Primary Hepatosplenic Tuberculosis in an Immunocompetent Adult and Domestic Literature Review

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Hepatic or splenic involvement of tuberculosis without other disseminated lesions is a very uncommon form of extrapulmonary tuberculosis, especially in an immunocompetent adult. We report a case of a 25 year-old-man who developed primary hepatosplenic tuberculosis not associated with the lung or other distant organs. He was initially diagnosed with esophageal candidiasis in local clinic. A computed tomographic scan of the abdomen showed hepatosplenomegaly and multiple microabscesses in the spleen. Our initial diagnosis, based on the clinical feature and radiologic findings, was hepatosplenic candidiasis. However, histopathology of the liver specimens revealed chronic granuloma with central caseous necrosis, strongly suggestive of tuberculosis. Although rare, splenic tuberculosis should be considered in the differential diagnosis of splenic abscess, especially in countries where tuberculosis is endemic.

Keywords: Tuberculosis, hepatic; Tuberculosis, splenic

INTRODUCTION

Tuberculosis (TB) remains a very important public health problem. In Korea, the estimated incidence of TB was 97 cases per 100,000 in 2009, and annually, 2,300 people died from TB. Extrapulmonary TB accounts for almost 17.1% of all cases, and appears to be gradually increasing. Pleural, lymphatic, abdominal, and bone-joints are common site for extrapulmonary TB [1]. Among extrapulmonary involvement, TB of the liver or spleen is rare and is usually a manifestation of miliary or pulmonary TB. Primary manifestation of hepatosplenic TB as a cause of splenic abscesses is unusual with only a few case reports and studies [2-5]. To review the reports of primary hepatic or splenic TB in Korea, we used KoreaMed and the Koreanstudies Information Service System search engines. In this report, we describe a case of hepatosplenic TB with no evidence of infection in the lung or other distant organs including the gastrointestinal tracts diagnosed by ultrasonography (USG)-guided percutaneous needle biopsy of the liver, followed by a review of the hepatosplenic TB reported cases in Korea.

CASE REPORT

A 25 year-old-man was admitted to our hospital with intermittent fever and night sweats for 5 weeks. Approximately one month prior, he underwent abdominal USG, gastroscopy and colonoscopy to evaluate for a fever focus in a local clinic. No significant findings were noted except for esophageal candidiasis. Upon further review, the patient did not use any inhaled or oral corticosteroids and had no history of using any immunosuppressants. He was healthy, without any history of human immunodeficiency virus (HIV) infection or chronic debilitating diseases such as diabetes. He was a non-smoker and did not take any medication. He has no known contacts with active TB patients and there was no family history of TB. Palpation of the abdomen revealed a palpable liver. The neck lymph nodes were not enlarged. Laboratory tests were noted as follows: hemoglobin, 10.8 g/dL; white blood count, 5,300/mm³ (neutrophil 83.1%, lymphocyte 11.2%, and monocyte 5.6%); platelet, 202,000/mm³; alanine aminotransferase, 72 U/L; aspartate aminotransferase, 119 U/L; total protein, 7.2 g/dL; albumin, 3.7 g/
dL; total bilirubin, 0.9 mg/dL; prothrombin time (PT), 14.8 seconds (PT 1.27%); erythrocyte sedimentation rate, 66 mm/hr; and c-reactive protein, 7.24 mg/dL. During admission, patient’s lymphocyte count was about 593/μL. However, the patient showed rapid recovery in the next 2 to 3 days. After one month, the patient showed full recovery. There was no laboratory finding indicating HIV infection. Sputum smear was negative on three consecutive early morning samples for acid-fast bacilli (AFB). The tuberculin skin test was negative, but Quantiferon-TB Gold test (Cellestis Ltd., Carnegie, VIC, Australia) was positive. Repeated blood cultures revealed no growth. A computed tomographic (CT) scan of the chest showed no evidence of cavitary or nodular lesion compatible with TB. An abdominal CT scan showed hepatosplenic megaly and multiple microabscesses in the spleen (Fig. 1). USG-guided percutaneous needle biopsy of the liver was performed. The polymerase chain reaction (PCR) and Ziehl-Neelsen stain of the liver specimen were negative for Mycobacterium tuberculosis. Mycobacteria failed to grow in liquid and solid culture. Histopathology of the liver specimens revealed wide central caseous necrosis and multinucleated giant cells with inflammatory cell infiltration, suggestive for TB (Fig. 2). The patient was diagnosed to have primary hepatosplenic TB and started on anti-TB drugs. A repeated CT after 11 months posttherapy revealed that hepatosplenomegaly was improved and the spleen nodules are nearly disappeared (Fig. 3). The patient has been followed for >1 year without any complications.

**DISCUSSION**

Hepatic or spleen TB is usually associated with concurrent pulmonary TB or disseminated disease. In one retrospective observational study, 200 cases of hepatic TB were studied, of which 180 cases (90%) involved miliary TB [6]. Case reports of primary hepatosplenic TB in which pathologic examination have been carried out are rare. In our case, a final diagnosis of primary hepatosplenic TB was made, as there were no other identified TB sources detected in the lung or gastrointestinal tract. Our patients initially presented with prolonged, intermittent fever. Radiologic findings revealed hepatosplenomegaly with splenic microabscess. The diagnosis of a primary hepatosplenic TB was established using USG-
Clinical features of 16 cases of primary hepatic or splenic tuberculosis in immunocompetent hosts in Korea

Table 1. Clinical features of 16 cases of primary hepatic or splenic tuberculosis in immunocompetent hosts in Korea

<table>
<thead>
<tr>
<th>No.</th>
<th>Citations</th>
<th>Presenting symptoms</th>
<th>Sex/age</th>
<th>ALP/GGT/AST/ALT</th>
<th>CT findings</th>
<th>Pathology</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kim et al. [2]</td>
<td>RUQ pain</td>
<td>M/18</td>
<td>NA</td>
<td>Multiple nodule</td>
<td>Granuloma with caseous necrosis</td>
<td>Medication</td>
</tr>
<tr>
<td>2</td>
<td>Kim et al. [2]</td>
<td>RUQ pain</td>
<td>M/52</td>
<td>NA</td>
<td>Mass</td>
<td>NA</td>
<td>Medication</td>
</tr>
<tr>
<td>3</td>
<td>Hwang et al. [7]</td>
<td>Fever</td>
<td>M/57</td>
<td>441/513/100/97</td>
<td>Multiple nodule</td>
<td>Granuloma</td>
<td>Medication</td>
</tr>
<tr>
<td>4</td>
<td>Hwang et al. [7]</td>
<td>Fever, anorexia</td>
<td>M/75</td>
<td>298/231/88/56</td>
<td>No lesion</td>
<td>Granuloma</td>
<td>Medication</td>
</tr>
<tr>
<td>6</td>
<td>Hwang et al. [7]</td>
<td>Fever</td>
<td>M/49</td>
<td>134/168/15/10</td>
<td>Abscess</td>
<td>Granuloma</td>
<td>Left lobectomy</td>
</tr>
<tr>
<td>8</td>
<td>Yeom et al. [10]</td>
<td>Weight loss</td>
<td>M/55</td>
<td>156/20/20/19</td>
<td>Mass</td>
<td>Granuloma with caseous necrosis, PCR + (liver)</td>
<td>Medication</td>
</tr>
<tr>
<td>9</td>
<td>Han and Park [8]</td>
<td>Abdominal pain, mass</td>
<td>F/25</td>
<td>NA/NA/26/13</td>
<td>Cystic abscess</td>
<td>Granuloma</td>
<td>Cystectomy</td>
</tr>
<tr>
<td>10</td>
<td>Moon et al. [9]</td>
<td>RUQ pain</td>
<td>M/37</td>
<td>1,379/505/65/40</td>
<td>Mass</td>
<td>Granuloma with caseous necrosis</td>
<td>Excision</td>
</tr>
<tr>
<td>11</td>
<td>Kim et al. [3]</td>
<td>Fever</td>
<td>F/32</td>
<td>712/95/65/52</td>
<td>Multiple nodules</td>
<td>Granuloma with caseous necrosis, AFB stain 1+ (spleen)</td>
<td>Splenectomy</td>
</tr>
<tr>
<td>12</td>
<td>Kim et al. [3]</td>
<td>Fever</td>
<td>M/22</td>
<td>108/NA/18/11</td>
<td>Multiple nodules</td>
<td>NA</td>
<td>Medication</td>
</tr>
<tr>
<td>13</td>
<td>Park et al. [5]</td>
<td>LUQ pain</td>
<td>M/33</td>
<td>124/22/31/28</td>
<td>Multiple nodules</td>
<td>Granuloma with caseous necrosis</td>
<td>Splenectomy</td>
</tr>
<tr>
<td>14</td>
<td>Lim et al. [4]</td>
<td>None</td>
<td>F/45</td>
<td>NA</td>
<td>Mass forming lesion</td>
<td>Granuloma with caseous necrosis</td>
<td>Splenectomy</td>
</tr>
<tr>
<td>15</td>
<td>Kim et al. [2]</td>
<td>LUQ mass</td>
<td>F/38</td>
<td>NA</td>
<td>Multiple small nodules</td>
<td>Fibroepithelioid lesion</td>
<td>Splenectomy</td>
</tr>
<tr>
<td>16</td>
<td>Present case</td>
<td>Fever</td>
<td>M/25</td>
<td>597/213/72/119</td>
<td>Multiple small nodules</td>
<td>Granuloma with caseous necrosis</td>
<td>Medication</td>
</tr>
</tbody>
</table>

ALP, alkaline phosphatase; GGT, gamma glutamyl transpeptidase; AST, aspartate transaminase; ALT, alanine transaminase; CT, computed tomography; RUQ, right upper quadrant; M, male; NA, not applicable; AFB, acid-fast bacilli; PCR, polymerase chain reaction; f, female; LUQ, left upper quadrant.

From 1983 to 2011, 16 patients (11 males and 5 females; mean age, 39.3 years; range, 22 to 75 years) were diagnosed with biopsy proven primary hepatic or splenic TB in previously healthy adults in Korea. Besides our patient, there was only one case of primary hepatosplenic TB [2]. In patients with TB involvement of the spleen, 5 of 6 patients (83.3%) had multiple abscesses and 1 patient (16.7%) had a mass forming lesion on ultrasound and CT. On the contrary, 6 of 10 patients (60%) with hepatic TB had mass lesions. A total of 7 patients (43.8%) were treated by surgical removal (4 patients, splenectomy; 3 patients, hepatic mass excision or hepatic cystectomy). A total of 9 patients (56.3%) were successfully treated with antituberculosis chemotherapy alone (Table 1).

According to the existing literatures, symptoms associated with hepatic or splenic TB include fever, anorexia, and weight loss, although there is no evidence supporting the clinical diagnosis. Fever was the most commonly reported symptom. Seven cases (43.7%), including our case, initially presented fever as a major symptom [3,7]. Most were diagnosed during the evaluation as a fever of unknown cause. However, hepatic or splenic TB may also be found incidentally in patients among various clinical settings such as a palpable mass [2,8], abdominal pain [2,5,8,9], unexplained weight loss [10], or discovered by accident, without any constitutional symptoms [11].

Histopathologic diagnosis is required to confirm or exclude TB from other chronic granulomatous diseases like sarcoidosis or fungal infections. In our case, USG-guided percutaneous needle biopsy of liver was carried out because of hemorrhagic complication of the spleen after biopsy. The use of a spleen biopsy is considered safe and efficient diagnostic tool [12]. However, some investigators believe that the procedure carries a substantial risk of hemorrhage or rupture which are thought to be higher when compared to biopsy of other abdominal organs [13,14]. Although, the patient had no microbiological evidence, diagnosis was made by the presence of typical caseous necrosis with epithelioid granuloma. According to several retrospective observational studies, the positivity of AFB on smear examination is 20% to 33%, PCR 75%, and AFB culture 7% in abdominal TB [6,7,15]. Among the reported cases in the literature, the diagnosis of hepatic or splenic TB was supported by CT findings of multiple abscesses, which confirms the presence of a hepatic or splenic mass with a typical hypodense appearance on contrast-enhanced CT images. The abscesses may be single or multiple, and the size of the lesion may vary from a few millimeters to several centimeters. The CT findings of splenomegaly, multiple lesions, or abscesses (Table 1) were suggestive of TB-containing lesions, and histopathologic examination confirmed the diagnosis.

The most common radiological finding is non-specific heptosplenomegaly. On USG, they may present as a “bright liver or spleen” pattern with diffuse hyperchogenicity [16]. Our patients CT findings included heptosplenomegaly with splenic multiple micronodular and focal hypoattenuating lesions consistent with TB. The most common radiological finding was multiple lesions, which could be confirmed in 4 patients (4/10; 40%). The CT findings of splenomegaly, multiple lesions, or abscesses (Table 1) were suggestive of TB-containing lesions, and histopathologic examination confirmed the diagnosis. The presence of multiple abscesses and the presence of a splenic mass (Table 1) were suggestive of TB-containing lesions, and histopathologic examination confirmed the diagnosis.

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Hepatosplenic TB has been categorized into either a micronodular or macronodular form, depending on whether it is smaller or larger than 10 mm. Micronodular splenic TB is more common and tends to have multiple nodules, and is usually seen in disseminated TB. Macronodular splenic TB is rare and could manifest as a singular abscess or multiple large nodules. Among 4 reported cases of primary splenic TB in Korea, there was only one mass forming splenic TB [4].

Hepatosplenomegaly and multiple small and circular or oval area of decreased attenuation are also characteristic findings of chronic disseminated candidiasis (CDC). This is because the main site of CDC is the liver and spleen. The primary symptom associated with CDC is fever. CDC presents very similarly to primary hepatosplenic TB [17]. In our case, the initial diagnosis was hepatosplenic candidiasis, based on his medical history of esophageal candidiasis and radiological findings, especially considering that the gastrointestinal tract can be a source for hematogenous candidiasis [18].

Because of the low pre-test probability of TB compared to other splenic infections, it is commonly misdiagnosed. In the review of reported cases in Korea, clinical presentation with fever and splenic abscess warranted splenectomy obtaining a diagnosis in 75% (3/4) of cases [3,5]. On the contrary, surgery was performed for hepatic TB in 30% (3/10) of cases. It is important to note that with anti-TB medication, most patients can recover without surgical intervention [3]. If a definite diagnosis can be made without surgical treatment, hepatosplenic TB can be treated with anti-TB medications alone.

We present a case of primary hepatosplenic TB mimicking CDC in an immunocompetent adult. A clinical diagnosis of primary hepatosplenic TB is difficult to establish owing to the rarity of the disease producing a low clinical index of suspicion. Although rare, clinicians should consider the possibility of primary hepatosplenic TB when facing patients with prolonged fever and hepatosplenomegaly, especially in countries where TB is endemic.

REFERENCES