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ORIGINAL ARTICLE

Prevalence and risk factors for unsuspected spontaneous ascitic fluid infection in cirrhotics undergoing therapeutic paracentesis in an outpatient clinic

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Abstract
Background Spontaneous bacterial peritonitis (SBP) has been typically described in hospitalized patients. There are little data on ascitic fluid infection in asymptomatic outpatients. The present study was aimed at determining the prevalence and risk factors for asymptomatic ascitic fluid infection among patients with liver cirrhosis attending an outpatient clinic.
Methods Between January 2008 and December 2009, consecutive patients with cirrhosis (n=110) undergoing therapeutic paracentesis in an outpatient setting were studied. Patients with fever, abdominal pain, hepatic encephalopathy, recent gastrointestinal bleeding, impaired renal function, previous history of SBP and on antibiotic treatment were excluded. Baseline demographic details, and etiology and severity of liver disease were recorded. Ascitic fluid cell count, culture and biochemical tests were done using standard laboratory techniques.
Results The causes of cirrhosis were alcohol (55.5%), hepatitis B (21.8%), hepatitis C (9.1%) and others (13.6%). A total of 278 paracenteses were done in them (average 2.5 [1.1] times per patient). Spontaneous ascitic fluid infection was found in 7 (2.5%) paracentesis, including spontaneous bacterial peritonitis in one (0.4%), monomicrobial nonneutrocytic bacterascites (MNB) in two (0.7%) and culture-negative neutrocytic ascites (CNNA) in four (1.4%). *Escherichia coli*, Klebsiella spp. and *Staphylococcus aureus* were grown. There was no difference between cirrhotic outpatients with and without infection in age, gender, alcohol consumption, etiology of cirrhosis, Child-Pugh score, serum albumin and ascitic fluid total protein. There was no death due to spontaneous ascitic fluid infection.
Conclusion Asymptomatic ascitic fluid infection was very infrequent in patients with cirrhosis attending an outpatient clinic and undergoing therapeutic paracentesis.

Keywords Ascitic fluid · Cirrhosis · Infection · Spontaneous bacterial peritonitis

Introduction

Ascites is a common complication of liver cirrhosis [1]. Patients with cirrhosis and ascites are more susceptible to bacterial infections, of which spontaneous bacterial peritonitis (SBP) is the most frequent and potentially life-threatening [2]. It has typically been described in hospitalized patients with cirrhotic ascites, with 7% to 27% of patients with cirrhotic ascites showing evidence of occult peritoneal fluid infection at the time of hospital admission [3–5]. One-third of patients with infected peritoneal fluid lack any overt signs or symptoms such as fever or abdominal pain at the time of initial presentation [4].

It has been recommended that inpatients and outpatients with cirrhosis and new-onset clinically apparent ascites should undergo ascitic fluid analysis to rule out peritoneal fluid infection [6]. However, the need for routine ascitic fluid analysis in asymptomatic cirrhotic patients undergoing therapeutic paracentesis in the outpatient setting remains unclear [7]. There are only a few published studies on ascitic fluid analysis in asymptomatic outpatients [8–12]. The present study was aimed at determining the prevalence and risk factors for asymptomatic peritoneal fluid infection in cirrhotic outpatients undergoing therapeutic paracentesis.

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Table 1 Characteristics of patients with ascitic fluid infection

Sr No	Age and sex	Etiology	Child-Pugh class	Cell count >250 cells/mm^3	Culture	Serum albumin (g/dL)	Ascitic fluid protein (g/dL)
1	52 M	Alcohol	B	No	Positive	2.6	1.0
2	49 M	Hepatitis B	C	No	Positive	3.1	1.3
3	48 F	Hepatitis C	C	Yes	Negative	2.3	1.1
4	47 M	Alcohol	B	Yes	Negative	3.0	1.2
5	48 M	Alcohol	B	Yes	Negative	3.0	1.2
6	47 M	Alcohol	B	Yes	Negative	2.8	1.0
7	47 F	Non alcoholic fatty liver disease	B	Yes	Positive	2.9	1.0

Methods

Between January 2008 and December 2009, consecutive outpatients with liver cirrhosis undergoing therapeutic paracentesis for relief of discomfort or respiratory embarrassment due to tense ascites were enrolled; for patients undergoing paracentesis on multiple occasions, each instance was analyzed separately. Patients with fever, abdominal pain, hepatic encephalopathy, gastrointestinal bleeding within the last month, impaired renal function, previous history of SBP, antibiotic treatment within 2 weeks, antibiotic prophylaxis for SBP or non-cirrhotic ascites were excluded. Diagnosis of cirrhosis was based on clinical, imaging and biochemical findings. Baseline demographic details including age, gender, literacy and socioeconomic status were collected. A detailed work up for the cause of cirrhosis was done. Child-Pugh class was used as a measure of disease severity.

Ascitic fluid was collected under strict aseptic precautions using an 18-G catheter. It was examined for total and differential leucocyte count, and total protein and albumin levels. For bacterial culture, the fluid was inoculated into aerobic and anaerobic blood culture bottles (10 mL in each) under strict aseptic precautions.

A diagnosis of SBP was made when there was a positive ascitic fluid culture and an elevated ascitic fluid absolute polymorphonuclear count (at least 250 cells/mm^3), with no evidence of an intra-abdominal surgically-treatable source of infection [13]. The criteria for diagnosis of monomicrobial nonneutrocytic bacterascites (MNB) included a positive ascitic fluid culture for a single organism, an ascitic fluid polymorphonuclear cell (PMN) count below 250 cells/mm^3, and no evidence of an intra-abdominal surgically treatable source of infection [14]. Culture–negative neutrocytic ascites (CNNA) was diagnosed when ascitic fluid culture grew no bacteria, ascitic fluid PMN count was 250 cells/mm^3 or greater, the patient had not received any antibiotics (not even one dose), and no other explanation for an elevated ascitic PMN count was forthcoming [15].

Patients with SBP were hospitalized and received intravenous cefotaxime for 5 days. Those with MNB and CNNA were treated with oral ofloxacin 400 mg twice a day for 5 days. A follow up paracentesis was done to confirm resolution of the infection. All study participants provided a written informed consent. The study was approved by ethical committee of the institution. Quantitative data were expressed in mean and SD, and qualitative data as frequencies.

Results

One hundred and ten patients (mean [SD] age 47.1 [9.6] years; 80 [72.7%] male) with cirrhosis underwent therapeutic paracentesis on 278 occasions (mean 2.5 [1.1] times

Table 2 Risk factors for asymptomatic ascitic fluid infection in cirrhosis

Factor	Ascitic fluid infection	
	Yes (n=7)	No (n=103)
Age (years)	48.3 (1.8)	47 (9.9)
Gender (male:female)	5:2	75:28
Cause of liver disease (alcohol: HBV:HCV:others)	4:1:1:1	57:23:9:14
Child-Pugh's class (B:C)	5:2	72:31
Serum albumin (g/dL)	2.8 (0.3)	2.8 (0.4)
Ascitic fluid protein (g/dL)	1.1 (0.1)	1.2 (0.2)

Data are shown as numbers or mean (SD)

per patient) in the outpatient setting during the study period. The duration of ascites before inclusion in the study was 3 months to 14 months. Fourteen patients had previously undergone paracentesis at other hospitals 3–6 months prior to enrollment in the current study. The causes of cirrhosis were: alcohol (61 [56%]), hepatitis B (24 [22%]), hepatitis C (10 [9%]) and others (15 [14%]). History of variceal bleeding and hepatic encephalopathy was found in 46 and 24 patients, respectively; 77 patients were in Child-Pugh class B and 33 in class C.

In 7 (2.5%) of 278 paracentesis, ascitic fluid showed evidence of peritoneal fluid infection (Table 1); these included SBP in one patient, MNB in two patients and CNNA in four patients. Bacterial culture showed *Escherichia coli* in one patient with SBP, and Klebsiella spp. and *Staphylococcus aureus* in one patient each with MNB. All patients had evidence of spontaneous infection at the time of their first therapeutic paracentesis. No deaths were observed due to spontaneous infection during a short term follow up of 12 weeks. There was no difference between cirrhotic outpatients with and without evidence of peritoneal fluid infection in age, gender, etiology, and severity of cirrhosis, and ascitic fluid protein level (Table 2).

Discussion

We found a very low frequency of peritoneal fluid infection among outpatients with cirrhotic ascites undergoing large volume paracentesis. Evans et al. [8] found the prevalence of SBP to be 1.4% and CNNA to be 2.1% in 427 cirrhotic patients attending an outpatient clinic without any symptoms or risk factors for SBP; the prevalence of MNB was 3%, and this condition was frequent in patients on selective intestinal decontamination. In another prospective study [9], ascitic fluid cell counts and cultures were obtained in outpatients with refractory ascites undergoing large volume paracentesis; of these, 2.5% had MNB and none had SBP. Runyon reported SBP in 2% of a series of 400 paracentesis performed over 2 years in an outpatient setting [10]. In a retrospective analysis of 37 outpatients undergoing large–volume paracentesis in a U.S. hospital, ascitic fluid cell counts and cultures did not reveal evidence of peritoneal fluid infection in any patient [11]. Similarly, in a prospective study from Barcelona, Spain, 173 ascitic fluid samples from 51 asymptomatic stable cirrhotics with refractory ascites were analyzed [12]; all the specimens had cell count below 250 PMN/mm^3 and only four (2.3%) grew bacteria and were classified as asymptomatic MNB.

SBP in asymptomatic outpatients differs from SBP in hospitalized patients. Ascitic fluid from the former patients more often grows Gram-positive bacteria [16], and not *E. coli* and *K. pneumoniae* that predominate among hospitalized patients. It has been proposed to be related to previous administration of norfloxacin prophylaxis or other interventions. Further, in these patients, co-existent type I hepatorenal syndrome is infrequent, recurrence of peritoneal fluid infection is unusual even in the absence of antibiotic prophylaxis, and 1 year mortality rate is low (33% vs. 50% to 70%) [8, 17, 18]. In our study, *E. coli*, Klebsiella spp. and *Staphylococcus aureus* were grown in three patients with ascitic fluid infection.

Though the outcome of SBP has improved over the last decade, the mortality rate in this condition remains high [4, 19, 20]. An early diagnosis of SBP may help by allowing early institution of treatment. AASLD practice guidelines recommend testing of ascitic fluid only for cell count and differential count for patients undergoing serial outpatient therapeutic paracentesis [6, 8, 9]. Bacterial culture is not necessary in asymptomatic patients.

The present study raises concern about the usefulness of routine ascitic fluid analysis in outpatient paracentesis on account of our observed low prevalence (2.5%). However, since the natural history of spontaneous infection without treatment was not studied, it may not be possible to assess the clinical utility of routine ascitic fluid cell count measurement in such patients.

In conclusion, our study confirms that asymptomatic spontaneous infection of peritoneal fluid is infrequent in cirrhotics undergoing therapeutic paracentesis on outpatient basis, and no predictors could be identified for occurrence of such infection. There is a need for studies to address the natural history of such infection without treatment to clearly define the role of routine ascitic fluid analysis in this setting.

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