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Research Article

Hepatic Cirrhosis: Characteristics of Spontaneous Bacterial Peritonitis

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Abstract

Objective: To establish the characteristics of spontaneous bacterial peritonitis in cirrhotic patients with ascites.

Method: We compiled information from clinical records of cirrhotic patients with ascites admitted to the gastroenterology service.

Results: The most common reason for consultation was increased abdominal circumference (69.2%); somnolence (29.9%), hematemesis (23.1%). Child-Pugh was 78.8% type B and 22.2% type C. There was evidence of association between coinfection and spontaneous bacterial peritonitis (p = 0.013).

Conclusion: EBP is a frequent and serious complication of patients with advanced liver cirrhosis and ascites. Early diagnosis and treatment have improved the prognosis in recent years.

Keywords: *Hepatic Cirrhosis; Ascites; Spontaneous Bacterial Peritonitis; Bacterioascitis; Neutrocytic Ascites*

Introduction

Spontaneous bacterial peritonitis (PBE) is a frequent and serious complication of patients with cirrhosis and ascites; with a hospital mortality of 30 - 50% and a risk of recurrence per year in patients who survive 70% [1]. The PBE was first described by Conn in 1964 when it differentiates this form of infection from surgical peritonitis, but it is not until 1975 that the elusive origin of this disease is demonstrated, and the same author and Correia coined this term and classify them into categories or subtypes based on cultures, neutrophil polymorphonuclear counts and the absence of a surgical origin of infection [2]. The incidence of SBP is between 66% and 88% of patients hospitalized with moderate to severe ascites. After presenting the first episode of this condition, long-term survival is very low (30 - 40%) and the probability of recurrence is 70% in the first year [3]. The clinical manifestations of spontaneous bacterial peritonitis are very variable, with abdominal pain, fever, chills and changes in mental state that can lead to hepatic encephalopathy, which can be expressed in very mild to very severe forms, even begin clinically as a septic shock [2,3].

The diagnosis is made by abdominal paracentesis and subsequent study of ascitic fluid in patients with hepatic cirrhosis, who present the clinical characteristics previously exposed or who are asymptomatic [2]. It has a recurrence rate of 70% during the first year, with mortality reaching 50 - 70% per year, which forces patients to recover from an episode of spontaneous bacterial peritonitis as potential candidates for liver transplantation [1]. After urinary tract infection, spontaneous bacterial peritonitis is the second most common infectious process in patients with advanced liver cirrhosis. It is developed in 3.5% of the patients who are treated as outpatients, its prevalence is 12% in hospitalized patients [4].

Spontaneous bacterial peritonitis is recognized as a marker of progression of underlying liver disease, which could define advanced liver disease [5]. Most episodes of PBE are caused by gram-negative aerobic germs, with the gut of the patients being the source of infection. This is due to the fact that patients with cirrhosis present severe alterations in the antibacterial defense mechanisms, both intestinal,

systemic and ascitic fluid itself [6]. Patients with cirrhosis present a slowing in intestinal transit time, which has been attributed to several factors. This disorder leads to a clearance failure that favors intestinal bacterial overgrowth (SBI) in cirrhosis (occurring in up to 40% of patients), especially in those with ascites and more advanced liver failure (Child-Pugh C). In fact, these patients have been shown to have a higher incidence of EBP at follow-up. Drugs that accelerate intestinal transit, such as prokinetics and propranolol, decrease the incidence of SBI [7]. In cases of experimental cirrhosis, it has been demonstrated that there is an oxidative stress of the mucosa of the small intestine, with an increase in the activity of xanthine oxidase and the lipid peroxidation of the brush border of the intestinal mucosa, altering its permeability. In addition, the immune defect in the clearance of translocated bacteria that occurs in cirrhosis is accompanied by an endotoxin-induced release of proinflammatory cytokines [8].

The cascade production of tissue necrosis factor and nitric oxide stimulated by endotoxins aggravates the oxidative damage in the intestinal epithelium [9]. In hepatic cirrhosis there is alteration in the function of circulating immunocompetent cells, and this knowledge is extrapolated to the intestinal immune system. Several *in vivo* and *in vitro* studies in human models of advanced cirrhosis have demonstrated deficiencies in the bacteriostatic and opsonic capacity of serum, in neutrophil phagocytes, and in the effector function of immunocompetent cells circulating in blood. In addition, splanchnic hyperemia associated with portal hypertension complicates the rolling, adhesion and migration of phagocytic cells in the mesenteric venules [10]. Ascitic fluid has an opsonizing and bactericidal activity, which is a basic defense mechanism against the development of infection. After the arrival of a germ to the ascitic fluid, this system is activated through the alternative route of the complement stimulated by the lipopolysaccharides of the wall of the gram-negative bacilli. The bactericidal capacity is in direct relation with the concentration of proteins and levels of complement, reason why those patients with albumin levels in ascites fluid of less than 1 g/dl or low levels of C3 are those that present greater predisposition for the development of PBE [11].

The key pathogenic mechanism that initiates bacteremia and subsequently the development of spontaneous bacterial peritonitis is bacterial translocation (TB). This is defined as the migration of microorganisms from the intestinal lumen to the mesenteric lymph nodes (GLM) and other extraintestinal organs. This migration of bacteria is a normal physiological phenomenon, but in healthy individuals, the immune system is able to eliminate the few germs that reach GLM. For TB to be a pathological phenomenon, bacterial migration must be associated with a local or systemic inflammatory response or with subsequent dissemination of bacteria from mesenteric lymph nodes to blood or lymph [12]. Its diagnosis is based on a count of polymorphonuclear leukocytes in ascitic fluid greater than 250 cells/µl; the frequent is that it is a monomicrobial infection, caused mostly by gram-negative germs of enteric origin, especially *Escherichia coli* and *Klebsiella* spp. A culture of positive ascitic fluid, which confirms the diagnosis, is obtained in 70% of the cases [1]. There are variants of spontaneous bacterial peritonitis. The neutrocyte ascites situation in which there is a PMN count greater than 250/µl in ascites fluid, but the culture is negative. However, these patients have similar signs, symptoms and prognosis as those with EBP and ascites fluid culture positive [13].

Bacterioascitis is characterized by bacterial colonization of ascitic fluid in the absence of an inflammatory reaction, i.e. there is a PMN < 250/µl count in ascitic fluid with a positive bacterial culture. Patients with bacterioascitis constitute a heterogeneous population. In some patients spontaneous colonization of the ascitic fluid occurs, while in others this colonization is secondary to an extraperitoneal infection [14]. The natural course of untreated bacterioascitis is also variable, from spontaneous resolution, which can occur in more than 60% of patients (especially in those who are asymptomatic), until the development of a true EBP. Usually, patients who develop PBE have signs or symptoms of infection at the time of paracentesis and should receive empiric antibiotic treatment pending the outcome of LA culture regardless of the PMN count [15].

General Objective

To establish the characteristics of spontaneous bacterial peritonitis in cirrhotic patients with ascites in the Gastroenterology Service of the Hospital Universitario de Caracas between January and December 2015.

Specific Objectives

1. Identify the most frequent germs in patients with spontaneous bacterial peritonitis.
2. Relate the presence of other previous infectious foci and spontaneous bacterial peritonitis.
3. To determine the frequency of spontaneous bacterial peritonitis.
4. Determine the frequency of bacteriascitis.
5. Determine the frequency of neutrocytic ascites.

Ethical aspects

This study was carried out in accordance with the Declaration of Helsinki. Likewise, it was submitted to a review by the Bioethics Commission of the University Hospital of Caracas for its consideration and acceptance.

Methods

Type of study: The research corresponded to a descriptive, retrospective cross-sectional study.

Population and sample: Patients with complicated liver cirrhosis with portal hypertension syndrome and ascites admitted to the Gastroenterology Service of the Hospital Universitario de Caracas in the period January-December 2015. The sample was intentional and non-probabilistic, was determined by the number of patients included in the study. period of time.

Inclusion criteria: Patients older than 18 years admitted with diagnosis of complicated liver cirrhosis with portal hypertension syndrome and ascites.

Exclusion criteria

- Patients with hepatic cirrhosis without portal hypertension.
- Patients with non-cirrhotic portal hypertension syndrome
- Patients with portosystemic shunts.

Procedures

The necessary information was collected by reviewing medical records requested from the Medical Records Archive. This information was collected using a data collection form, then tabulated and analyzed, interpreting the results, determining conclusions and recommendations.

Proposed statistical treatment

The mean and standard deviation of age were calculated; in the case of the nominal variables, their frequencies and percentages were calculated. The results were arranged in one-and two-input tables. The relationship of the presence of PBE and type of infection was carried out with the chi-square test of Pearson. It was considered a significant value if $p < 0.05$. The data were analyzed with JMP-SAS version 12.

Variables	**n**	
n	52	
Age (years) (mean ± standard deviation)	57 ± 14	
Gender	**n**	**%**
Male	32	61,5%
Female	20	38,5%

Table 1: *Characteristic of the sample according to epidemiological indicators.*

Etiology of cirrhosis	n	%
Alcohol	34	65,4
Hepatitis C	7	13,5
NASH	4	7,7
Secondary biliary cirrhosis	3	5,8
Autoimmune hepatitis	3	5,8
Hepatitis B	1	1,9

Table 2: *Distribution of Hepatic Cirrhosis according to its causes.*

Reason for consultation	n	%
Increased abdominal circumference	36	69,2
Somnolence	14	26,9
Hematemesis	12	23,1
Abdominal pain	7	13,5
Jaundice	6	11,5
Fever	6	11,5
Rectorragia	3	5,8
Cough	1	1,9

Table 3: *Distribution of the sample according to reasons for consultation.*

Comorbilities	n	%
None	39	75
DM II	6	11,5
Secondary sclerosing cholangitis	2	4
Psoriasis	1	1,9
Primary sclerosing cholangitis	1	1,9
Choledocholithiasis	1	1,9
Scleroderma	1	1,9
LOE pelvic	1	1,9

Table 4: *Characteristic of the sample according to type of comorbidity.*

Variables	n	%
Child-Pugh		
A	0	0,0
B	41	78,8
C	11	21,2

Table 5: *Sample characteristic according to Child-Pugh score.*

Variables	n	%
Spontaneous bacterial peritonitis	13	25
Ascites Neutrocytic	33	63,5
Bacterioascitis	6	11,5
Isolated germ		
Absent	46	88,5
Escherichia coli	3	5,8
Staphylococcus aureus	1	1,9
Escherichia coli BLEE	1	1,9
Klebsiella	1	1,9
Infection		
Absent	39	75,0
ITU	9	17,3
IPPB	3	5,8
IRB	1	1,9
Results of culture*		
Without culture	43	82,7
*Escherichia col*i	5	9,6
Sin crecimiento	4	7,7

Table 6: *Characteristic of the sample according to bacteriological indicators.*

**coinfection culture*

	Spontaneous bacterial peritonitis			
	With		Without	
Infection	**n**	**%**	**n**	**%**
Absent	7	53,8	32	82,1
IPPB	3	23,1	0	0,0
IRB	0	0,0	1	2,6
ITU	3	23,1	6	15,4
Total	13	100,0	39	100,0
p = 0,013				

Table 7: *Relationship of presence of coinfection and presence of SBP.*

Discussion

Cirrhotic patients with ascites may develop EBP. The prevalence of SBP in patients with cirrhosis ranges from 10% to 30%. Corresponding to our study, where a prevalence of 25% of patients with EBP was observed. Similarly, at the General Hospital of the West "Dr. José Gregorio Hernández" from Caracas, a study was carried out with 90 patients admitted with ascites, of whom 76 had a diagnosis of liver cirrhosis, 11 with intra-abdominal tumors and 3 with heart failure, where it was concluded that ascitic fluid infection was more frequent in cirrhotic patients, with a prevalence of 7.9% for PBE, 6.6% for neutrocytic ascites and 1.3% for bacterioascitis [16]. The prevalence in this study was conditioned, since all patients with ascites were included, without discriminating the etiology of the disease. In our

study, neutrocytic ascites and Grade B Child-Pugh classification were more frequently observed. Because patients who develop EBP are patients with more impaired hepatocellular function as indicated by a higher Child-Pugh score, presence of hepatic encephalopathy at the time of diagnosis of infection, and a low concentration of proteins in ascitic fluid. In contrast, neutrocytic ascites occurs in patients with a more conservative hepatocellular function, and its clinical course and prognosis are better than in patients with an EBP. This data is related to the decrease in the opsonization of ascitic fluid and, therefore, a decrease in the capacity to eliminate both bacterial and bacterial products that reach the ascitic fluid through the bacterial translocation phenomenon [17]. Despite the use of sensitive methods, culture of ascitic fluid is negative in up to 60% of patients with clinical manifestations suggestive of EBP and neutrophil count in high ascites [18]. Most patients have symptoms or signs suggestive of peritoneal infection, especially abdominal pain, fever and impaired gastrointestinal motility. Other patients may present with hepatic encephalopathy or renal failure which may be the predominant or only characteristic. In other cases, SBP may be asymptomatic or have only minor symptoms [19]. In contrast, the main symptom reported by patients included in our study was increased abdominal circumference, followed by drowsiness, which led to their hospital admission, determining presence or not of PBE. Similarly, this is related to advanced liver disease, since both are parameters to determine the degree of Child-Pugh classification. Also, in a study conducted by Kavita., *et al*. The most frequent symptoms were abdominal pain (45%), fever (38%), jaundice (36%), upper gastrointestinal bleeding (10%) and altered state of consciousness (8%). One of the cases with PBE was admitted with grade IV hepatic encephalopathy [5]. With early diagnosis of the disease and timely and appropriate antibiotic treatment, hospital mortality due to EBP has been reduced to approximately 20%. Most episodes of spontaneous bacterial peritonitis are monomicrobial and produced by enteric bacteria. Of these episodes, 67% involve gram-negative bacteria, *Escherichia coli* is the most frequently isolated microorganism [20]. Similarly, our study showed that *Escherichia coli*, with 5.8%, being this more frequent germ of the gastrointestinal tract.

Likewise, *Staphylococcus aureus* was isolated in 1.9% of cases. Although the most frequent infections caused by *Staphylococcus aureus* are cutaneous, urinary or respiratory, the occurrence of PBE by *Staphylococcus aureus* has been described in recent years. 17 - 29% of hospitalized cirrhotic patients have been identified as nasal carriers of *Staphylococcus aureus*. *Staphylococcus aureus* colonization in cirrhotic patients occurs frequently during hospitalization and is associated with the practice of invasive maneuvers and previous administration of antibiotics [1]. Inoculation of ascitic fluid in blood culture bottles often show *Escherichia coli* and *Streptococcus* species. Ascites with negative culture is observed in 60% of the patients, despite clinical signs of SBP and neutrophil count > 250 cells / L. These patients should still be treated as if they had PBE [21].

The probability of having a first episode of SBP in patients with bilirubin in serum greater than 2.5 mg/dl becomes 43% and with protein levels in ascites less than 2.5 g/dl is 15 - 45 %. When the level of protein in ascites is high (> 2.5 g/dl), the risk of EBP is insignificant and antibiotic prophylaxis is not considered necessary [22]. Although not reported as a variable in our study, data were collected on total protein levels in ascitic fluid, evidencing protein levels lower than 2.5 g/dl in 89.5% of the cases. The probability of having a first episode of SBP in patients with bilirubin in serum greater than 2.5 mg/dl becomes 43% and with protein levels in ascites less than 2.5 g/dl is 15 - 45 %. When the level of protein in ascites is high (> 2.5 g/dl), the risk of EBP is insignificant and antibiotic prophylaxis is not considered necessary [22]. Although not reported as a variable in our study, data were collected on total protein levels in ascitic fluid, evidencing protein levels lower than 2.5 g/dl in 89.5% of the cases.

Conclusions

- The most common reason for consultation was increased abdominal circumference.
- According to the Child-Pugh Scale, the most frequent grade was grade B.
- According to the presence of PBE and its variants, the most frequent was neutrocytic ascites.
- The most common germ isolated in ascitic fluid culture was Escherichia coli.
- It was determined that there is a statistically significant relationship between the presence of coinfection (urinary tract infection) and EBP.

Recommendations

- Follow-up of patients with liver cirrhosis complicated with portal hypertension syndrome, facilitating the control of chronic liver disease and determining early behavior avoiding complications related to this pathology.
- Perform diagnostic paracentesis for all patients with hepatic cirrhosis, portal hypertension syndrome and ascites, and perform an early diagnosis of spontaneous bacterial peritonitis.
- Use more sensitive culture media, in order to improve the detection of causative germs and indicate adequate antibiotic therapy, avoiding bacterial resistance.
- Improve asepsis methods at the time of paracentesis, avoiding secondary complications.
- Indicate antibiotic therapy for all patients suffering from spontaneous bacterial peritonitis and its variants.
- Perform a study to determine the relationship between the severity of hepatic cirrhosis and spontaneous bacterial peritonitis.
- Indicate antibiotic therapy independently of the findings of spontaneous bacterial peritonitis and its variants.

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