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Spontaneous bacterial peritonitis variants

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INTRODUCTION

Spontaneous bacterial peritonitis (SBP) is defined as an ascitic fluid infection without an evident intraabdominal surgically-treatable source; it primarily occurs in patients with advanced cirrhosis [1-3]. The diagnosis is established by a positive ascitic fluid bacterial culture and an elevated ascitic fluid absolute polymorphonuclear leukocyte (PMN) count (≥250 cells/mm^3).

When faced with a patient who appears to have SBP, the clinician should at least consider the possibility that the patient might have a surgically-treatable source for the infection (eg, a ruptured peptic ulcer) (see "Spontaneous bacterial peritonitis in adults: Diagnosis"). This distinction is crucial because the mortality of secondary bacterial peritonitis in the presence of ascites approaches 100 percent, if treated only with antibiotics with no surgical intervention [1]. Conversely, if a patient with SBP receives an unnecessary exploratory laparotomy, the mortality is approximately 80 percent [4]. With appropriate antibiotic treatment of SBP, infection-related mortality approaches zero [5]. (See "Spontaneous bacterial peritonitis in adults: Treatment and prophylaxis".)

There are three variants of SBP that are also "spontaneous" (ie, there is no surgically treatable source for the infection) (table 1) [6]:

- Culture-negative neutrocytic ascites
- Monomicrobial non-neutrocytic bacterascites
- Polymicrobial bacterascites

These variants are distinguished from classic SBP largely by ascitic fluid analysis (table 1). Separate labeling of each of these variants may seem artificial, but probably has clinical relevance. Research efforts to explain the differences between these subgroups have led to improvements in culture technique and advancement in our understanding of the sequence of events that lead to ascitic fluid infection.

CULTURE-NEGATIVE NEUTROCYTIC ASCITES

The phrase culture-negative neutrocytic ascites (CNNA) was proposed in 1984 [7]. This diagnosis was made when a patient had an elevated ascitic fluid absolute polymorphonuclear leukocyte (PMN) count (≥250 cells/mm^3) with a negative ascitic fluid culture (in the absence of antibiotic therapy or pancreatitis) and no evident intraabdominal surgically treatable source of infection. A PMN threshold of 500/mm^3 was initially used, but this was subsequently revised to 250/mm^3. Although a PMN count above 100/mm^3 is probably pathologic, there is enough error in the manual count and differential to justify a higher threshold. (See "Spontaneous bacterial peritonitis in adults: Diagnosis".)

Since the original publication, it has become apparent that a number of disorders other than spontaneous bacterial peritonitis (SBP) can produce a somewhat similar picture. These include:

- Tuberculous peritonitis [8].
- Malignancy-related ascites [9].
- Any process that leads to death of cells (eg, lysing tumor cells) can activate complement or cytokines that can attract PMNs into the peritoneal cavity.

However, in the absence of an active bacterial infection, there is usually not a predominance of PMNs in these settings. In contrast, there is almost always a PMN predominance in SBP.

One potential source of error is that hemorrhage into the ascitic fluid, as in a traumatic paracentesis, leads to red cell and white cell entry into the fluid. A corrected PMN count should be calculated if there is bloody fluid: One PMN is subtracted from the absolute PMN count for every 250 red cells/mm^3 [10]. PMNs lyse rapidly, much more so than red cells. Thus, if the bleeding episode occurred prior to rather than during paracentesis, the PMNs that entered the fluid may have lysed and the corrected PMN count may be a negative number.

Paracentesis should **precede** the initiation of antibiotic therapy. However, it has been our experience that patients are frequently inappropriately given one or more doses of a parenteral antibiotic before they undergo paracentesis, in particular in the emergency department. It is common for the emergency department physician to use clinical characteristics and physician

assessment and to rule out SBP; this has been shown to be insufficient [11]. Paracentesis is mandatory. The potential impact of antimicrobial therapy on culture results was shown in a study of patients with SBP with culture-positive fluid prior to treatment: 86 percent of repeat ascitic fluid cultures grew no bacteria when fluid was obtained six hours after a single 2 g dose of intravenous cefotaxime [1].

Importance of culture technique — Within 10 years of the original publication on CNNA, it became clear from multiple studies that the inability of the culture to grow bacteria was largely due to insensitive culture technique [6,12]. The older method of culture was based on the erroneous assumption that infected ascitic fluid was usually a high-colony-count, polymicrobial infection, as in surgical peritonitis. However, most ascitic fluid infections are "spontaneous," with a low colony count, and are monomicrobial similar to bacteremia [12]. Culturing ascitic fluid as if it were blood (ie, bedside inoculation of ascitic fluid into blood culture bottles) has been shown to increase the culture-positivity of the ascitic fluid of patients with an ascitic fluid PMN count ≥250 cells/mm^3 (in the absence of prior antibiotic treatment, pancreatitis, tuberculous peritonitis, or malignancy-related ascites) from about 50 percent (with the conventional method) to approximately 80 percent [6]. (See "Spontaneous bacterial peritonitis in adults: Diagnosis", section on 'Culture'.)

The volume of fluid cultured also has a dramatic impact on the sensitivity of the culture in detecting bacterial growth. In one report, for example, inoculation of 10 or 20 mL of fluid into 100 mL blood culture bottles led to a much higher culture-positivity rate than a 1 mL inoculum (93 versus 53 percent) [12].

Culture-independent techniques may be able to detect bacterial DNA or toxins, when no live bacteria are present [13]. While these diagnostic tests are Food and Drug Administration (FDA)-approved to detect pathogens in food, they cannot distinguish among different strains of bacteria.

Thus, in the care of the 20 percent of patients who have neutrocytic ascites and grow no bacteria have one or more of the following probably occur:

- Unrecognized treatment (as is common in emergency departments) occurred with one or more doses of antibiotic.
- Culture technique was inadequate, with an inadequate volume of fluid in the inoculum.
- One of the other causes of culture-negative neutrocytic ascites took place (eg, hemorrhage into the fluid, tuberculous peritonitis, pancreatitis, and malignancy).

- SBP resolved spontaneously; in such patients, late paracentesis may be performed at a time when the bacterial count has been reduced below the threshold of detectability by our current culture techniques (figure 1) [14].

Course — The short-term natural history of CNNA was assessed in a prospective study in which paracentesis was repeated within about eight hours of the initial tap and prior to initiation of antibiotic therapy [14]. In 19 (66 percent) of 29 well-characterized episodes of CNNA, the second culture was also negative with a falling PMN count in 18 (figure 1). The follow-up culture grew bacteria in the remaining 10 who progressed to SBP.

Similar conclusions were reached in another report that focused on 427 asymptomatic patients with cirrhosis who underwent paracentesis as outpatients [15]. The authors observed spontaneous resolution (ie, without antibiotics) in four episodes in which the ascitic fluid neutrophil count was ≥250 cells/mm^3 but <500 cells/mm^3 (one of which was culture positive).

The observation that ascitic fluid infection may spontaneously resolve may explain the lower mortality of CNNA compared with SBP [16,17]. However, recognition of this phenomenon should not decrease the enthusiasm for empiric treatment of patients with an ascitic fluid PMN count ≥250 cells/mm^3. (See "Spontaneous bacterial peritonitis in adults: Treatment and prophylaxis".)

These findings and our experience indicate that there is always an explanation for an elevated ascitic fluid PMN count. PMNs do not enter the ascitic fluid without a reason to be there. Spillover from the circulation is not an explanation, since patients with profound peripheral leukocytosis do not have PMNs in their ascitic fluid [18].

MONOMICROBIAL NON-NEUTROCYTIC BACTERASCITES

Monomicrobial non-neutrocytic bacterascites (MNB) usually represents the colonization phase of ascitic fluid infection [19]. The flora are similar to those of SBP [19]. MNB may progress to spontaneous bacterial peritonitis (SBP), or in 62 to 86 percent of cases, resolve spontaneously (figure 1) [19,20].

An increase in the number of paracenteses that is currently being performed has led to enhanced recognition of this variant. The high spontaneous resolution rate suggests that the clinician may not need to know about all colonization episodes. A study in which routine bacterial cultures were performed at the time of therapeutic paracentesis in outpatients without symptoms of infection demonstrated that 2 percent of patients had bacterascites comprised of skin flora that were probably contaminants [15]. In the absence of signs or

symptoms of infection, bacterial cultures are probably not necessary when performing a therapeutic paracentesis.

The symptoms of the patient help predict who will progress to SBP and who will resolve the colonization. Patients destined to progress to SBP in general have fever at the time of the initial tap; in contrast, patients destined to resolve the colonization are usually asymptomatic [19,20].

Progression from MNB to SBP can occur very rapidly. One study documented a 50- to 170-fold rise in polymorphonuclear leukocyte (PMN) count within 40 to 70 minutes [19].

POLYMICROBIAL BACTERASCITES

Polymicrobial bacterascites is caused by a traumatic paracentesis in which the bowel is entered by the paracentesis needle and bacteria leak, usually transiently, from the gut into the fluid [21]. This complication is recognized when air or frank stool is aspirated during attempted paracentesis or when multiple bacteria are seen on Gram stain or grow on culture of non-neutrocytic ascites (ie, polymorphonuclear leukocyte [PMN] count <250 cells/mm^3). It occurs once in approximately 1000 paracenteses, usually occurs when the operator is inexperienced, the needle is placed too close to a surgical scar (with bowel adherent to the abdominal wall), or ileus is present. We have never encountered an episode of this variant in which surgical intervention was required.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Portal hypertension and ascites".)

SUMMARY AND RECOMMENDATIONS

- Spontaneous bacterial peritonitis (SBP) is defined as an ascitic fluid infection without an evident intraabdominal surgically-treatable source; it primarily occurs in patients with advanced cirrhosis.
- There are three variants of SBP, which are distinguished from classic SBP largely by ascitic fluid analysis (table 1). It is important to recognize these variants in at-risk patients who do not fulfill classical definitions of SBP.

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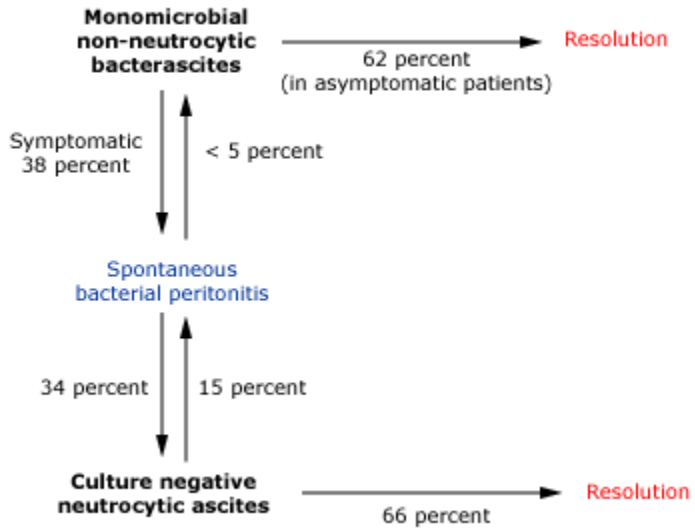
GRAPHICS

Spontaneous bacterial peritonitis and its variants that do not require surgery

Variant	Ascitic fluid culture	Absolute PMN per mm3
Spontaneous bacterial peritonitis	Positive	≥250
Culture-negative neutrocytic ascites	No growth	≥250
Monomicrobial non-neutrocytic bacterascites (single organism)	Positive	<250
Polymicrobial bacterascites	Positive	<250

Graphic 77418 Version 1.0

Natural history of ascitic fluid infection



Relation between spontaneous bacterial peritonitis and its variants as shown by the short-term, untreated natural history of the different conditions.

Adapted from McHutchison JG, Runyon BA. Spontaneous bacterial peritonitis. In: Gastrointestinal and Hepatic Infections, Surawicz CM, Owen RL (Eds), WB Saunders, Philadelphia, 1994, p. 455.

Graphic 56516 Version 2.0

Contributor Disclosures

Bruce A Runyon, MD, FAASLD No relevant financial relationship(s) with ineligible companies to disclose. **Keith D Lindor, MD** Consultant/Advisory Boards: Pliant [DSMB member]. All of the relevant financial relationships listed have been mitigated. **Kristen M Robson, MD, MBA, FACG** No relevant financial relationship(s) with ineligible companies to disclose.

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