karsen MD1, Fazilet Duygu MD2, Kubilay Yapıcı MD3, Ali İrfan Baran MD3, Huseyin Taskiran MD4, İrfan Binici MD3

Abstract

Background: We aimed to examine cases of brucellosis that presented with severe thrombocytopenia and hemorrhagic diathesis.

Methods: A total of 10 brucellosis cases with severe thrombocytopenia were included in this case-series study. Patients' files were reviewed for their clinical and laboratory findings, as well as clinical outcomes and complications. Platelet counts of < 20000/mm³ were diagnosed as severe thrombocytopenia.

Results: The lowest thrombocyte count was 3000/mm³ while the highest was 19000/mm³ (mean: 12000/mm³). Patients had the following symptoms: epistaxis (7 cases), petechia with epistaxis (4 cases), bleeding gums (3 cases), ecchymosis with epistaxis (2 cases), melena and renal failure (2 cases), and hematuria (1 case). Patients were given rifampicin and doxycycline along with supportive hematological therapy. All were treated successfully with no evidence of recurrence at follow-up visits.

Conclusion: Since brucellosis is endemic in developing countries, it must be considered in the differential diagnosis of cases that present with severe thrombocytopenia and hemorrhagic diathesis.

Keywords: Brucellosis, hemorrhagic diathesis, severe thrombocytopenia


Introduction

Brucellosis is a multisystem disease with a wide variety of symptoms that include hematological abnormalities such as anemia, thrombocytopenia, pancytopenia and leucopenia. Disseminated intravascular coagulation (DIC) and hemorrhagic diathesis are rarely seen. Various rates of thrombocytopenia due to brucellosis have been reported; however, to the best of our knowledge, all published studies except for case-reports regarding severe thrombocytopenia due to brucellosis were pediatric case-series, until now. In this paper, 10 adults cases with severe thrombocytopenia and hemorrhagic diathesis due to brucellosis have been presented.

Materials and Methods

This was a case-series study. Patients' files were reviewed for their clinical and laboratory findings, symptoms, prognosis, age and gender as well as complications and clinical outcomes. The study protocol was approved by the local research committee for ethics. The Brucella Wright test; blood culture; complete blood count; erythrocyte sedimentation rate (ESR); C-reactive protein (CRP); liver and renal function profiles; urinalysis; IgM antibodies against brucella with a titer of ≥ 1:160 by the standard tube agglutination test (Brucella abortus antisera, Cromatest, Linear Chemicals, Barcelona, Spain) and/or by isolation of brucella from blood (BACTEC, Becton Dickinson, USA) in addition to clinical symptoms consistent with brucellosis. Anemia, thrombocytopenia, and leucopenia were defined as hemoglobin (Hb) levels of < 12 g/dL, a platelet count of < 150000/mm³, and leucocyte count of < 4000/mm³, respectively. Platelet counts < 20000/mm³ were considered as severe thrombocytopenia.

Results

There were 4 male and 6 female patients with severe thrombocytopenia. Patients' mean age was 35.24 ± 6.12 years (range: 18 to 64 years). Standard agglutination test was positive in all patients, however B. melitensis was present in the blood cultures of only 3 patients.

Pancytopenia was present in 5 cases, bicytopenia (thrombocytopenia and anemia or thrombocytopenia and leucopenia) was seen in 4 cases, and there was only one case of isolated thrombocytopenia. The lowest thrombocyte count was 3000/mm³ while the highest was 19000/mm³ (mean: 12000/mm³). The mean Hb level was 9.17 g/dL and white blood cell level was 5720/mm³. Totally, the mean decrease in thrombocytes was 92% while it was 23.6% in Hb levels. There was no decrease in white blood cell count.
As seen in Table 1, clinical symptoms were as follows: epistaxis (7 cases), petechia with epistaxis (4 cases), bleeding gums (3 cases), ecchymosis with epistaxis (2 cases), melena and renal failure (2 cases), and hematuria (one case). The following elevated laboratory abnormalities were present: ESR (6 cases), CRP (10 cases), PT (7 cases), PTT (2 cases), and PT together with aPTT and INR (one case). The one case which had elevated PT, aPTT and INR also had a low fibrinogen result. All patients were treated with rifampicin and doxycycline and platelet suspensions. Hb levels were < 8 gr/dL in 4 patients and each of them received whole blood transfusions. All cases were negative for CCHF, enteric fever, malaria, acute viral hepatitis, and toxoplasmosis.

### Discussion

Mild hematological abnormalities such as anemia and leucopenia are common in the course of human brucellosis. Severe thrombocytopenia, acute hemolysis, DIC, hemorrhagic diathesis, immune thrombocytopenia, capillary leak syndrome (CLS), thrombotic thrombocytopenic purpura (TTP), and Evan’s syndrome are rarely seen.4–10 In our study, the mainly affected blood elements were thrombocytopenia (TTP), and Evan’s syndrome are rarely seen in brucellosis,4,6,15 in our study all cases had severe thrombocytopenia and bleeding disorder due to brucellosis have been reported.16–18 Although severe thrombocytopenia, bleeding disorder, DIC, and thrombotic thrombocytopenic purpura (TTP) are rarely seen in brucellosis,4,6,15 in our study all cases had severe thrombocytopenia and bleeding disorders, 2 cases had TTP, and one case had DIC.

According to a study by Kiki et al., a 19-year-old woman presented with complaints of headache, fever, sweating, malaise, and jaundice. Her clinical signs and laboratory findings were consistent with TTP. She received plasma exchange and antibiotic therapy.17 In a case presented by Erdem et al., a 51-year-old man had complaints of moderate confusion, depressed mood and dysarthria, fever (38.5°C), jaundice, and petechial-purpuric skin lesions. Laboratory tests showed white blood cell count of 9600/mm³, Hb 7.1 g/dL, and platelets 18000/mm³. He received a plasma infusion and antimicrobial treatment.18

The clinical picture of our fifth case was as follows: confusion and speech disturbance, fever of 38.8°C, thrombocyte count of 10000/mm³, Hb of 5.5 mg/dL, creatinine level of 9.1 mg/dL (normal: 0.8 – 1.2), total bilirubin of 4.1 mg/dL (normal: 0.2 – 1.2), and indirect bilirubin of 3.4 mg/dL (normal: 0 – 0.75). He received thrombocyte infusion and antimicrobial treatment.

Our eighth case had the following clinical symptoms: convulsion and hallucinations, loss of consciousness, fever of 39.8°C, thrombocyte count of 16000/mm³, Hb of 4.7 mg/dL, creatinine level of 2.52 mg/dL, total bilirubin level of 4.8 mg/dL, and indirect bilirubin level of 4 mg/dL. He received antimicrobial treatment, platelet suspensions and whole blood transfusions.

Our third patient presented with DIC, whose laboratory findings were: PT 26 sec (normal: 10 – 15), active partial thromboplastin time (aPTT) 59 sec (normal: 26 – 41) and INR 1.8 (normal: 0.8-1.22), fibrinogen 67 mg/dL (normal: 150 – 400), and D-dimer 4.05 ug/mL (normal: 0 – 0.4). He received antibiotics, platelet suspensions and fresh-frozen plasma.

Bleeding disorders such as epistaxis and hematuria have rarely been reported.19 We have not seen any case report of brucellosis-induced melena, gum bleeding, and ecchymosis in the literature. As mentioned in Table 1, in addition to severe thrombocytopenia, our cases had complaints of epistaxis, ecchymosis, melena, hematuria, gum bleeding, neuropsychiatric symptoms, and renal failure. The symptoms of our brucellosis cases were similar to those of hematologic malignancies and hemorrhagic viral diseases.

Therefore, hematologists, ENT specialists, psychiatrists, dermatologists, dentists, urologists, and gastroenterologists should bear in mind the possibility of brucellosis in patients who present with bleeding.

We agree with some authors who have suggested that thrombocytopenia is a result of immunological reactions.19 In some of our cases thrombocytopenia had developed as a result of an immunological mechanism, which was the main reason for severe thrombocytopenia. Hemorrhage results from either a decrease in platelet counts or platelet dysfunction. Thrombocytopenia is rare; only in very rare cases of brucellosis is it severe enough to cause bleeding.22 The high rates of bleeding in our cases (100%) warrant attention. After 4 days of treatment with antibiotics (rifampicin and doxycycline) and platelet suspensions, the hemorrhage stopped in all our cases with bleeding. Fortunately, the severe thrombocytopenia which occurs in brucellosis is responsive to antibiotics and hematological supportive therapy.

Within 2 weeks, thrombocytopenia improved in the majority of cases. At the end of the third week, platelet counts were > 150000/mm³ in all patients. At the end of the fourth week of treatment with anti-brucellosis drugs, hematological abnormalities as well as renal insufficiency, neuropsychiatric symptoms, and other symptoms had completely disappeared. Akdeniz et al. have reported that platelet counts returned to normal within 2 – 3 weeks of initiating

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<table>
<thead>
<tr>
<th>Case Number</th>
<th>Platelet (mm³)</th>
<th>Hb (g/dL)</th>
<th>WBC (mm³)</th>
<th>Complications seen in cases</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>3000</td>
<td>12.4</td>
<td>9000</td>
<td>Epistaxis, petechia, neuropsychiatric symptoms</td>
</tr>
<tr>
<td>2</td>
<td>7000</td>
<td>8.9</td>
<td>2700</td>
<td>Melena, gum bleeding</td>
</tr>
<tr>
<td>3</td>
<td>9000</td>
<td>10.6</td>
<td>73000</td>
<td>Epistaxis, ecchymosis</td>
</tr>
<tr>
<td>4</td>
<td>10000</td>
<td>9.5</td>
<td>4900</td>
<td>Epistaxis, ecchymose, gum bleeding</td>
</tr>
<tr>
<td>5</td>
<td>10000</td>
<td>5.5</td>
<td>3900</td>
<td>Melena, hematuria, renal failure, psychiatric symptoms</td>
</tr>
<tr>
<td>6</td>
<td>13000</td>
<td>7</td>
<td>3700</td>
<td>This case had no bleeding symptoms</td>
</tr>
<tr>
<td>7</td>
<td>15000</td>
<td>7.8</td>
<td>7600</td>
<td>Neuropsychiatric symptoms</td>
</tr>
<tr>
<td>8</td>
<td>16000</td>
<td>4.7</td>
<td>10900</td>
<td>Epistaxis, petechia, renal failure, psychical symptoms</td>
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<tr>
<td>9</td>
<td>18000</td>
<td>12.7</td>
<td>3700</td>
<td>Epistaxis, petechia</td>
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<tr>
<td>10</td>
<td>19000</td>
<td>13</td>
<td>3500</td>
<td>Epistaxis</td>
</tr>
</tbody>
</table>

Hb: Hemoglobin, WBC: White blood cell
antibiotics. Dilek et al. have reported restoration of thrombocyto-
penia to normal ranges within one week after initiation of anti-
microbial therapy. We have completed the antimicrobial treatment to
penicillin within one week after initiation of antimi-
6 weeks in all patients.

All our patients were treated successfully then discharged. Pa-
patients were followed monthly for 12 months with clinical and
follow-ups.

Some authors have reported successful results with the adminis-
tration of plasma, plasma exchange, intravenous gamma globulin,
and steroids in conjunction with brucellosis treatment. How-
ever, in our cases, those treatment modalities were not necessary.

In conclusion, since brucellosis is endemic in developing coun-
tries, it must be considered in the differential diagnosis of viral
hemorrhagic diseases and cases presenting with severe thrombo-
cytopenia and bleeding disorders. Even with the development of
severe thrombocytopenia and bleeding in patients with brucellosis,
successful results can be obtained with antibiotics and hematologic
supportive therapy.

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