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ORIGINAL ARTICLE

Analysis of ascitic fluid lactoferrin levels in the diagnosis of spontaneous bacterial peritonitis after systemic antibiotic treatment



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KEYWORDS

Antibiotic treatment; Ascites; Lactoferrin **Summary** Aims: Spontaneous bacterial peritonitis (SBP) is one of the most frequent complications of liver cirrhosis. Ascitic fluid lactoferrin has been proved to be a good diagnostic tool for SBP. However, lactoferrin in ascites may be checked after antibiotic treatment in these patients. Our study aims to assess the utility of ascitic fluid lactoferrin levels for the diagnosis of SBP after antibiotic treatment.

Materials and methods: Twenty-two ascites samples were collected from patients with cirrhosis. Samples were examined for bacterial culture, lactoferrin concentration, and polymorphonuclear leukocyte count. Clinical symptoms and indications for ascitic paracentesis were obtained from medical records. The diagnosis of SBP was based on an elevated ascitic fluid polymorphonuclear leukocyte count of ≥ 250 cells/mm³.

Results: Four (18.1%) samples fulfilled the diagnostic criteria for SBP. Three ascites samples showed a positive result for bacterial culture. Patients who received antibiotics for treatment of SBP constituted Group B (n=9), whereas those who did not receive any antibiotics comprised Group A (n=9). Lactoferrin concentration was significantly elevated (mean: $261.69 \pm 145.5 \, \text{ng/mL}$) in the three cases with a positive bacterial culture compared to those without SBP, in both Group A (mean: $19.64 \pm 6.32 \, \text{ng/mL}$, p=0.002) and Group B (mean: $23.64 \pm 9.53 \, \text{ng/mL}$, p=0.001).

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Conclusion: After systemic antibiotic treatment, elevated lactoferrin levels in the ascites of cirrhotic patients appear to be a promising predictor for the presence of SBP having positive ascitic bacterial culture.

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Introduction

Liver cirrhosis represents a terminal clinical stage of chronic liver disease. Patients with liver cirrhosis are susceptible to a variety of complications. Ascites or accumulation of fluid within the peritoneal cavity is one of the most common complications [1]. Spontaneous bacterial peritonitis (SBP) is the infection of pre-existing ascitic fluid without evidence of a secondary infection. The diagnosis of SBP is based on a polymorphonuclear leukocyte (PMN) count in ascitic fluid of \geq 250 cells/mm³, irrespective of whether the ascitic fluid indicates positive results on bacterial culture [2].

SBP leads to hospitalization of 10—30% of cirrhotic patients, and the mortality rate in this group approaches 30% [3,4]. Owing to the high mortality rate, patients with SBP should be started on empiric, broad-spectrum antibiotics immediately. According to the 2012 American Association for the Study of Liver Disease guidelines, in patients with suspected SBP, empiric therapy should be initiated promptly to maximize patient survival [5].

Lactoferrin is an iron-binding protein found in human mucosal secretions as well as in the specific granules of PMNs [6]. A previous study demonstrated the sensitivity and specificity of fecal lactoferrin concentration for the detection of intestinal inflammation [7]. In addition, measurement of ascitic fluid lactoferrin levels is a reliable biomarker for the presence of PMNs and detection of SBP in patients with cirrhosis [8]. However, as prompt antibiotic treatment is recommended when SBP is suspected, the therapy may be initiated prior to abdominal paracentesis for the collection of ascitic fluid in most cases, which can adversely affect the lactoferrin concentration. Therefore, the diagnostic role of ascitic lactoferrin levels after antibiotic treatment may be compromised and is unclear. Moreover, patients with advanced cirrhosis are prone to develop bacterial infections other than SBP, such as pneumonia or urinary tract infection, and may require antibiotic treatment [9]. In the present study, we aimed to identify the lactoferrin level after systemic antibiotic treatment for SBP and other systemic infections.

Materials and methods

Patients

The inclusion criteria were a known diagnosis of cirrhosis and the presence of ascites. The major indication for abdominal paracentesis was symptom relief to minimize the

feeling of abdominal fullness. Exclusion criteria included the presence of other causes of neutrocytic ascites, such as rupture of hepatocellular carcinoma, peritoneal carcinomatosis, and hemorrhagic ascites.

Paracentesis

Paracentesis was performed under aseptic conditions, with the patient in supine position and the puncture site in the left or right lower quadrant. Ultrasonography was performed prior to needle insertion to visualize the intra-abdominal structures. No immediate or delayed complications such as bleeding or hollow organ perforation were noted after the abdominal puncture procedure. Concurrent collection of an ascites fluid sample was performed. The ascites samples were used to measure total cell counts, PMN count, and albumin levels, and for performing aerobic and anaerobic cultures.

Methods

A total of 22 patients with cirrhosis and ascites, who were admitted to Chang Gung Memorial Hospital, Taoyuan, Taiwan and fulfilled the inclusion criteria, were assessed. The diagnosis of liver cirrhosis and ascites was based on clinical and biochemical data, and ultrasonography findings. The diagnosis of SBP was based on the PMN count during the first paracentesis, when SBP was suspected, as the symptoms such as fever, abdominal pain, or sepsis existed and the samples were examined for cell counts and bacterial culture. All the ascites samples collected during the second paracentesis, which was performed for symptom relief, were also examined for cell counts, bacterial culture, and lactoferrin concentration. Patients were classified into three groups: nine patients with an ascitic fluid PMN count of <250 cells/mm³, who did not initially receive systemic antibiotic treatment (Group A); nine patients with an ascitic fluid PMN count of <250 cells/mm³, who initially received antibiotic treatment for reasons other than SBP (Group B); and four patients with an ascitic fluid PMN count of \geq 250 cells/mm³ (Group C). Group C was further subdivided into culture-negative SBP (defined as Group Cn) and culture-positive SBP (defined as Group Cp) groups. Bacteriological culture was performed using aerobic and anaerobic standard blood culture bottles. The medical history of all patients was recorded, and all patients underwent a clinical examination, routine laboratory investigations, and an abdominal ultrasonographic examination. Aspirated ascitic fluid samples were immediately processed for cell counts (including total and differential cell counts), bacterial cultures, and biochemical assays. The lactoferrin

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