Prevalence and Diagnosis of Spontaneous Bacterial Peritonitis

Thesis

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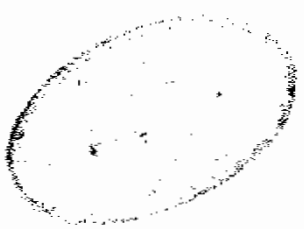

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I thank the patients for their cooperation and patience, and to whom I dedicate this work.

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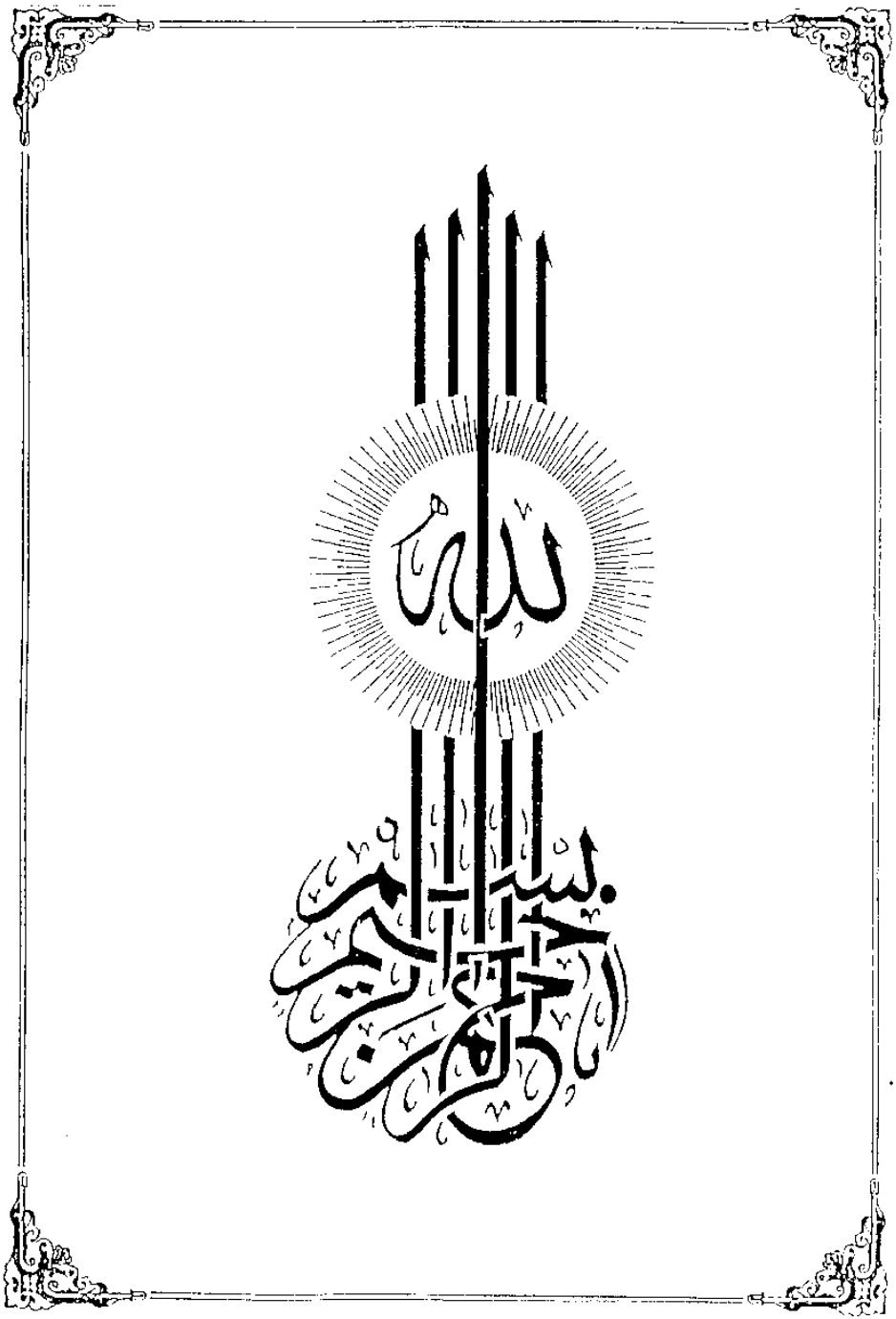

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Introduction and Aim of the Work

Ascites refers to accumulation of fluid within the penitoneal cavity, ascitic fluid is "normally" sterile. Spontaneous bacterial peritonitis is defined as infected ascitic fluid in the absence of a recognizable secondary cause of peritonitis *(Hoefs et al., 1982)*.

It has a special predilection for cirrhotic patients with ascites *(Runyon, 1985)*.

Some factors render cirrhotic patients particularly liable to develop spontaneous peritonitis; patients with cirrhosis are predisposed to bacteraemia. Bacteria, particularly intestinal could reach the general circulation either by passing through a faulty hepatic filter or through portal-systemic collaterals *(Sherlock, 1993)*.

Ascitic fluid favours bacterial growth, opsonic activity is low and resolution of infection by peritoneal macrophages fails *(Runyon et al., 1985)*.

Clinical presentation of the disease may be subtle; but increasing awareness of this entity is leading to earlier diagnosis in atypical cases *(Zakim and Boyer, 1990)*.

SBP should always be considered in any ascitic patient with deteriorating renal or hepatic function and worsening encephalopathy.

SBP and its variants bacterascites and culture negative neutrocytic ascites are significant causes of morbidity in patients with chronic liver disease; the mortality may exceed 50% *(Hurwich et al., 1993)*.

A positive bacteriological culture of ascitic fluid is the "gold standard" for the diagnosis of SBP. However, it requires 24 to 72 hours before a positive culture can be obtained. It is often necessary to initiate antibiotics on the basis of clinical impressions or preliminary laboratory analysis of ascitic fluid *(Stassen et al., 1986)*.

Most of the studies have been carried on patients with alcoholic liver disease. The main goals of this study were to determine the prevalence of spontaneous bacterial peritonitis in our Egyptian ascitic patients admitted to the hospital with liver cirrhosis and to evaluate the currently available methods for diagnosis.

Review of Literature

Spontaneous Bacterial Peritonitis

Definition

Spontaneous bacterial peritonitis (SBP) is defined as sudden onset of acute bacterial peritonitis without any apparent external or intra-abdominal focus of infection in patients with ascites *(Hallak, 1989)*.

SBP can also be defined as infected ascitic fluid in the absence of a recognizable secondary cause of peritonitis *(Sherlock, 1993)*.

SBP of the cirrhotic patient is not a "new" syndrome. Correia and *Conn, (1975)*, believe that Ludwig von Beethoven was the first recorded victim. Since it is a complication of a complication, its occurrence may have not been perceived in patients admitted in the terminal stage of their liver disease.

Conn, (1964), was the first to define the entity known as the syndrome of SBP in cirrhotic patients.

The reported incidence of SBP has been increased over the past two decades, which may be related to an increased awareness, and greater familiarity of this complication *(Hallak, 1989)*.

Variants of SBP

1. **Culture-Negative Neutrocytic Ascites (CNNA):** according to *Runyon and Hoefs, 1984*. The diagnosis of CNNA was applied to patients who met all of the following criteria.

a) An ascitic fluid PMN count greater than 500 cells per mm^3 (the figure of 500 was chosen in an attempt to exclude "technical" error in determination of the cell counts).

b) Negative ascitic fluid culture(s).

c) Absence of an intra-abdominal source of infection.

d) No antibiotic treatment within 30 days.

e) No alternative explanation for an elevated PMN e.g. pancreatitis, haemorrhage into ascites, peritoneal carcinomatosis, ascites from pancreatitis or serositis (i.e., systemic lupus erythematosus).

There is similarity between patients with CNNA and SBP as regard signs, symptoms, ascitic fluid analysis, blood culture positivity rate and mortality.

The response in the ascitic fluid PMN count (in all cases of CNNA in which a repeat paracentesis was performed) to antibiotic treatment is consistent with bacterial infection, of course non infectious inflammatory conditions can result in neutrocytic ascites, as in the example of a penetrating duodenal ulcer reported by *Harty et al., 1978*. Cholecystitis or diverticulitis presumably could also result in an elevated ascitic fluid neutrophil count without actual contamination of the fluid. Some patients with uninfected ascites may have unexplained chemotactic factors in their

fluid which result in neutrocytic ascites; however, such factors should not respond to therapy with antibiotics *(Runyon and Hoefs, 1984)*.

Some instances of CNNA may represent the resolution phase of SBP where the host defenses have eliminated the organism without the aid of antibiotics, but the elevated neutrophil count is still present *(Hoefs et al., 1982)*. Twenty-four percent of the survivors of CNNA either had a documented episode of spontaneous bacterial peritonitis before their culture-negative episode or developed SBP after their culture-negative episode *(Runyon, 1985)*.

Perhaps the bacterial inoculum into the ascitic fluid is below the threshold of detectability by current culture techniques *(Runyon and Hoefs, 1984)*. For comparison, 20% of suspected infective endocarditis patients *(Pesanti and Smith, 1979)*, and 25% of suspected acute septic arthritic patients *(Ward et al., 1960)*, have negative cultures.

The management of patients with CNNA should include a careful history and physical examination in an attempt to exclude inflammatory conditions near the peritoneum. Blood and urine cultures should be obtained before antibiotics are started. An ascitic fluid amylase would help to exclude pancreatogenous ascites.

If the above evaluation fails to explain the elevated neutrophil count, antibiotic coverage will have to be considered. If blood or urine cultures are positive, antibiotics can be chosen based on those sensitivities. If all cultures are negative, the choice of antibiotics is more difficult and should

depend on the local sensitivities of the organisms that are usually responsible for SBP e.g., E. coli, streptococcus species and klebsiella pneumonia *(Runyon and Hoefs, 1984)*.

2. **Bacterascites** which is defined as culture positivity in ascites with polymorphonuclear cell count less than 250/mm^3. Monomicrobial, non-neutrocytic bacterascites may resolve without treatment but can progress to SBP *(Figure 1) (Runyon, 1990)*.

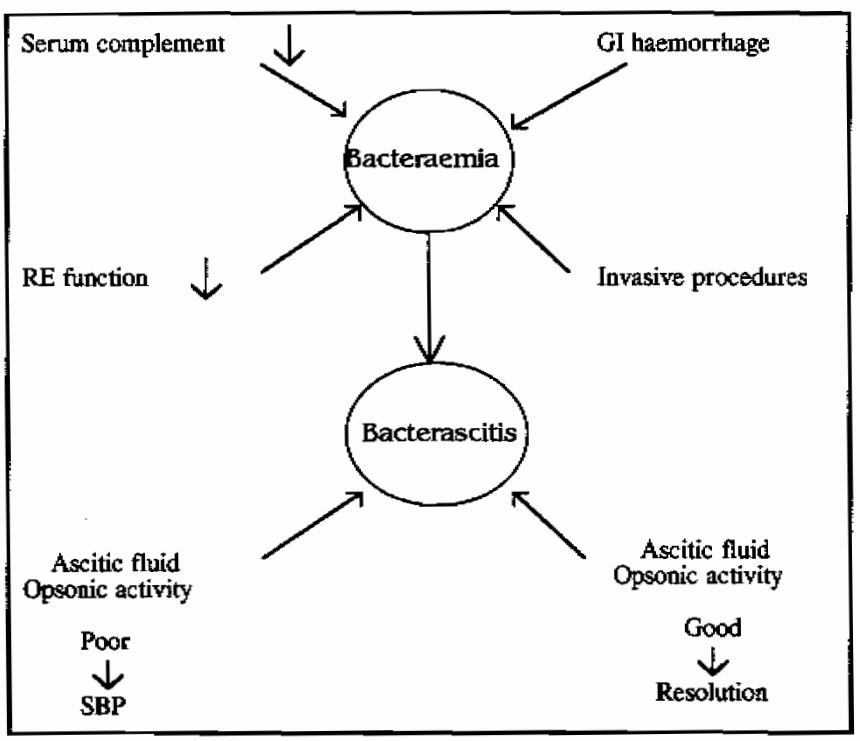

Figure 1

The pathogenesis of spontaneous bacterial peritonitis (SBP) in patients with cirrhosis *(Sherlock, 1993)*

Presumably at an early stage, the organisms in the ascitic fluid can be eradicated by host defenses by means of specific and nonspecific opsonins

and macrophages without an influx of neutrophils. In some instances, however, the infection persists and chemotactic factors are released, initiating a polymorphonuclear response. The chemotactic factors include by-products of complement activation.

Some ascitic fluids are profoundly complement deficient and infection may progress in the absence of a marked leukocytic response. In that sense, bacterascites may be either an early stage of infection (colonization) or one in which the stimulus for chemotaxis is deficient (i.e., uncontrolled infection) *(Runyon, 1985)*.

Most authors consider bacterascites as an early stage of colonization. However, it was found that patients with a low leukocyte response have the same mortality as those with a greater response *(Hoefs et al., 1982)*.

Pathogenesis

Causative Organisms (table 1)

The infection is monomicrobial in 90% of the patients *(Sherlock, 1993)*.

The offending organism is predominantly of enteric origin usually Escherichia coli *(Zakim and Boyer, 1990)*. *Soriano et al., (1993)*, studied cirrhotic Patients with SBP caused by E. coli and strains were serotyped, they found that 63.6% of E. coli isolated were encapsulated and 31% with K_1 capsular polysaccharide, patients with encapsulated E. coli showed a higher number of complications per patient than those with nonencapsulated strains and higher mortality (35.7% versus 25%). In spite of similar clinical and analytical data in both groups; they also found that patients with serotype K_1 E. coli showed a greater incidence of renal insufficiency than encapsulated non-K_1 strains (100% versus 42.8%) and higher mortality (42.8% versus 28.5%). Encapsulated serotypes of E. coli mainly those with K_1 capsular polysaccharide have been related to increased virulence *(Soriano et al., 1993)*.

Streptococci and Klebsiella are also common to be found, pneumococci are responsible for most attacks in children and 20% of cases in adults *(Rolando and Wyke, 1991)*.

Staphylococcus aureus infection accounts for 38% of cases SBP in patients with a Le Veen Shunt *(Rimland and Prokesch, 1983)*.

Other Gram-negative organisms than E. coli and klebsiella have been isolated e.g., H. influenza, Proteus, Pseudomonas, Aerobacter and Citrobacter *(Clark, 1984)*.

Table 1

Bacteria isolated from the ascitic fluid in 267 Episodes of SBP in 246 patients *(Runyon, 1985)*

Bacteria	No. of isolates	%
Escherichia coli	131	43
Klebsiella pneumoniae	26	8
Streptococcus pneumoniae	24	8
Alpha-hemolytic streptococcus	17	5
Group D streptococcus	17	5
Unclassified streptococcus	13	4
Beta-hemolytic streptococcus	12	4
Enterobacteriaceae	8	3
Pseudomonas	6	2
Staphylococcus aureus	5	2
Miscellaneous	48	16
Total	**307**	**100**

N.B.: 28 of cases (10%) were polymicrobial.

Of the 267 episodes reported in seven large series, 28 (10%) were polymicrobial, i.e., more than one organism was cultured from the ascitic fluid sample that was diagnostic of infection. These polymicrobial infections usually include one or more isolates typical of SBP plus one or