

# Spontaneous Bacterial Peritonitis Caused by Infection with *Listeria monocytogenes*

Michael Vincent F. Tablang

Department of Internal Medicine, University of Connecticut Health Center,  
Farmington, Conn., USA

## Key Words

Ascites · Cirrhosis · Listeria · Peritonitis · Sepsis

## Abstract

Spontaneous bacterial peritonitis is a severe and life-threatening complication in patients with ascites caused by advanced liver disease. The organisms most commonly involved are coliform bacteria and third-generation cephalosporins are the empiric antibiotics of choice. This is an uncommon case of spontaneous bacterial peritonitis caused by *Listeria monocytogenes* in a female patient with liver cirrhosis from autoimmune hepatitis. She did not improve with ceftriaxone and her course was complicated by hepatic encephalopathy, seizures and multi-organ failure. This case emphasizes that a high index of suspicion should be maintained for timely diagnosis and treatment. Listerial peritonitis should be suspected in patients with end-stage liver disease and inadequate response to conventional antibiotics within 48–72 h. Ampicillin/sulbactam should be initiated while awaiting results of ascitic fluid or blood culture.

## Introduction

Spontaneous bacterial peritonitis (SBP) is the most common life-threatening infectious complication in patients with ascites caused by liver cirrhosis. The diagnosis is established by an elevated ascitic fluid polymorphonuclear count  $\geq 250$  cells/mm<sup>3</sup> and a positive ascitic fluid bacterial culture. The organisms most commonly involved in this infection are *Escherichia coli*, *Klebsiella pneumoniae*, and other Gram-negative enteric organisms, which account for the majority of cases [1].

*Listeria monocytogenes* is an uncommon cause of peritonitis, with less than 50 cases reported in the medical literature. Early recognition and treatment are critical because of the high mortality rate. Cefotaxime, or other third generation cephalosporins, has been the mainstay of empiric treatment for SBP, but it is an inadequate treatment for *Listeria*

peritonitis. Ampicillin alone or in combination with gentamicin is the preferred treatment for *L. monocytogenes* [2].

In this case report we describe the clinical presentation and treatment of a patient with long-standing ascites who developed SBP with *Listeria*.

### Case Report

A 72-year-old Hispanic woman with cirrhosis caused by autoimmune hepatitis, who had suffered prior episodes of hepatic encephalopathy and ascites, was admitted to our hospital with a 2-day history of bilious vomiting, diffuse abdominal pain, oliguria, and headache. She had recently had esophagogastroduodenoscopy showing gastritis and grade IV esophageal varices. Her current medications included nadolol, spironolactone, furosemide, azathioprine, esomeprazole and lactulose.

Her vital signs showed a temperature of 36.06°C, blood pressure of 82/32 mm Hg, and a regular pulse of 92 beats/min. Physical examination revealed lethargy, bibasilar rales, and tender abdomen with tense ascites. No jaundice, lower extremity edema, or focal neurological deficits were noted.

The patient had a white blood count of 9,400 cells/mm<sup>3</sup> but with significant bandemia (61% bands, 93.6% neutrophils, 4.4% lymphocytes, and 1.8% monocytes). She also had macrocytic anemia and thrombocytopenia with hemoglobin of 9.6 g/dl (12–16 g/dl), hematocrit of 28.5% (35–47%), platelets of 116,000/μl (150,000–400,000/μl), and MCV of 115.9 fl (80–100 fl). Her INR was 1.98 (0.8–1.2) and the prothrombin time was 16 s (10–13 s).

The patient was found to have new-onset renal failure (creatinine 5 mg/dl; 0.6–1.2 mg/dl) and metabolic acidosis (pH 7.39; HCO<sub>3</sub> 13.4; PCO<sub>2</sub> 22.8; PO<sub>2</sub> 77.8). Her lactic acid was 6.7 mmol/l (0.4–1.9 mmol/l) while her serum ammonia was 16 μmol/l (11–32 μmol/l). The rest of her metabolic profile showed the following: sodium 128 meq/l (137–144 meq/l); potassium 5 meq/l (3.6–4.8 meq/l); chloride 101 meq/l (100–111 meq/l); bicarbonate 13 meq/l (23–32 meq/l), and BUN 70 mg/dl (8–24 mg/dl).

The results of her abdominal CT scan showed a cirrhotic liver, splenomegaly and ascites. No ruptured viscus or obstruction was seen. Large volume paracentesis was performed and 2 l of serosanguinous ascitic fluid were drained. The albumin concentration in the fluid was <1 mg/dl, whereas serum albumin was 2.6 mg/dl (3.8–5.3 mg/dl). The serum-ascites albumin gradient was >1.1. The total white and red cell counts in the ascitic fluid were 2,889/mm<sup>3</sup> and 20,111/mm<sup>3</sup>, respectively.

Urine studies were suggestive of a prerenal cause but her renal function did not improve with aggressive volume resuscitation with normal saline. Her urine sodium was less than 10 meq/l. Both kidneys were structurally normal on ultrasound. Her clinical picture was consistent with hepatorenal syndrome. She did not respond to midodrine and octreotide. Vancomycin and ceftriaxone were given initially; however, when cultures of blood and ascitic fluid grew *L. monocytogenes*, the antibiotics were changed to ampicillin-sulbactam. Gentamicin was held because of her renal failure.

She deteriorated clinically within 48 h and was transferred to the intensive care unit where she went into respiratory failure requiring mechanical ventilation. She had multiple generalized tonic-clonic seizures. Lumbar tap was not performed because of her worsening coagulopathy. Comfort measures were instituted after family discussions. The patient died 4 days after admission from multi-organ failure caused by *Listeria* sepsis.

### Discussion

*L. monocytogenes* is the only strain among the seven known *Listeria* species that infects humans. It is an aerobic, facultatively anaerobic, non-spore-forming, Gram-positive rod. Despite being an ubiquitous environmental organism, it is an uncommon cause of illness in the general population, with an annual incidence of 0.7 case per 100,000 [3].

The risk of listeriosis is markedly higher among newborns, pregnant women, and the elderly. Likewise, patients with impaired cell-mediated immunity such as organ transplant recipients, AIDS, malignancy and on chronic steroid therapy are predisposed to develop

this infection. However, up to 30% of adults contracting listeriosis have no apparent immunocompromising condition [3, 4].

The most common manifestations of *Listeria* infection are bacteremia and meningitis, although endocarditis, gastroenteritis and other localized infections have also been described [4, 5]. Listerial peritonitis is a rare but dangerous form of listeriosis. Interestingly, the majority of reported cases occurred in Spain, although the reason for the high incidence rate in that country is unclear. Geographic predisposition, a mild climate, and diets rich in raw fruits and vegetables and multiple types of dairy products are possible causes [6].

The pathogenic mechanisms for *Listeria* to cause SBP are not clear but most likely similar to Gram-negative organisms. Since only half of the infections with *Listeria* SBP were bacteremic, it seems reasonable to presume that transmission of *Listeria* is by the fecal-oral route with resulting gut colonization. Subsequent transluminal migration of bacteria through the intestinal wall occurs, however less efficient compared to Gram-negative enterics. Consequently, in some cases, bacteremia and disseminated infection may occur [1, 6].

It is well established that iron both in vivo and in vitro promotes the growth of *Listeria*. Patients with hemochromatosis and transfusional overload have increased incidence of infection with *Listeria* [7]. Individuals with end-stage liver disease of many causes have increased body iron stores, and this may account for the increased incidence of *Listeria* SBP in patients with cirrhosis [8].

An intact cell-mediated immunity is the primary defense against *L. monocytogenes*. Patients with physiologic and pathologic defects in this immunity have an increased risk of listeriosis, and SBP is the culmination of the inability of the gut and the immune system to contain intestinal bacteria [1, 9].

The overall mortality of cirrhotic patients with listerial infected ascites has been estimated to be 30% and patients die within six days after contracting the infection [6]. The increasing incidence of *L. monocytogenes* requires early recognition and specific treatment. Infection with *L. monocytogenes* should be suspected in patients with end-stage liver disease and inadequate response to conventional medical treatment within 48–72 h. A high index of suspicion should also be maintained in patients with hemochromatosis, impaired cell-mediated immunity, exposure to farm animals and Gram-positive-like organisms in peritoneal fluid or blood [8].

The usual treatment of infection by *L. monocytogenes* is with ampicillin alone or in combination with gentamicin. Current empiric use of third generation cephalosporins such as cefotaxime as the first-line treatment regimen may not give adequate antimicrobial coverage. About 5–10% of organisms including anaerobes, diphtheroids, staphylococci, and *Listeria* are resistant. Thus, the use of ampicillin/sulbactam as initial therapy to cover the most common isolates and unusual cases such as *Listeria* should be studied [1, 8].

Patients with prior history of SBP have a high rate of recurrence, and secondary prophylaxis with norfloxacin is standard treatment. Since *Listeria* is resistant to norfloxacin, trimethoprim-sulfamethoxazole is recommended after an initial episode of listerial SBP [8, 10].

There is no adequate data that defines the duration of therapy, but most physicians would treat longer than 10–14 days. Resolution of neutrocytic ascites and sterilization of both blood and ascitic cultures may be used as treatment endpoints [2].

### **Conclusion**

Patients with chronic liver disease have been recently identified as a risk group for invasive listeriosis, including SBP. The risk of listeriosis is markedly increased among newborns, pregnant women, the elderly, and patients with impaired cell-mediated immunity. Iron overload in end-stage liver disease may predispose to SBP caused by *Listeria*.

*Listeria* is resistant to third-generation cephalosporins, the standard empiric treatment for SBP. Ampicillin/sulbactam and gentamicin should be instituted early, particularly in patients who do not respond promptly to conventional antibiotic regimen.

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