A case of brucellosis presenting with acute hepatitis and bicytopenia

Un caso di brucellosi con presentazione clinica di epatite acuta e pancitopenia

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INTRODUCTION

Brucellosis is a zoonotic infection transmitted from animals to humans caused by Gram-negative coccobacilli of the genus Brucella. The disease, non-specific symptoms and signs, may present with different clinical manifestations. Holding one or more organs can mimic many diseases [1]. Although liver involvement is frequently seen in brucellosis, acute hepatitis is a rare clinical entity [2-5]. Haematological course of the disease are not specific findings can be seen in various degrees [1]. We report a case of brucellosis with acute hepatitis and bicytopenia without anemia.

CASE REPORT

A 19-year-old male Turkish farmer presented with a 2-week history of fever, sweating, low back and leg pain, lassitude, loss appetite, nausea and vomiting. He gave a history of raw milk ingestion and animal contact. On examination he was febrile with temperature of 40.3°C, tachycardia (at a heart rate of 120 beats/min), and tachypnea (breathing rate of 25 breaths/min). His blood pressure was 100/70 mmHg. Physical examination showed signs of icteric skin and sclera, tenderness in the right hypochondriac region and hepatosplenomegaly. Other system examination was normal. Laboratory findings showed bicytopenia without anemia with WBCs 3500/mm³ (polymorphs 63% and lymphocytes 33%), Hb 13.8 g/dL and platelets 89000/mm³. Biochemical tests showed with AST 771 U/L, ALT 471 U/L, ALP 355 U/L, GGT 432 U/L, total bilirubin 2.61 mg/dL, direct bilirubin 1.45 mg/dL and albumin 3.7 g/dL. The other haematological parameters showed with PTT 18.3 s, INR 1.71, aPTT 55.4 s, ESR 19 mm/h, CRP 21.7 mg/dL (N<0.8 mg/dL). Viral hepatitis markers found as negative (HBsAg, anti-HBc total, anti-HBc IgM, anti-HAV IgM, and anti-HCV). The patient’s laboratory findings are given in Table 1. Blood culture grew Brucella melitensis. Brucella agglutinin antibodies were positive for Brucella melitensis with a titer of 1:160 on the second day of admission.

In upper abdominal ultrasonography, liver size was minimally increased (160 mm), and its parenchymal echogenicity was diffusely decreased. The wall of gall bladder was diffusely increased (4.5 mm) and spleen became larger (179x69 mm). He was started on tetracycline 500 mg per oral four times daily and streptomycin 1 g intramuscularly once daily. Fever subsided after 5 days and symptoms were relieved. General condition was improved. He was followed up for two weeks. At discharge, his symptoms and findings excluding lassitude were totally improved. Leukopenia and thrombocytopenia returned normal levels on the 28th day. Tetracycline 500 mg orally four times daily for 6 weeks and streptomycin 1 g i.m. once daily for 21 days. After one year of follow-up, no relapse was observed.
A case of brucellosis presenting with acute hepatitis and bicytopenia

**DISCUSSION**

Brucellosis, primarily as a zoonosis, and infected animals, meat, infected milk and milk products, direct contact with infected animals, is transmitted to people infected with inhalation of aerosols or conjunctiva inoculation. The main clinical findings are fever with chills, muscle and joint pain, sweating, weight loss, fatigue, headache [1]. Liver involvement is common in brucellosis, as determined by elevated transaminase levels but acute hepatitis clinic is a rare condition [2-5]. Hepatomegaly and splenomegaly is seen, in 20-60% and 25-30% of patients with brucellosis, respectively. In addition, patients with hepato-renal syndrome, acute cholecystitis, pancreatitis and peritonitis can be seen [6]. Liver function tests of case at admission were significantly higher levels. Transaminases and bilirubin increased gradually until the seventh day of hospitalization, icterus has become more pronounced in skin and sclera but the general view of the clinic did not deteriorate. From the second week of treatment, clinical and laboratory findings observed a dramatic improvement in the patient, although liver function tests decreased to normal levels in 28th day of hospitalization.

In a prospective study by Colmenero et al. on complications associated with *Brucella melitensis* infection in 530 patients, hepatic involvement was observed in 2.5% of patients [7]. In some Turkish studies, AST and ALT elevation ranging from 12% and 43.6% has been reported [8-12]. In a retrospective evaluation and review of the literature of clinical manifestations and complications in 1028 cases of brucellosis, Buzgan et al. reported hepatomegaly in 20.6% of cases, splenomegaly in 14.5%, and hepatosplenomegaly in 10.3% [11]. In their evaluation of 140 cases with brucellosis, Gursoy and colleagues found acute hepatitis in 1.6% of patients, elevated transaminase levels in 27.9%, hepatomegaly in 8.6%, splenomegaly in 10.7%, and hepatosplenomegaly in 3.6% [13]. In a prospective evaluation of 120 adult patients with brucellosis, Namiduru et al. observed acute hepatitis in only 1 patient (0.8%), and hepatomegaly and splenomegaly in 63.3% and 56.6%, respectively [14]. Haematologic findings are non-specific and can be seen in varying degrees during the course of brucellosis. Microangiopathic haemolytic anemia, thrombocytopenia, leukopenia was observed in the majority of patients with brucellosis, whereas pancytopenia and bicytopenia without anemia was detected in rare cases. Rarely, haematologic abnormalities, occurring in the early period of infection, may mask the etiology of infection, resembling primary haematologic abnormalities. These haematologic abnormalities are transient, and return to normal with appropriate antimicrobial therapy [15]. In some Turkish studies, leukopenia and thrombocytopenia rates in detected cases of brucellosis ranged between 2.1 and 20% and between 0.5 and 13.3%, respectively [11-13, 15]. Patient haematologic findings with infection was detected early in bicytopenia (WBC: 3500/mm³, platelet: 89000/mm³). An additional treatment without the need for treatment of brucellosis with only leukopenia, while normal on the seventh day of hospitalization (4400/mm³), thrombocytopenia on the fourth day of hospitalization reached the normal number of platelets (242000/mm³) is observed.

In conclusion, we suggest that bicytopenia/pancytopenia and acute hepatitis in brucellosis cases should take into consideration in our country, endemic for brucellosis.

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**Keywords:** Brucellosis, acute hepatitis, bicytopenia.

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**Table 1 - The patient’s laboratory findings.**

<table>
<thead>
<tr>
<th>Duration</th>
<th>WBC/mm³</th>
<th>PLT/mm³ (x10³)</th>
<th>AST* (U/L)</th>
<th>ALT* (U/L)</th>
<th>ALP* (U/L)</th>
<th>GGT* (U/L)</th>
<th>Bilirubin* (Total/Direct) (mg/dL)</th>
<th>PTZ/INR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>3500</td>
<td>89</td>
<td>771</td>
<td>471</td>
<td>355</td>
<td>432</td>
<td>2.61/1.45</td>
<td>18.3/1.71</td>
</tr>
<tr>
<td>3rd day</td>
<td>3100</td>
<td>63</td>
<td>801</td>
<td>450</td>
<td>284</td>
<td>356</td>
<td>3.58/2.21</td>
<td></td>
</tr>
<tr>
<td>7th day</td>
<td>4400</td>
<td>125</td>
<td>837</td>
<td>699</td>
<td>519</td>
<td>529</td>
<td>6.14/2.84</td>
<td>21.1/1.86</td>
</tr>
<tr>
<td>14th day</td>
<td>7500</td>
<td>242</td>
<td>111</td>
<td>253</td>
<td>280</td>
<td>221</td>
<td>2.34/1.04</td>
<td>13.2/1.12</td>
</tr>
<tr>
<td>28th day</td>
<td>7300</td>
<td>261</td>
<td>41</td>
<td>29</td>
<td>113</td>
<td>56</td>
<td>1.61/0.30</td>
<td></td>
</tr>
</tbody>
</table>

Although liver involvement is frequently seen in brucellosis, acute hepatitis is a rare clinical entity. In its progress, haematological findings are non-specific and vary in respect to severity. In this paper, we present a case of brucellosis with acute hepatitis and bicytopenia without anaemia. A 19-year-old man presented with a 2-week history of fever, sweating, low back and leg pain, lassitude, loss appetite, nausea and vomiting. He gave a history of raw milk ingestion and animal contact. Physical examination showed signs of icteric skin and sclera, tenderness in the right hypochondriac region and hepatosplenomegaly. On admission to hospital, laboratory tests showed WBC 3500/mm³ (polymorphs 63% and lymphocytes 33%), haemoglobin 13.8 g/dL, platelet 89000/mm³, erythrocyte sedimentation rate 19 mm/h, and C-reactive protein 21.7 mg/dL (N<0.8 mg/dL). Biochemical tests were as follows: AST 771 U/L, ALT 471 U/L, ALP 355 U/L, GGT 432 U/L, total bilirubin 2.61 mg/dL, direct bilirubin 1.45 mg/dL and albumin 3.7 g/dL. Viral hepatitis markers were found to be negative (HBsAg, anti-HBc total, anti-HBc IgM, anti-HAV IgM, and anti-HCV). Blood culture grew Brucella melitensis. Leukopenia and thrombocytopenia returned to normal levels at the 7th and 14th day of his admission, respectively. Liver function tests improved at the 28th day. Treatment of the brucellosis was performed with antibiotics (tetracycline 500 mg orally four times daily for 6 weeks and streptomycin 1 g IM once daily for 21 days). Finally, a case of brucellosis with acute hepatitis and bicytopenia was treated with a successful outcome. In conclusion, we suggest that due consideration be taken of bicytopenia/pancytopenia and acute hepatitis in brucellosis cases in Turkey, an endemic region.

REFERENCES