Case Report

Acute acalculus cholecystitis and hepatitis caused by *Brucella melitensis*

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**Abstract**

Acute cholecystitis is a very rare presentation of brucellosis. A case of acalculous cholecystitis caused by *Brucella melitensis* is reported with a review of previously reported cases.

**Keywords:**


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**Introduction**

Brucellosis is a zoonotic infection with a worldwide distribution. It is endemic in many parts of the world. Areas of high endemicity include the Mediterranean basin, the Arabian peninsula, the Indian subcontinent, parts of Mexico, and Central and South America [1]. Human brucellosis is a multisystemic disease with a wide range of clinical manifestations [2]. Cholecystitis is a rare complication of brucellosis. In this report, a patient who presented with a classical picture of acute cholecystitis and from whom *Brucella melitensis* was cultured from blood is reported. Other previously reported cases of brucella cholecystitis are reviewed.

**Case report**

A 45-year-old previously healthy Saudi male presented to the emergency department of King Khalid University Hospital with a five-day history of fever, rigors and crampy abdominal pain. The abdominal pain started in the epigastric area and became localized to the right upper quadrant area. The patient had pruritis and produced dark urine. There was no history of vomiting or diarrhoea. On physical examination, the patient was febrile (temperature of 39°C), toxic, and jaundiced. Abdominal examination showed tender epigastric area and a positive Murphy’s sign. Laboratory data at the time of admission were as follows: total bilirubin 109 µmol/L; direct bilirubin 91 µmol/L; alkaline phosphatase 322 U/L; alanine aminotransferase 159U/L; aspartate aminotransferase 149 U/L; γ glutamyl transferase 331U/L; serum amylase 23U/L; leukocyte count 8x10⁹/L with 70% neutrophils, 64% lymphocyte, 16% monocyte; hemoglobin 9g/dl; platelets 75x10⁹/L; PT 16; PTT 37.9; and fibrinogen assay 4.12g/L. Ultrasound scan showed a thickened gallbladder wall with no evidence of stones and mild inflammation of the adjacent liver parenchyma (Figure 1). As the patient was septic with raised liver enzymes, computed tomography (CT-scan) of the abdomen was performed to rule out liver abscess; the CT-abdomen revealed no liver lesions. The patient was therefore managed as a case of acute cholecystitis and ascending cholangitis complicated with sepsis and reactive hepatitis. After three blood cultures were obtained, intravenous tazocin 4.5 g was

**Figure 1.** Abdominal ultrasound revealed thickened wall of the gallbladder.
commenced. The abdominal pain disappeared gradually and the patient’s temperature returned to normal within three days. On day 9 after admission, one blood culture was positive. It grew small colonies of Gram-negative bacilli that were later identified as *B. melitensis*. Standard tube agglutination test (STA) and coombs anti-Brucella test were 1:80 and 1:2560, respectively. The patient was treated with a combination of doxycycline 200 mg twice daily for six weeks and streptomycin 1gm IM for two weeks. He remained asymptomatic during a six-week follow-up period with no evidence of relapse.

**Discussion**

Focal forms of brucellosis are present in approximately 30% of patients [3]. The most common gastrointestinal complication is reactive hepatitis with or without granulomas [4]. Other less frequent complications include peritonitis [5], intraabdominal abscesses [6], ileitis [7], colitis [8], pancreatitis [9], and appendicitis [10]. Cases of acute cholecystitis occurring as a complication of brucellosis are rare. In a review of literature (MEDLINE 1934-2005), only 16 cases have been reported to date (Table 1). As in our case, most reported cases are due to *B. melitensis* and describe both lithiastic and acalculous cholecystitis. Twelve of the sixteen cases were male patients and four were females. The average age was 49 years (range 6-72 years). All the patients had clinical symptoms of acute cholecystitis and had history of fever days or weeks prior to admission. Six patients had *B. melitensis* and one had *Brucella abortus* isolated in the bile. In one patient *Brucella suis* was isolated from both blood and bile cultures [11]. In six

### Table 1. Details of reported cases of acute cholecystitis associated with *brucella species*.

<table>
<thead>
<tr>
<th>No</th>
<th>Author(ref)</th>
<th>Age/Sex</th>
<th>Risk factor</th>
<th>Blood culture</th>
<th>Bile culture</th>
<th>Gallstones</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mettier [12]</td>
<td>57/M</td>
<td>No</td>
<td><em>B. melitensis</em></td>
<td><em>B. melitensis</em></td>
<td>Absent</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>White [16]</td>
<td>58/M</td>
<td>No</td>
<td>Negative</td>
<td><em>B. abortus</em></td>
<td>Present</td>
<td>Streptomycin</td>
</tr>
<tr>
<td>3</td>
<td>Valenzuela [14]</td>
<td>56/M</td>
<td>Sheep and goat contact</td>
<td>NA</td>
<td>NA</td>
<td>Absent</td>
<td>Tetracycline + streptomycin</td>
</tr>
<tr>
<td>4</td>
<td>Morris [11]</td>
<td>34/M</td>
<td>Microbiologist</td>
<td><em>B. suis</em></td>
<td><em>B. suis</em></td>
<td>Present</td>
<td>Tetracycline + streptomycin</td>
</tr>
<tr>
<td>5</td>
<td>Berbegal [17]</td>
<td>33/M</td>
<td>No</td>
<td><em>B. melitensis</em></td>
<td>Negative</td>
<td>Absent</td>
<td>Tetracycline + streptomycin</td>
</tr>
<tr>
<td>6</td>
<td>Shaheen [18]</td>
<td>42/F</td>
<td>No</td>
<td><em>B. melitensis</em></td>
<td><em>B. melitensis</em></td>
<td>Absent</td>
<td>Tetracycline + streptomycin</td>
</tr>
<tr>
<td>7</td>
<td>Colmenero [2]</td>
<td>58/M</td>
<td>Shepherd</td>
<td><em>B. melitensis</em></td>
<td>Negative</td>
<td>Present</td>
<td>Doxycycline + streptomycin</td>
</tr>
<tr>
<td>8</td>
<td>Fasquelle [13]</td>
<td>72/F</td>
<td>Contaminated milk or dairy products</td>
<td><em>B. melitensis</em></td>
<td><em>B. melitensis</em></td>
<td>Present</td>
<td>Doxycycline + rifampin</td>
</tr>
<tr>
<td>9</td>
<td>Serrano [19]</td>
<td>59/M</td>
<td>No</td>
<td><em>B. melitensis</em></td>
<td>Negative</td>
<td>Present</td>
<td>Doxycycline + streptomycin</td>
</tr>
<tr>
<td>10</td>
<td>Ashley [20]</td>
<td>6/M</td>
<td>No</td>
<td><em>B. abortus</em></td>
<td>NA</td>
<td>Absent</td>
<td>TMP/SMX + rifampin</td>
</tr>
<tr>
<td>11</td>
<td>Miranda [15]</td>
<td>34/M</td>
<td>Sheep and goat contact</td>
<td>Negative</td>
<td><em>B. melitensis</em></td>
<td>Present</td>
<td>Doxycycline + rifampin</td>
</tr>
<tr>
<td>12</td>
<td>Andriopoulos [10]</td>
<td>72/M</td>
<td>No</td>
<td><em>B. melitensis</em></td>
<td><em>B. melitensis</em></td>
<td>Absent</td>
<td>Doxycycline + streptomycin</td>
</tr>
<tr>
<td>13</td>
<td>Lopez-Prieto [21]</td>
<td>56/F</td>
<td>No</td>
<td>Negative</td>
<td><em>B. melitensis</em></td>
<td>Present</td>
<td>Doxycycline + streptomycin</td>
</tr>
<tr>
<td>14</td>
<td>Kanafani [22]</td>
<td>55/M</td>
<td>No</td>
<td><em>Brucella spp</em></td>
<td><em>Brucella spp</em></td>
<td>Present</td>
<td>Doxycycline + rifampin</td>
</tr>
<tr>
<td>15</td>
<td>Kanafani [22]</td>
<td>29/F</td>
<td>No</td>
<td>Negative</td>
<td><em>Brucella spp</em></td>
<td>Present</td>
<td>Doxycycline + rifampin</td>
</tr>
<tr>
<td>16</td>
<td>Alotaibi (PR)</td>
<td>42/M</td>
<td>Raw milk ingestion</td>
<td><em>B. melitensis</em></td>
<td>NA</td>
<td>Absent</td>
<td>Doxycycline + streptomycin</td>
</tr>
</tbody>
</table>
patients, both blood and bile cultures were positive at the time of the infection. In five of the cases diagnosis was made on growth of the microorganism in the blood. Gallstones were present in nine patients. Thirteen patients underwent cholecystectomy. Histopathological examination of the gallbladder showed signs of acute and/or chronic inflammation. Three cases showed the presence of granulomas in the gallbladder wall [2,10,12]. Five patients had a brucellosis risk factor. Three patients had history of contact with animals [2,14,15] and one was a microbiologist [15]. In one case reported by Fasquelle [12], brucellosis was linked to contaminated milk and dairy products. In our patient brucellosis was not suspected at the time of admission. The diagnosis was reached only after blood cultures were performed due to the patient’s fever. On further questioning of the patient, he gave a history of ingestion of raw milk one month prior to his illness.

The most commonly used antibiotic combination was doxycycline/streptomycin and tetracycline/streptomycin. The duration of therapy ranged from eight days to six months. All patients made uneventful recovery.

Brucella species, as in the case of Salmonella species, are usually associated with bacteremia and systemic infection. Both organisms are intracellular and may cause latent infection with subsequent clinical symptoms months or years after their onset. Involvement of the gallbladder in such systemic infections may occur via the lymphatic spread or as part of bacteremia. However, unlike Salmonella species in which the gallbladder acts as a reservoir for the microorganism, no reports on chronic carriage of Brucella in the gallbladder has been made. Localized brucellosis may result as a complication of bacteremia or may be the only manifestation of chronic infection [11]. In this case, it is unclear whether acute cholecystitis associated with brucellosis is a complication of a chronic latent infection or simply a localized form of acute brucellosis.

In conclusion, brucellosis should be considered in the differential diagnosis of acute cholecystitis in regions where brucellosis is an endemic disease.

References
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