CASE REPORT

Disseminated tuberculosis presenting as tuberculous peritonitis and sepsis tuberculosa gravissima in a patient with cirrhosis of the liver: A diagnosis of challenge

Chun-Yuan Lee a, Hung-Chin Tsai a,b, Susan Shin-Jung Lee a,b, ChengLen Sy a, Yao-Shen Chen a,b,*

a Division of Infectious Diseases, Department of Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan
b Faculty of Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan

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We report the case of an 81-year-old man diagnosed with liver cirrhosis complicated by spontaneous bacterial peritonitis and septic shock. Mycobacterium tuberculosis complex was isolated from the ascites, sputum, and blood culture 1 month after the patient died. Clinicians should be aware of the unusual diagnosis of sepsis tuberculosa gravissima presenting with tuberculous peritonitis, which is easily misdiagnosed as spontaneous bacterial peritonitis and Gram-negative bacillus sepsis in patients with cirrhosis. Clinicians should cautiously evaluate the patient’s sputum, gastric contents, urine, cerebrospinal fluid, and bone marrow for early diagnosis of disseminated tuberculosis in patients with a high degree of suspicion of this diagnosis.

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Introduction

Tuberculous peritonitis is a rare presentation of extrapulmonary tuberculosis (TB). Although some reports have discussed the epidemiology and clinical manifestations of tuberculous peritonitis in Taiwan, it continues to pose a significant challenge due to its protean manifestations and
overlapping presentations with other diseases. The mean duration from presentation to diagnosis is about 1 month and the mortality rate is 60% among patients for whom treatment is not started within 30 days of presentation. Infection with Mycobacterium tuberculosis rarely presents as septic shock with multiple organ failure, i.e., sepsis tuberculosa gravissima, the behavior of which is similar to that of Gram-negative bacillus (GNB) sepsis.

We report here a case of disseminated TB presenting with tuberculous peritonitis and sepsis tuberculosa gravissima in a patient with cirrhosis of the liver, which was initially misdiagnosed as spontaneous bacterial peritonitis (SBP) with GNB sepsis.

Case report

An 81-year-old man with diabetes mellitus, hypertension, and previous cerebrovascular accident was brought to our emergency department with stupor for 1 day. He reported progressive abdominal distension, anorexia, and limb edema for 2 weeks prior to presentation. There was neither fever nor cough with sputum. One day prior to admission, he developed stupor.

In the emergency department, his initial physical examination showed a blood pressure of 138/61 mmHg, body temperature 37.3°C, heart rate 123 beats/minute, and respiratory rate 21 breaths/minute. The initial Glasgow Coma Scale score was E3V2M3. Pale conjunctiva, abdominal distension with shifting dullness, spider angioma over the chest wall, and palmar erythema were also found. There was no focal neurological sign such as eye deviation or limb weakness. A computed tomography scan of his brain disclosed several tiny hypodense lesions involving bilateral basal ganglia and left periventricular white matter in favor of old lacunar infarction.

His laboratory tests showed a white blood cell count of 15.19 x 10^9/L with 84% granulocytes, 12% lymphocytes, and 4% monocytes. Hemoglobin was 10.1 g/dL, the mean corpuscular volume was 88.4 fL/red cell, and the platelet count was 332,000/mm^3. Serum electrolyte levels were 139 mmol/L Na (normal range 135–147 mmol/L), 3.8 mmol/L K (normal range 3.4–4.7 mmol/L), and 8.3 mg/dL Ca (normal range 8.4–10.6 mg/dL). The renal function test showed 34 mg/dL blood urea nitrogen (normal range 7–20 mg/dL) and 2.1 mg/dL serum creatinine (normal range 0.7–1.5 mg/dL). Liver function tests showed 10 U/L glutamate pyruvate transaminase (normal range 0–40), 91 U/L γ-glutamyl transpeptidase (normal range 8–60 U/L), 89 U/L alkaline phosphatase (normal range 42–128 U/L), and 57 μg/dL serum ammonia (normal range 12–66 μg/dL). The viral hepatitis test gave a negative result for anti-HCV antibody and HBs antigen and a positive result for anti-HBs antibody. The family did not report a history of alcoholism in the patient.

A chest radiograph showed a band-like lesion over the right lower lung field (Fig. 1). Chest radiograph taken in the emergency department showing a band-like lesion over the right lower lung field.

Shock with acute respiratory failure developed on Day 1 of hospitalization and the patient was intubated, ventilated mechanically, and given fluid resuscitation and inotropic drugs. An initial sputum smear showed a high polymorphonuclear (PMN) cell count with a predominance of GNB. With a diagnosis of liver cirrhosis complicated with SBP, multiple organ failure, and GNB pneumonia, antibiotic treatment was changed to cefotaxime 2 g every 8 hours.

Table 1 gives the serial analysis of the ascites fluid. Initially, the patient’s vital signs and level of consciousness improved gradually and the repeat analysis of ascites also showed a reduction in the PMN cell count. On Day 4 of hospitalization, however, his clinical condition deteriorated again and shock with multiple organ failure was exacerbated despite fluid hydration and the use of inotropic drugs. The sputum culture grew Enterobacter cloacae. Four sets of ascites bacterial cultures showed negative results. Based on culture-negative neutrocytic ascites, tuberculous peritonitis and malignancy could not be excluded. An abdominal computed tomography scan showed no evidence of a primary tumor with peritoneal carcinomatosis. We looked for other evidence of disseminated TB and collected TB culture from sputum, ascites fluid, urine, and blood, but...
the families declined lumbar puncture. The sputum acid-fast staining was positive (3+). We changed the antibiotic treatment to cefepime and started antituberculous treatment with isoniazid, rifampin, ethambutol, and pyrazinamide on Day 4 of hospitalization. On Day 6 of hospitalization, the patient died due to refractory shock and multiple organ failure. One month later, *Mycobacterium tuberculosis* complex was isolated from the blood, ascites, and sputum culture.

**Discussion**

This case highlights the difficulty in the diagnosis of disseminated TB presenting as tuberculous peritonitis and sepsis tuberculosa gravissima in a patient with cirrhosis with symptoms of SBP and fulminant sepsis.

Liver cirrhosis is a known risk factor for tuberculous peritonitis in addition to patients with end stage renal disease receiving continuous ambulatory peritoneal dialysis, and patients with diabetes mellitus. However, tuberculous peritonitis often goes unsuspected and undiagnosed in patients with concomitant cirrhosis with ascites. It is not uncommon for patients with cirrhosis with tuberculous peritonitis to be misdiagnosed as having SBP, which is more common in these patients.

The diagnosis of tuberculous peritonitis is complicated by the variability of its presentation and the limitations of the available diagnostic tests. The clinical manifestations of SBP and tuberculous peritonitis overlap and they can both present with fever, abdominal discomfort or pain, and altered mental status. The onset of tuberculous peritonitis may be insidious, although acute presentations resembling bacterial peritonitis also occur, as in our patient. It is difficult to differentiate tuberculous peritonitis from SBP based on clinical findings alone.

Currently available methods for diagnosing tuberculous peritonitis include ascitic fluid analysis, ascites smear and culture, and polymerase chain reaction (PCR), but they have several limitations. Acid-fast staining of ascites is easy to perform, but is often inconclusive. Yeh et al. showed lymphocyte ≥50% and SAAG ≤1.1 in most patients (59.6% and 72.3%, respectively). However, the diagnosis of tuberculous peritonitis cannot be excluded based on PMN cell count predominance, especially among patients with comorbid liver cirrhosis, end stage renal disease receiving continuous ambulatory peritoneal dialysis, and malignancy. Acid-fast staining of ascites is positive in <3% of patients, but the yield rate may be enhanced by centrifuging large volume of ascites, such as those reported for peritoneal TB in patients receiving peritoneal dialysis. The sensitivity of ascites culture is around 30%, but it is time consuming, leading to delayed diagnosis. The sensitivity of PCR reaches up to 95% in smear-positive patients, but the sensitivity is low (48%) in smear-negative patients. However, the sensitivity of acid-fast staining of ascites is <3% of patients, reflecting the low sensitivity of PCR for overall cases of tuberculous peritonitis.

**Table 1** Serial analysis of ascites fluid from admission Day 1 to Day 5. Serial analysis of the ascites fluid showed a predominance of PMNs with an initial increase in PMNs and then a >25% reduction after 2 days of treatment with antibiotics.

<table>
<thead>
<tr>
<th>Day</th>
<th>WBC (mm³)</th>
<th>RBC (mm³)</th>
<th>PMNs (%)</th>
<th>Lymphocytes (%)</th>
<th>Monocytes (%)</th>
<th>LDH (U/L)</th>
<th>Protein (g/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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<td>120</td>
<td>65</td>
<td>30</td>
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<tr>
<td>2</td>
<td>5310</td>
<td>90</td>
<td>57</td>
<td>41</td>
<td>2</td>
<td>296</td>
<td>2.0</td>
</tr>
<tr>
<td>3</td>
<td>1210</td>
<td>40</td>
<td>83</td>
<td>7</td>
<td>10</td>
<td>272</td>
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</tr>
<tr>
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<td>860</td>
<td>810</td>
<td>63</td>
<td>18</td>
<td>19</td>
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<tr>
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<td>360</td>
<td>80</td>
<td>11</td>
<td>9</td>
<td>284</td>
<td>1.5</td>
</tr>
</tbody>
</table>

LDH = lactate dehydrogenase; PMN = polymorphonuclear cell count; RBC = red blood cell count; WBC = white blood cell count.

![Abdominal computed tomography scan taken in the emergency department showing bilateral pleural effusion, a coarse liver surface, and much ascites, compatible with the imaging of liver cirrhosis.](image-url)
The response of SBP to antibiotic treatment is usually assessed clinically and by reduced PMN cell counts in ascitic fluid. A decrease in PMN cell counts of <25% in ascitic fluid after 2 days of antibiotic treatment compared with pretreatment values is considered to be a failure of treatment or incorrect diagnosis. It is unknown why serial ascitic fluid analysis showed a >25% reduction in PMN cell count after 2 days of ineffective cefotaxime treatment in our patient (Table 1). This may have resulted from concomitant bacterial peritonitis, although no bacteria were isolated from ascites fluid.

TB peritonitis results from either hematogenous spread from active pulmonary TB or spreading from adjacent intestinal foci or abdominal lymph nodes. Tuberculous peritonitis may be a presentation of disseminated TB, and cautious evaluation of sputum, gastric contents, peripheral lymph nodes, urine, cerebrospinal fluid, and blood may facilitate the diagnosis of disseminated TB. The coexistence of pulmonary TB is reported in >50% of patients with tuberculous peritonitis. In a recent review of 211 patients with tuberculous peritonitis in Taiwan, 77% of patients had abnormalities on chest radiographs. In our patient, sputum acid-fast staining provided an opportunity for the early diagnosis of disseminated TB, even though the chest radiograph did not present with typical findings compatible with reactivation of pulmonary TB.

In the absence of other foci of TB, peritoneal tissue must often be obtained to make the pathological diagnosis of tuberculosis peritonitis. An image-guided percutaneous peritoneal biopsy with a sensitivity >80% has been reported. Direct visualization and targeted biopsy of the peritoneum by early laparoscopy have shown that the sensitivity and specificity of diagnosing tuberculous peritonitis exceeded 90%. Prompt diagnosis with peritoneal biopsy is an effective method of early diagnosis of tuberculous peritonitis.

In rare conditions, sepsis tuberculosis gravissima can present with acute onset and a rapid clinical course, leading to septic shock with multiple organ failure masquerading as fulminant GNB sepsis. Described mostly in patients with AIDS, rare cases have been observed among patients without overt immunosuppression and have involved cases of disseminated or pulmonary TB.

In conclusion, clinicians must be aware of sepsis tuberculosis gravissima presenting with tuberculosis peritonitis, which is easily misdiagnosis as SBP and GNB sepsis in patients with cirrhosis. Even in patients with PMN-predominant ascites, SAAG >1.1 g/dL, and a >25% decrease in the PMN cell count in ascitic fluid after 2 days of empirical antibiotic treatment, for patients with culture-negative neutrocytic ascites and a deteriorating clinical course and concomitant abnormalities on chest radiographs, clinicians should cautiously evaluate any body fluid for the early diagnosis of disseminated TB and prescribe timely treatment with antituberculous drugs.

Conflicts of interest

The authors have no conflicts of interest to declare.

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