

Study of Frequency of Spontaneous Bacterial Empyema in Cirrhotic Patients With Hepatic Hydrothorax

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ABSTRACT

AIM: The aim of this work was to assess the frequency of spontaneous bacterial empyema in cirrhotic patients with ascites and determine the possible associated risk factors of spontaneous bacterial empyema in those patients.

MATERIALS AND METHODS: 322 cirrhotic patients with ascites and pleural effusion were enrolled. Spontaneous bacterial empyema was diagnosed by positive pleural fluid culture or, if negative, a pleural fluid PMNL count >500 cells/mm³ without radiographic evidence of pneumonia or a contiguous infection process on chest radiography.

RESULTS: The frequency of spontaneous bacterial empyema (SBEM) among cirrhotic patients with ascites and hepatic hydrothorax was 14.3% (46 out of 322 cirrhotic patients). E.Coli was the commonest organism (54.8%) responsible for SBEM in positive culture cases.

CONCLUSION: SBEM was recognized in 14.3% of cirrhotic patients with ascites and hepatic hydrothorax. So, it is a frequent but underdiagnosed complication of hepatic hydrothorax and has a poor prognosis.

Key words: Spontaneous bacterial empyema; cirrhosis; hydrothorax

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INTRODUCTION

Despite the advancement in medical care for patients with advanced liver disease in the past decades, bacterial infections remain very common and account for significant morbidity and mortality (approximately 30%) in these patients^[1,2].

Spontaneous bacterial empyema (SBEM) is the infection of a pre-existing hydrothorax in which pneumonia has been excluded. It has been reported to be present in 10% -20% of hospitalized patients with hepatic hydrothorax^[3-5]. SBEM can occur either with SBP, through trans-diaphragmatic spread, or without SBP through hematogenous spread^[6].

Some factors may contribute to development of SBEM in patients with cirrhosis such as the presence of SBP, low pleural fluid protein and complement (C3) levels, low serum albumin and advanced liver disease (high child pugh score)^[4,7].

Any patient with hydrothorax who develops fever, pleuritic pain, encephalopathy or unexplained deterioration in renal function should undergo thoracentesis, as SBEM is suspected. Thoracentesis should be done when an infection is suspected in cirrhotic patients with ascites and hydrothorax, particularly in those with non-infected ascites^[8].

Hospital mortality has been reported as 20%-40% in cirrhotic patients with SBEM^[3,5]. So, treatment with an intravenous third generation cephalosporin antibiotic such as first line therapy: cefotaxime 2gm/12 h IV or ceftriaxone 1gm/12-24IV for 7-10 days should be initiated immediately when pleural fluid PMN \geq 250

cells/mm³ while awaiting culture result^[9,6]. Chest Tube drainage is contraindicated in patients with hepatic hydrothorax and SBEM because of the risk of life threatening fluid depletion, protein loss and electrolyte imbalance^[10,3].

The aim of this work was to assess the frequency of spontaneous bacterial empyema in cirrhotic patients with ascites and determine the possible associated risk factors of spontaneous bacterial empyema in those patients.

PATIENTS AND METHODS

This cross sectional study was performed in Tropical Medicine Department, Internal Medicine Department, Zagazig University and Hepatology Department, El-Ahrar hospital in the period between May 2013 to May 2014.

Administrative design was done and an informed consent was taken from each patient before inclusion in this study.

322 cirrhotic patients with ascites and pleural effusion were enrolled. The diagnosis of liver cirrhosis was established histologically (120 patients) or based on the presence of at least 2 of the following: characteristic imaging features, esophageal and/or gastric varices, ascites or increased international normalized ratio (INR) that could not be attributed to any other cause. The severity of the liver disease was assessed according to the Child-Pugh classification.

Patients with evidence of pneumonia or pleural effusion due to cardiac and pulmonary diseases before the infections episode were excluded from the study.

All patients were subjected to:

1 history taking;

2 full clinical examination and;

3-Laboratory investigations: A- Complete blood picture; B- Liver function tests; C-Renal function test; D-Viral markers: Hepatitis B surface antigen (HBs Ag), and Hepatitis C virus Ab (HCV Ab) using third generation ELISA test; E-Anti mitochondrial antibody (AMA), anti smooth muscle antibodies (ASMA), antinuclear antibodies (ANA) and anti liver kidney microsomal antibodies (LKMA) in cases suspecting autoimmune hepatitis; F-Serum ceruloplasmin and 24 hours urinary copper in cases suspecting of Wilson disease; G-Serum iron and transferrin saturation in cases suspecting of hemochromatosis; H-Serum alpha-fetoprotein level: In cases suspecting hepatocellular carcinoma.

4 Imaging study: I. Abdominal Ultrasound: The abdominal ultrasonography was used to assess liver size, shape and texture, focal lesion and portal vein diameter. Also to assess the size of spleen in addition to detection of ascites and pleural effusion; II. Chest X-ray: Chest radiography, post-anterior and lateral view for the effusion and to exclude pneumonia. C.T Chest was done if indicated in some cases.

5 Diagnostic thoracentesis: The pleural fluid is collected under aseptic conditions in a sterile container and sent to the laboratory immediately and processed for leukocyte count, cytology, Gram staining and both aerobic and anaerobic bacterial cultures.

Spontaneous bacterial empyema was diagnosed by positive pleural fluid culture or, if negative, a pleural fluid PMNL count >500 cells/mm³ without radiographic evidence of pneumonia or a contiguous infection process on chest radiography.

6 Paracentesis of the ascitic fluid: The ascitic fluid is collected at the same time and processed in the same way as the pleural fluid.

The diagnosis of spontaneous bacterial peritonitis was established by positive ascitic fluid culture or, if negative, an ascitic fluid PMNL count >250 cells/mm³, with an absence of findings suggesting secondary peritonitis.

RESULTS

Cirrhosis are caused by HCV infection in 289 (89.8%) patients, HBV infection in 20 (6%) patients, non-alcoholic steatohepatitis in 5 (1.6%) patients, autoimmune hepatitis in 2 (0.6%) patients and undiagnosed cirrhosis in 6 (1.9%) patients.

Child classification were more commonly presented with statistically significant value in patients with SBEM in comparison to patients with sterile pleural effusion (Table 1).

The frequency of spontaneous bacterial empyema (SBEM) in cirrhotic patients with ascites was 14.3% (Table 2).

Table 3 shows the types of microorganisms isolated in culture +ve SBEM in which E. Coli is more frequent (54.8%) followed by Klebsiella, Streptococci, Pseudomonas and then Clostridium.

Table 4 shows the types of microorganisms isolated in culture +ve SBP in which E. Coli is more frequent.

Table 1 Demographic data and Child classification in patients with sterile pleural effusion and SBEM.

Variable	Sterile pleural effusion (N=276)	SBEM (N=46)	X2	P
Sex			1.031	0.31(NS)
Male	158 (57.2%)	30 (65.2%)		
Female	118 (42.8%)	16 (34.8%)		
Age	Mean ± SD	56.76 ± 6.23	t: 0.247	0.805(NS)
Child classification			11.438	0.001(S)
Child A	0	0		
Child B	92(33.3%)	4 (8.7%)		
Child C	184 (66.7%)	42 (91.3%)		

S: Significant ($p < 0.05$); NS: Non significant ($p > 0.05$).

Table 2 Frequency of spontaneous bacterial peritonitis (SBP), pleural effusion and spontaneous bacterial empyema(SBEM) in the studied group.

Variable	Number	Percentage
SBP	108	33.5%
Pleural effusion		
Right sided	282	87.6%
Left sided	29	9%
Bilateral	11	3.4%
SBEM	46	14.3%

SBP: spontaneous bacterial peritonitis; SBEM: spontaneous bacterial empyema.

Table 3 Pleural fluid examination in the studied group.

Pleural fluid	Number	Percentage
Culture +ve SBEM	31	9.6%
Culture -ve SBEM	15	4.7%
Sterile pleural effusion	276	85.7%
PMNL count/mm ³	65 (Median)	6 -1475 (Range)

Culture +ve SBEM (n=31)	Number	Percentage
E. Coli	17	54.8%
Klebsiella	9	29%
Streptococci	2	6.5%
Clostridium	1	3.2%
Pseudomonas	2	6.5%

SBEM: spontaneous bacterial empyema; PMNL: polymorphonuclear leukocytes.

Table 4 Organisms found in ascitic fluid in culture +ve SBP.

Culture +ve SBP (n=21)	Number	Percentage
E. Coli	8	38.1%
Klebsiella	4	19%
Streptococci	4	19%
Enterococci	3	14.3%
Pseudomonas	2	9.5%

No statistically significant difference between the distribution of Pleural effusion in patients with sterile pleural effusion and SBEM. However there was highly statistically significant increase of right sided pleural effusion in patients with spontaneous bacterial empyema (SBEM).

There was statistically highly significant difference in levels of PMNLs count in patients with spontaneous bacterial empyema (SBEM) when compared to those without (Table 5).

Treatment with an intravenous third generation cephalosporin antibiotic such as cefotaxime 2gm/12 h IV or ceftriaxone 1gm/12-24IV for 7-10 days should be initiated immediately when pleural fluid PMN ≥ 250 cells/mm³ while awaiting culture result.

Table 6 shows antibiotic susceptibility in culture positive SBEM.

Table 5 The distribution of Pleural effusion and PMNLs count in patients with sterile pleural effusion and SBEM.

Pleural effusion	Sterile pleural effusion (N=276)	SBEM (N=46)	X2	P
Right	240(86.9%)	42(91%)		
Left	27(9.7%)	2(4.5%)	1.515	0.469 (NS)
Bilateral	9(3.4%)	2(4.5%)		

Variable	Sterile pleural effusion (N=276)	SBEM (N=46)	Mann-Whitney test	P
PMNLs count (cell/cm ³)	Median 60 Range 6-87	765 415-1475	-10.867	0.000(HS)

Table 6 Antibiotic susceptibility in culture +ve SBEM.

Culture +ve SBEM (n=31)	Number	Percentage
Meropenem	31	100%
Ceftriaxone	20	64.5%
Cefotaxime	18	58.4%
Levofloxacin	16	51.6%
Ciprofloxacin	18	58%

DISCUSSION

In the absence of cardiac or lung disease, the presence of a pleural effusion in a cirrhotic patient is known as hepatic hydrothorax^[11]. Spontaneous bacterial empyema, (SBEM) is the infection of a pre-existing hydrothorax in which pneumonia has been excluded. It has been reported to be present in 10%-20% of hospitalized patients with hepatic hydrothorax. Comparable to spontaneous bacterial peritonitis (SBP), SBEM is associated with a deteriorating prognosis with an estimated mortality rate over 20%^[12].

In the present study the frequency of spontaneous bacterial empyema (SBEM) among cirrhotic patients with ascites and hepatic hydrothorax was 14.3% (46 out of 322 cirrhotic patients). This percentage is closely near to Xiol *et al*^[3] and Chen *et al*^[4] who reported that the incidence of spontaneous bacterial empyema (SBEM) in patients with liver cirrhosis was between 13% and 16%, with a higher incidence in more advanced stages of the liver disease. However this result was less than that reported by Makhlof *et al*^[13] who found that the prevalence was 26.2% and Gur *et al*^[14] who also reported a higher prevalence reaching 30%. The variation in incidence of spontaneous bacterial empyema in cirrhotic patients may be explained by the different diagnostic methods or the criteria for patient selection.

In the present study, the demographic data of cases with spontaneous bacterial empyema showed that the old aged male patients predominated than females patients (65.2% vs 34.8%) respectively. This result was similar to those reported by Chen *et al*^[4] who found that males were 70% and females were 30% and Mansour

et al^[15] who reported that males were 57.1% and females were 42.9%.

The present study showed that 91.3% from cirrhotic patients with spontaneous bacterial empyema were Child class C and 8.7% were Child class B. This result is in agree with Makhlof *et al*^[13] who reported that 93.8% from cirrhotic patients with spontaneous bacterial empyema were Child C. Chen *et al*^[4] showed that advanced liver disease as expressed by high child scores was risk factor for the occurrence of SBEM.

As regard development of pleural effusion (hepatic hydrothorax) in cirrhotic patients with SBEM, we found that all patients had ascites, 91% of patients had right sided pleural effusion, 4.5% of patients had left sided pleural effusion and 4.5% of patients had bilateral pleural effusion secondary to passage of ascites from the abdomen to the pleural space via defects in the diaphragm^[11,16]. This result is agree with Mansour *et al*^[15] who reported that 85.8% of patients had right sided pleural effusion, 7.1% of patients had left sided pleural effusion and 7.1% of patients had bilateral pleural effusion. But Chen *et al*^[4] showed that 4% of patients had hydrothorax without ascites and Makhlof *et al*^[13] showed that 25% of patients had hydrothorax without ascites.

In the present study it was found that 63% of cirrhotic patients with spontaneous bacterial empyema had spontaneous bacterial peritonitis. Makhlof *et al*^[13] reported that about 56.3% of patients had spontaneous bacterial peritonitis (SBP), also Chen *et al*^[4] reported that only 47% of patients had spontaneous bacterial peritonitis (SBP).

As regard pleural fluid examination in the present study, a high PMNL count was documented in all cases of SBEM, that PMNL count is the earliest and most reliable marker for SBEM. Pleural fluid culture was found to be positive in 31 patients with SBEM and 15 patients had culture negative SBEM (PMNL count >500 cells/mm³), and our results are close to those reported by Xiol *et al*^[3].

The bacteria responsible for SBEM are usually E.Coli, Klebsiella, Clostridium, Streptococci and pseudomonas^[17]. In the present study, E.Coli was the commonest organism (54.8%) responsible for SBEM in positive culture cases. Xiol *et al*^[3] and Chen *et al*^[4] reported that E Coli was the commonest organism for SBEM in positive culture cases (44.4% and 20% respectively).

CONCLUSION

SBEM was recognized in 14.3% of cirrhotic patients with ascites and hepatic hydrothorax. So, it is a frequent but underdiagnosed complication of hepatic hydrothorax and has a poor prognosis. More studies are required to elucidate the underlying pathogenetic mechanism and the natural course of SBEM. Meanwhile, its possible occurrence should be borne in mind in cases of hepatic hydrothorax who develop fever, encephalopathy or unexplained deterioration of renal functions, particularly if they have high Child-Pugh score with or even without SBP.

CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

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