Candida albicans in Peritoneal Fluid in a Patient with Hepatic Encephalopathy

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Candida albicans is a common human fungal pathogen [1]. Candida peritonitis is usually a disease of critically ill surgical patients [2]. Isolation of fungus from ascites in cirrhotic patients is an uncommon event [3] and the clinical significance is unknown. We describe the case of a cirrhotic patient who presented with hepatic encephalopathy. She was diagnosed as having spontaneous fungal peritonitis, and the subsequent treatment led to a temporary good clinical response. We review the literature and discuss the issues regarding the diagnosis and treatment.

PATIENT DESCRIPTION

A 62 year old woman was admitted to the Internal Medicine department due to hepatic encephalopathy. She had been diagnosed a year earlier as having cirrhosis secondary to hepatitis C virus infection. Complications included ascites, esophageal varices, splenomegaly, hypoalbuminemia and hyperbilirubinemia. She had had recurrent episodes of hepatic encephalopathy, including an episode in the week before her admission secondary to Escherichia coli infection treated with ertapenem.

The patient was admitted in a comatose state that required intubation. She was afebrile and hemodynamically stable. The most striking physical finding apart from encephalopathy was ascites. The spleen was non-palpable due to the ascites. There were no obvious triggers for her encephalopathy, such as acute infection, gastrointestinal bleeding, bowel obstruction or use of sedatives. As shown in the Table, the patient had pancytopenia, mildly elevated liver enzymes and impaired synthetic function.

Paracentesis was performed. The ascitic fluid cell count was 140 white blood cells (WBC)/µl, with 25 polymorphonuclear cells (PMN)/µl (18%). Gram stain and bacterial cultures were negative. The patient was treated with levolac and neomycin.

Three days after admission, Candida albicans was identified in fungal culture from peritoneal fluid. Intravenous fluconazole was initiated and the patient was sufficiently stabilized to allow extubation. After 4 days of treatment the encephalopathy resolved. The subsequent ascitic fluid sample revealed 120 WBC/µl with 43 PMN/µl (36%); Gram stain and cultures were negative for both bacteria and fungi.

Nevertheless, within a few days the patient again became encephalopathic despite treatment and she died within a few hours from septic shock attributed to extended spectrum beta-lactamase E. coli bacteremia. Ascitic fluid was not sampled again; the last sample was taken 3 days before her death.

Table 1. Blood tests on admission

<table>
<thead>
<tr>
<th>Component</th>
<th>Normal</th>
<th>Patient</th>
<th>Normal</th>
<th>Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaline phosphatase (U/L)</td>
<td>30–120</td>
<td>122</td>
<td>2.5</td>
<td>4.8–10.8</td>
</tr>
<tr>
<td>Gammaglutamyl transpeptidase (U/L)</td>
<td>7–49</td>
<td>94</td>
<td>9.1</td>
<td>12–16</td>
</tr>
<tr>
<td>Aspartate aminotransferase (U/L)</td>
<td>7–37</td>
<td>42</td>
<td>29.1</td>
<td>37–47</td>
</tr>
<tr>
<td>Alanine aminotransferase (U/L)</td>
<td>0–40</td>
<td>47</td>
<td>40</td>
<td>150–400</td>
</tr>
<tr>
<td>Amonia (µmol/L)</td>
<td>10–60</td>
<td>74</td>
<td>12.4</td>
<td>PT (sec)</td>
</tr>
<tr>
<td>Bilirubin total (mg/dl)</td>
<td>0.2–1.5</td>
<td>3</td>
<td>77</td>
<td>80–127</td>
</tr>
<tr>
<td>Bilirubin direct (mg/dl)</td>
<td>0–0.5</td>
<td>1</td>
<td>25</td>
<td>21–32</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>3.5–5.5</td>
<td>2.2</td>
<td>1.1</td>
<td>INR</td>
</tr>
</tbody>
</table>

PT = prothrombin time, PTT = partial thromboplastin time, APTT = activated partial prothrombin time, INR = international normalized ratio

COMMENT

Candida albicans is a common human fungal pathogen. It normally serves as a harmless commensal yet may function as a pathogen among immunocompromised patients or secondary to use of intravenous catheters [1]. Candida peritonitis is usually a disease of critically ill surgical patients. It results from hollow viscus perforation or the treatment of such an event and is associated with significant mortality [2].

Isolation of a fungus from ascitic fluid in cirrhotic patients is an uncommon event. Choi and co-researchers [4] reviewed the cases of 21 cirrhotic patients with ascitic cultures positive for Candida spp. Ten patients with clinical features of peritonitis were described as having spontaneous Candida peritonitis, while 11 patients were considered to have spontaneous fungal peritonitis.
 classified as having asymptomatic Candida isolated from ascites. None of the patients received antifungal therapy. Within 1 year of diagnosis all patients with spontaneous Candida peritonitis died, compared with 54.5% in the asymptomatic group. Ascitic fluid PMN > 315 cells/µl demonstrated 100% sensitivity in diagnosing spontaneous Candida peritonitis [4].

In a recently published study, spontaneous fungal peritonitis was found in 15 of 416 patients (3.6%) diagnosed with spontaneous peritonitis; all of them had a neutrophil count of at least 250 cells/µl. Sixty percent of the patients received antibiotic therapy 90 days prior to the fungal infection. Nosocomial spontaneous peritonitis was significantly more common in the spontaneous fungal peritonitis cohort than in the spontaneous bacterial peritonitis cohort (80% versus 35%, P = 0.0009). Only five patients were treated with appropriate antifungal therapy, and one of them improved. Patients with spontaneous fungal peritonitis had significantly higher 30 days mortality than spontaneous bacterial peritonitis patients (73% vs. 29%) [5].

Previously published data included patients with a higher ascitic neutrophil count than in our patient, and most of the patients did not receive antifungal treatment. Our case is unique because the patient was treated appropriately although she had a very low neutrophil count, her condition improved substantially and the culture became negative, suggesting that in her case it was truly an infection rather than colonization alone. Unfortunately, she died a few days later due to septic shock and bacteremia.

Candida peritonitis is a rare complication in cirrhotic patients. The definition of an infection versus colonization and its clinical significance and need for appropriate treatment is under debate. After reviewing the literature, we believe that primary fungal peritonitis is under-diagnosed. We suggest that in patients at high risk for fungal peritonitis (prolonged antibiotic therapy, recent hospitalization, and no improvement with empiric antibiotic therapy) [5] fungal cultures from ascitic fluid should be sent to the microbiology laboratory, regardless of neutrophil count. Empiric antifungal therapy should be considered in selected severely ill patients.

Patients with this disorder are rare and the diagnosis is difficult to ascertain, but our case raises the possibility that positive fungal cultures from ascitic fluid in cirrhotic patients are an indication of infection and not simply a harmless colonization, and the appropriate treatment should be administered. Therefore, larger scale studies are needed to determine both diagnostic and treatment guidelines for this condition. It seems, however, that regardless of treatment, Candida peritonitis is associated with a poor prognosis in cirrhotic patients.

References