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Case report

Listeria peritonitis and bacteremia in a patient with cholangiocarcinoma

Mohamed Eisa*, Kibrewessen Tefera, Anahita Alvanpour

Wellstar Atlanta Medical Center, United States

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ABSTRACT

We are presenting a case of *Listeria monocytogenes* spontaneous bacterial peritonitis (SBP) monomicrobial non-neutrocytic bacterascites (MNS) in a patient with malignant ascites secondary to cholangiocarcinoma who underwent peritoneal catheter placement. *Listeria* peritonitis is uncommon, with cancer patients at a higher risk. *Listeria* infection should be suspected in susceptible patients once there is no response to empiric antibacterial or if the initial culture report shows gram positive bacilli, the antibacterial of choice is ampicillin.

Introduction

Among patients with ascites in the United States, most (85%) have cirrhosis and portal hypertension [1]. Malignancy-related ascites is much less common, accounting for or contributing to ascites formation in approximately 7–10% of patients.

Spontaneous bacterial peritonitis (SBP) is defined as an ascites fluid infection without an evident intra-abdominal surgically treatable source; it primarily occurs in patients with advanced cirrhosis [2]. Peritonitis also can occur in patients treated with continuous ambulatory peritoneal dialysis [3]. The diagnosis is established by a positive ascites fluid bacterial culture and an elevated ascites fluid absolute polymorphonuclear leukocyte (PMN) count ($\geq$250 cells/mm^3). There are three variants of SBP that are also "spontaneous" (i.e., there is no surgically treatable source for the infection) [4]: Culture-negative neutrocytic ascites, monomicrobial non-neutrocytic bacterascites and polymicrobial bacterascites.

The organisms most commonly involved in this infection are gram-negative bacilli like *Escherichia coli* and *Klebsiella pneumoniae*, and gram-positive bacteria like *Streptococcus pneumoniae* and *Staphylococcus aureus*. *Listeria monocytogenes* is an uncommon gram-positive bacillus implicated in infections in neonates, pregnant females, the elderly and immunocompromised patients. *Listeria monocytogenes*-induced SBP is rare with total of 110 cases reported in the literature (including foreign languages Spanish, German and French) from 1966 to 2017 according to Medline search. Monobacterial non-neutrocytic bacterascites (MNB) is a variant of SBP, where the ascites fluid culture is positive but the ascites neutrophil count is less than 250/mm^3. Forty percent of these patients will subsequently have SBP [5].

Monomicrobial non-neutrocytic bacterascites (MNB) usually represents the colonization phase of ascitic fluid infection [6]. The floras are similar to those of SBP [6]. MNB may progress to spontaneous bacterial peritonitis (SBP), or in 62–86% of cases, resolve spontaneously.

Listeria monocytogenes is an important bacterial pathogen in neonates, immunosuppressed patients, older adults, pregnant women, and occasionally, previously healthy individuals. The importance of underlying diseases was illustrated in a series of 165 adults with culture-proven *Listeria* infection: 69% of cases in non-pregnant adults occurred in patients with cancer, AIDS, organ transplant recipients, or corticosteroid therapy [7].

Case report

A 64 year old Asian male with the recent diagnosis of cholangiocarcinoma with peritoneal and mesenteric implants presented to our facility following a fall with altered mental status for 3 days. He had received his first course of chemotherapy before admission, consisting of gemcitabine/cisplatin on day 1 and day 8. His family reported multiple episodes of recorded fever, lethargy and loss of appetite. 2 days before his admission he had seen his oncologist and subsequently had a peritoneal catheter placed. EMS on arrival reported a temperature of 103, HR of 120 and BP of 110/70. Upon arrival to the hospital he was confused, disoriented to time/place and person. There was no asterixis and abdominal examination revealed distention with peritoneal catheter in place.

* Corresponding author.
E-mail address: dr.moe.eisa@gmail.com (M. Eisa).

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His initial labs showed WBC 4500 (Absolute neutrophil count 4248), hemoglobin 11.1, platelets of 27,000 and ammonia level of 44. His liver enzymes were normal, Albumin 2.9, bilirubin 2.2 and alkaline phosphatase was normal. His thrombocytopenia was contributed to the recent history of chemotherapy. CT abdomen showed a percutaneous drainage catheter overlying the lower part of the abdomen, extensive ascites, likely malignant, and multiple poorly defined intrahepatic masses; the CT head was negative for acute changes. He received ceftriaxone and piperacillin/tazobactam, subsequently the ceftriaxone was changed to vancomycin when he was transferred to the ICU. Ascitic fluid analysis revealed absolute neutrophil count of 36 and blood culture grew gram positive bacilli later during the clinical course confirmed to be *Listeria monocytogenes*. A suspicion of *Listeria* meningitis was raised, however given the thrombocytopenia; the family refused lumbar puncture because of the bleeding risk, and also refused an MRI of the brain to exclude metastasis. At that point the ascites fluid culture grew *Listeria monocytogenes*, ampicillin was started. His temperature curve normalized dramatically after the first dose of ampicillin although he remained critically ill, and his hospital course was complicated with atrial arrhythmia and hypotension requiring high doses of pressers support. He continued to deteriorate despite the maximum supportive care in form of acute kidney injury and electrolytes disturbances; his family refused further vasopressers and made him DNR with discontinuation of the pressers support. He died a few hours following de-escalation of care.

Discussion

Listeria monocytogenes is the only *Listeria* species that regularly infects humans, although rare cases of human infections with *Listeria ivanovii* (a pathogen of ruminants) and *Listeria grayi* have been reported [8,9]. *Listeria* is an aerobic and facultatively anaerobic, beta-hemolytic, non–spore-forming, short gram-positive rod that exhibits characteristic tumbling motility by light microscopy [10,11]. *Listeria* occurs singly or in short chains. On Gram stain, *Listeria* may resemble *Pneumococci* (diplococci), *Enterococci*, or *Diphtheroids* (*Corynebacteria*) or be gram variable and be confused with *Haemophilus* species [10,11]. In particular, when a positive blood or cerebrospinal fluid culture is preliminarily identified as *Diphtheroids*, the clinician should consider the possibility that the isolate represents *Listeria* [10].

Listeria monocytogenes, although an uncommon cause of illness in the general population, is an important pathogen in pregnant patients, neonates, elderly individuals, and immunocompromised individuals. Patients with cancer, particularly those of blood, are also at high risk for *Listeria* infection [12]. It is typically a food-borne organism. *Listeria* is also a common veterinary pathogen, being associated with abortion and encephalitis in sheep and cattle. It can be isolated from soil, water, and decaying vegetation. The most common clinical manifestation is diarrhea. A mild presentation of fever, nausea, vomiting, and diarrhea may resemble a gastrointestinal illness. The microorganism has gained recognition because of its association with epidemic gastroenteritis. In 1997, an outbreak of noninvasive gastroenteritis occurred in 2 schools in northern Italy, involving more than 1500 children and adults [13]. Bacteremia and meningitis are more serious manifestations of disease that can affect individuals at high risk. Unless recognized and treated, *Listeria* infections can result in significant morbidity and mortality.

Most cases of *Listeria monocytogenes*–induced SBP occur in patients with chronic liver disease. It has also been reported after bowel wall injury resulting from paracentesis, Esophagogastroduodenoscopy (EGD), malignancy, hepatic transplantation, and continuous ambulatory peritoneal dialysis [3]. Despite the worldwide prevalence of listeriosis, two thirds of the cases of SBP caused by *Listeria monocytogenes* have been reported from Spain. The exact reason for this regional predilection is not known, though dietary habits have been implicated in its pathogenesis [14].

Although cirrhosis is the cause of ascites formation in most patients (approximately 85% of cases), 7%–10% of patients develop ascites secondary to a malignancy [15]. Approximately 50% of patients with malignant ascites have peritoneal carcinomatosis with an additional 13% of patients having extensive liver metastases resulting in portal hypertension [16]. Spontaneous bacterial peritonitis (SBP) occurs more often in ascitic fluid with low protein concentrations. Isner et al in 1977, reported one patient with gastric adenocarcinoma who developed SBP after chemotherapy. At autopsy, 75% of the patient's liver parenchyma was replaced by tumor [17]. After that, less than 10 cases of SBP in malignant ascites have been reported. Five of the cases had extensive metastasis to the liver [17–20]. A case report of SBP in a patient with gastric carcinoma without liver metastasis, prompted the author to consider gastro-intestinal bleeding as a risk factor for SBP in malignant ascites [21]. Alfonso et al in 2005 believed that two of the cases which were reported earlier, should not be considered as SBP because they did not have more than 250 PMN/mm3 in the peritoneal fluid. These cases should be classified as “monomicrobial non-neutrocytic bacterascites” [22].

Intravenous antibacterials must be started immediately when the diagnosis is suspected or confirmed. Diagnosis is established by culture of the organism from blood, CSF, or other sterile body fluid. Person-to-person transmission does not occur; therefore, isolation precautions are not necessary. Ampicillin is the drug of choice. It interferes with bacterial cell wall synthesis during active multiplication, causing bactericidal activity against susceptible organisms. Gentamicin is an adjunctive therapy that can be used in conjunction with ampicillin. Penicillin-allergic patients should be skin tested and desensitized if necessary or treated with trimethoprim-sulfamethoxazole, which inhibits bacterial synthesis of dihydrofolic acid by competing with paraaminobenzoic acid, which results in inhibition of bacterial growth.

Conclusion

Listeria monocytogenes peritonitis is rare with only few cases having been reported thus far. *Listeria* infection should be suspected once there is no response to the empirical antibacterial in 24–48 h or initial cultures report showing Gram positive rods or diphtheroids. It should be especially suspected in malignancy and immunosuppresed patients.

Authors contribution

Eisa, Mohamed: The first author, who wrote the case report, participated in the literature review and wrote the manuscript.

Kibrewessen, Tefera: The attending who was taking care of the case, revised the final draft of the case report.

Alvanpour, Anahita: The resident who was taking care of the patient and participated in the literature review.

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