A Rare Case of Listeria Septicemia and Meningitis in Liver Cirrhosis

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Patient: Male, 64-year-old
Final Diagnosis: *Listeria monocytogenes* infection • Listeria septicemia • meningitis • shock
Symptoms: Encephalopathy • sepsis • shock
Medication: —
Clinical Procedure: —
Specialty: Critical Care Medicine

Objective: Rare coexistence of disease or pathology
Background: Sepsis is a leading global cause of mortality, with the most common causative agents being *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Escherichia coli*. In septic patients with liver cirrhosis, the mortality rates are higher than in the general population due to altered liver function and an excessive innate immune response. In this demographic, sepsis is typically caused by spontaneous bacterial peritonitis or urinary tract infections and the causative agents are very predictable owing to known dysregulated immunological pathways studied in patients with cirrhosis. *Listeria monocytogenes* is not only a less common cause of sepsis, but also a rare cause in patients with cirrhosis. Moreover, concurrent meningitis and septicemia is even less common in this demographic.

Case Report: Herein we present a patient with known liver cirrhosis from chronic alcohol use who presented with generalized complaints and was admitted to the Intensive Care Unit with septic shock and concomitant liver failure. Although his changes in mentation were initially attributed to sepsis with superimposed hepatic encephalopathy, he was also diagnosed with meningitis. Cultures from the cerebral spinal fluid and blood serum were positive for *Listeria monocytogenes*. The patient’s family reported that he had not recently consumed deli meat, cheeses, or raw chicken, and there were no known outbreaks in the area at the time of diagnosis.

Conclusions: This report illustrates a rare case of concurrent septicemia and meningitis secondary to *Listeria monocytogenes* in a patient with liver cirrhosis and reviews current literature.

Keywords: *Listeria monocytogenes* • Liver Cirrhosis, Alcoholic • Meningitis, Bacterial • Sepsis • Hepatic Encephalopathy • Hepatitis

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Background

Sepsis is an infection of the bloodstream, which can lead to multi-organ failure and death [1-5]. This disease has a major global healthcare impact and is associated with a greater than 40% mortality rate, regardless of causative agents [2]. Despite appropriate measures to reduce the spread of infections worldwide, the incidence of sepsis remains high [2]. Early recognition and diagnosis is imperative to prevent death [2]. Circulating proinflammatory cytokines and acute phase reactants alter microvascular blood flow, leading to sepsis-induced multi-organ failure [3]. Global tissue dysoxia is caused by a reduction in functional capillary density, increased permeability and apoptosis of the endothelial cells, adherence of activated neutrophils to the endothelial layer, activation of clotting cascades, and deposition of microthrombi [3]. During shock, all macrovascular blood flow is decreased by approximately 50% [3]. The liver plays a major role in metabolizing host defense mechanisms and toxins during sepsis; however, with underlying liver cirrhosis, there is not only liver dysfunction but also an excessive response of the innate immune system [3,4]. Previous studies have demonstrated increased mortality from sepsis in patients with cirrhosis, regardless of bacterial pathogen [4].

Listeria monocytogenes is the third most common pathogen of sepsis affecting adults; however, patients are typically immunocompromised due to various medications, prior splenectomies, underlying malignancies, autoimmune diseases, or HIV [6]. One large prospective study in Taiwan observed that the mean age of non-perinatal Listeria infection was 63.9±15.3 years and that it predominantly occurred in men [7]. Of the 115 non-perinatal cases, Listeria infections were most commonly in patients with solid malignancies (47.1%), followed by hematological malignancies (27%), and then steroid use (39.1%) [7]. Only 17% of patients had underlying liver cirrhosis, making liver cirrhosis a less common comorbidity of Listeria infections [7]. The 30-day mortality was 25.2%, which did not differ based on underlying condition in this study; however, other studies have demonstrated higher rates of mortality in sepsis, specifically in those patients with liver cirrhosis [4,7].

Alcohol abuse can also suppress the immune system owing to depressed phagocytic activity against gram-negative and gram-positive bacteria, and, due to underlying poor liver function, the ability to remove toxins is also impaired [1]. This increases the risk of sepsis and meningitis, even from Listeria monocytogenes [1,6]. A study of 11 adult patients with Listeria meningitis demonstrated that 4 patients with cirrhosis and/or alcoholism had concomitant bacteremia [8]. Five of the patients with cirrhosis and/or alcoholism presented with altered levels of consciousness, while 4 only had seizures [8]. The accepted treatment for Listeria meningitis is amoxicillin, ampicillin, or penicillin G for at least 21 days. Also, the addition of an aminoglycoside has been debated; however, is not a part of standard therapy owing to the incidence of acquired renal failure following treatment [6].

Case Report

A 64-year-old man with a past medical history of hypertension with medication non-adherence and liver cirrhosis with active alcohol use disorder, presented to the Emergency Department with acute mild and intermittent chest pain associated with dizziness, nausea, and palpitations. The pain started the morning prior to presentation and initially resolved spontaneously but re-emerged throughout the next day. His last shot of alcohol was 3 days prior to admission, and he reported drinking 1 shot of ethanol 3 times weekly. The patient reported a recent increased use of acetaminophen for generalized chronic body aches as well, although he was unable to quantify the amount. Additionally, the patient denied use of herbal supplements, vitamins, and other over-the-counter medications. On arrival, the patient was alert and oriented and the examination was unremarkable, per the admitting team. He was hemodynamically stable with the following vital signs: temperature of 38.7°C (temporal artery), heart rate of 94 beats per min, respiratory rate of 18 breaths per min, blood pressure of 113/55 mmHg, and peripheral oxygen saturation of 97% on room air. Admission laboratory results were significant for an elevated high sensitivity troponin (57 pg/mL), normocytic anemia (hemoglobin 9.2 g/dL, MCV 84 fL), thrombocytopenia (26 K/mm3), hypertriglyceridemia (227 mg/dL, HDL <8 mg/dL), hyponatremia (133 mEq/L), hypoalbuminemia (3.2 g/dL), elevated liver function enzymes (ALP 117 unit/L, AST 900 unit/L, ALT 169 unit/L), and hyperbilirubinemia (4.8 mg/dL). Creatinine kinase, brain natriuretic peptide, and lipase levels were all within normal limits. Of note, the patient’s baseline hemoglobin was approximately 9 to 10 g/dL, baseline platelets were 20 to 30 K/mm3, and he initially did not require transfusion while inpatient, as there was no indication of an active bleed. An electrocardiogram showed normal sinus rhythm with left axis deviation that was unchanged from previous imaging and no ST- or T-wave changes. The chest X-ray was unremarkable. He was admitted to the medical floors with non-ST-elevation myocardial infarction and demand ischemia. A 2-dimensional echocardiogram and transesophageal echocardiogram revealed preserved ejection fraction with severe left ventricular hypertrophy, impaired diastolic dysfunction, and no evidence of valvular defects or stigmata of infective endocarditis. The patient was scheduled for a stress test; however, he was noted to be lethargic the day following admission, for which the Critical
Care Unit was consulted for acute encephalopathy. During assessment, the patient was intermittently agitated, confused, and lethargic on examination. He was slightly febrile, with a temperature of 39.2°C, and tachycardic (108 beats per min), and had a blood pressure of 76/41 mmHg. He was euvoletic, with scleral icterus and jaundice, and the abdomen was soft and non-tender with normocytic, normochromic anemia, and a blood count of 8.9 × 10^6/mm^3, with segmented neutrophils of 78% and bands of 17%. He was transferred to the Intensive Care Unit for liver shock and multi-factorial encephalopathy. A computed tomography scan of the brain without contrast did not reveal gross intracranial hemorrhage, midline shift, or hydrocephalus. Owing to worsening lethargy, the patient was intubated for airway protection and started on vasopressors (norepinephrine) for hemodynamic instability secondary to sepsis. The patient was initially treated with NAC, rifaximin, and lactulose and placed on empiric antibiotics (intravenous vancomycin 1000 mg daily and cefepime 500 mg daily), until blood cultures returned positive for *Listeria monocytogenes*. Due to his recent alcohol use, the patient was not a candidate for liver transplantation. Further workup showed no acute or chronic viral hepatitis, with evidence of previous immunity from vaccinations, and no evidence of HIV, CMV, EBV, or HSV infections. His hospitalization was immediately complicated with acute blood loss anemia in the setting of possible gastrointestinal hemorrhage, requiring multiple transfusions of platelets, red blood cells, and fresh frozen plasma. The patient underwent an emergency esophagogastroduodenoscopy, showing 2 actively bleeding grade II esophageal varices, which were banded. An abdominal venous ultrasound demonstrated no portal vein thrombosis; however, there was bidirectional flow in the right hepatic vein, representing intrinsic liver disease. An abdominal paracentesis was performed, and there was no evidence of spontaneous bacterial peritonitis. An EEG revealed severe diffuse encephalopathy, and in the setting of *Listeria* septicemia with worsening mentation, a lumbar puncture was performed. At this stage, the patient was treated with intravenous ampicillin 2000 mg every 6 h and gentamicin 80 mg daily when the cerebral spinal fluid (CSF) cultures returned positive for *Listeria monocytogenes*; however, due to worsening renal function, gentamicin was discontinued after 2 days. The CSF also contained 2290 mm^3 red blood cells, 658 mm^3 white blood cells with 95% segmented neutrophils, and glucose and protein were 19 mg/dL and 68 mg/dL, respectively. His hospital course was further complicated by rhabdomyolysis (creatinine 6.9 mg/dL, CK 1493 unit/L) secondary to sepsis and liver shock, for which the patient required hemodialysis. At this stage, the lactic acid and procalcitonin had entirely normalized, and the patient was extubated and transferred back to the medical floors. There he continued to receive hemodialysis 3 times weekly, with minimal improvement in his kidney function, and continued to receive 21 days of intravenous ampicillin 2000 milligrams every 6 h, and lactulose 3 times daily, with minimal improvement in his mentation. A repeat ammonia level at this stage was still elevated at 78 mcg/dL, with total bilirubin of 33.4 mg/dL. As his encephalopathy, hemodynamic instability, and hepatic and renal failure did not improve, despite the treatment mentioned above, he was ultimately seen by the Palliative Care Unit and transitioned to comfort care. The patient’s family reported that he had not recently consumed deli meat, cheeses, smoked fish, or raw chicken, and there were no known outbreaks in the area at time of diagnosis.

**Discussion**

Bacterial infections are an important complication of cirrhosis, especially in hospitalized patients, as they are prone to sepsis-related organ failure, including ischemic hepatitis [3,4]. During sepsis, the liver metabolizes, produces, and releases cytokines and acute phase reactants leading to structural and functional injury [3]. The sinusoidal cells become swollen and clogged with acute phase reactants, causing leakage of albumin and toxins and directly damaging tissue [4]. Additionally, alterations in the hepatic macro- and microcirculation are present during sepsis owing to high amounts of circulating nitric oxide, endothelin-1, and carbon monoxide [3]. This is problematic in cirrhosis because patients with cirrhosis tend to have high cardiac output, low arterial pressure, and low systemic vascular resistance. Thus, the presence of these toxins will further decrease perfusion and blood flow velocity in the liver sinusoids and allow endothelial invasion of neutrophils and microthrombi, which ultimately exacerbate tissue ischemia and induce damage [1,3]. Infection is more common in decompensated liver cirrhosis than in compensated liver cirrhosis because the ability to present antigens via monocyte HLA-DR expression is downregulated and there are deficiencies in complement expression [1]. Moreover, in alcohol-induced cirrhosis, specifically, there is depressed neutrophil phagocytosis and intracellular killing of gram-positive or gram-negative bacteria [1]. High amounts of circulating proinflammatory cytokines also lead to the development of renal failure, acute lung injury, hepatic encephalopathy, sepsis-induced hyperglycemia, defective arginine vasopressin secretion, adrenal insufficiency, and compartmental syndrome [1]. This was the case in our patient, who developed renal failure from acute tubular necrosis and rhabdomyolysis in the setting of sepsis, rather than any underlying heart disease. Additionally, our patient...
developed hepatic encephalopathy with elevated ammonia levels and altered mental status, which unfortunately did not improve despite treatment with NAC, rifaximin, and lactulose.

The most common bacterial infection in liver cirrhosis is spontaneous bacterial peritonitis, which is frequently caused by *Escherichia coli*, *Klebsiella pneumoniae*, or *Streptococcus pneumoniae* bacteria [1]. Other common infections include urinary tract infections, pneumonia, or cellulitis, of which up to 60% of cases are caused by gram-negative bacilli [1]. Gram-positive cocci account for 60% of cases of sepsis induced by therapeutic procedures; *Listeria monocytogenes* is rarely a causative agent [9,10]. *Listeria* is a gram-positive rod, which is transmitted through contaminated food products [5]. Pregnant women, newborns, and elderly and immunocompromised individuals are at a higher risk of acquiring *Listeria* infections, and the most common manifestations are sepsis and meningitis [5,10]. However, *Listeria* is still an uncommon cause of both sepsis and meningitis in patients with cirrhosis [5,10]. One study investigated the findings of bacterial meningitis in patients with liver cirrhosis over the course of 16 years and discovered that the MELD and Child-Pugh scores predicted prognosis [11]. At least 2 of the following presenting symptoms were present in 84% of cases: fever, nuchal rigidity, and an obtunded status; however, only 39% of cases had an alternate source of infection, including sepsis [11]. Our patient did have an alternate source of infection, and his clinical presentation manifested similarly with fever and altered mental status; however, we are still unsure of the exact mechanism by which the patient acquired *Listeria* bacteremia and/or meningitis. To the best of our knowledge, only 3 other reported cases of *Listeria* septicemia and concomitant *Listeria* meningitis exist in patients with cirrhosis, and their cases were complicated by diabetes mellitus, chronic myeloid leukemia, recent steroid use, or other immune-suppressive diseases [5,10]. This makes our case unique, as our patient did not have an underlying immunosuppressive disease or immunocompromised status; however, as described above, the presence of alcoholic liver cirrhosis can depress phagocytic activity against any gram-negative or gram-positive bacteria, and thus may explain the presence of *Listeria* in any capacity.

Conclusions

In this case report, we present a patient with liver cirrhosis who developed multi-factorial encephalopathy and liver shock in the setting of *Listeria* septicemia and concomitant *Listeria* meningitis. Not only is *Listeria* an uncommon cause of sepsis, especially in liver cirrhosis, but meningitis is also a rare manifestation of cirrhotic disease. The severity of the liver disease corresponds to the excessive innate immune response in sepsis, leading to poorer outcomes and multi-organ failure. When superimposed with other infections, such as meningitis, the prognosis is grim.

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