LISTERIA MONOCYTOGENES SEPTICEMIA IN A NEUTROPENIC PATIENT: A CASE REPORT

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Abstract:

Introduction: Listeria monocytogenes is a gram-positive facultative intracellular bacterium, commonly transmitted through the consumption of contaminated food. In immunocompetent individuals, it typically results in self-limiting gastroenteritis, whereas in immunocompromised patients, it can lead to more severe manifestations, including septicemia, meningitis, and encephalitis. Clinically, listeriosis may present with altered mental status, and seizures occur in approximately 25% of cases. Despite appropriate antimicrobial therapy, the mortality rate for listeriosis remains around 30%.

Case presentation: We report the case of a 60-year-old female with a 5-day history of high-grade fever (up to 40°C), headache, nausea, watery diarrhea, fatigue, and myalgia, who presented to the Infectious Diseases Emergency Department at UHC "Mother Teresa" in January 2024. The patient had a known history of diffuse infiltrative carcinoma of the gastric fundus and was undergoing chemotherapy. Laboratory investigations revealed severe leukopenia with a white blood cell (WBC) count of 1.0 K/μL. Despite the initiation of empirical antimicrobial therapy with ciprofloxacin and metronidazole, the treatment regimen was adjusted to target Listeria after blood cultures confirmed the presence of Listeria monocytogenes. On the fourth day of hospitalization, the patient developed 3-4 episodes of generalized tonic-clonic seizures, characterized by eye fixation and limb rigidity. Neurological evaluation, including a head computed tomography (CT) scan and lumbar puncture (LP), showed no abnormalities in cerebrospinal fluid (CSF) analysis. The patient was subsequently transferred to the intensive care unit (ICU) and intubated. However, despite aggressive treatment, her clinical condition continued to deteriorate, with a further decline in WBC count to 0.2 K/μL. Unfortunately, on the seventh day of hospitalization, the patient succumbed to the infection, resulting in Exitus Letalis.

Conclusion: Chemotherapy-induced intestinal paralysis, malnutrition, and myeloablation significantly increase the risk of bacterial translocation and sepsis, exacerbating the severity and worsening the prognosis of listeriosis. These factors must be carefully considered when selecting empirical anti-listerial antibiotic therapy for patients undergoing cytotoxic treatment. Although Listeria monocytogenes infections are rare, they represent a substantial threat to immunocompromised patients, often leading to severe and fatal outcomes, as demonstrated in this case.

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Introduction

Listeriosis, a severe foodborne infection caused by Listeria monocytogenes, affects approximately 1,600 individuals annually, resulting in around 260 deaths. Although L. monocytogenes infrequently causes illness in the general population, a significant proportion of affected individuals, including up to 30% of adults and 54% of children and young adults, lack apparent immunocompromising conditions (Cohen et al., 2017). Populations at highest risk include pregnant women and their neonates, the elderly (those over 65 years of age), and individuals with compromised immune systems (Centers for Disease Control and Prevention, 2022).

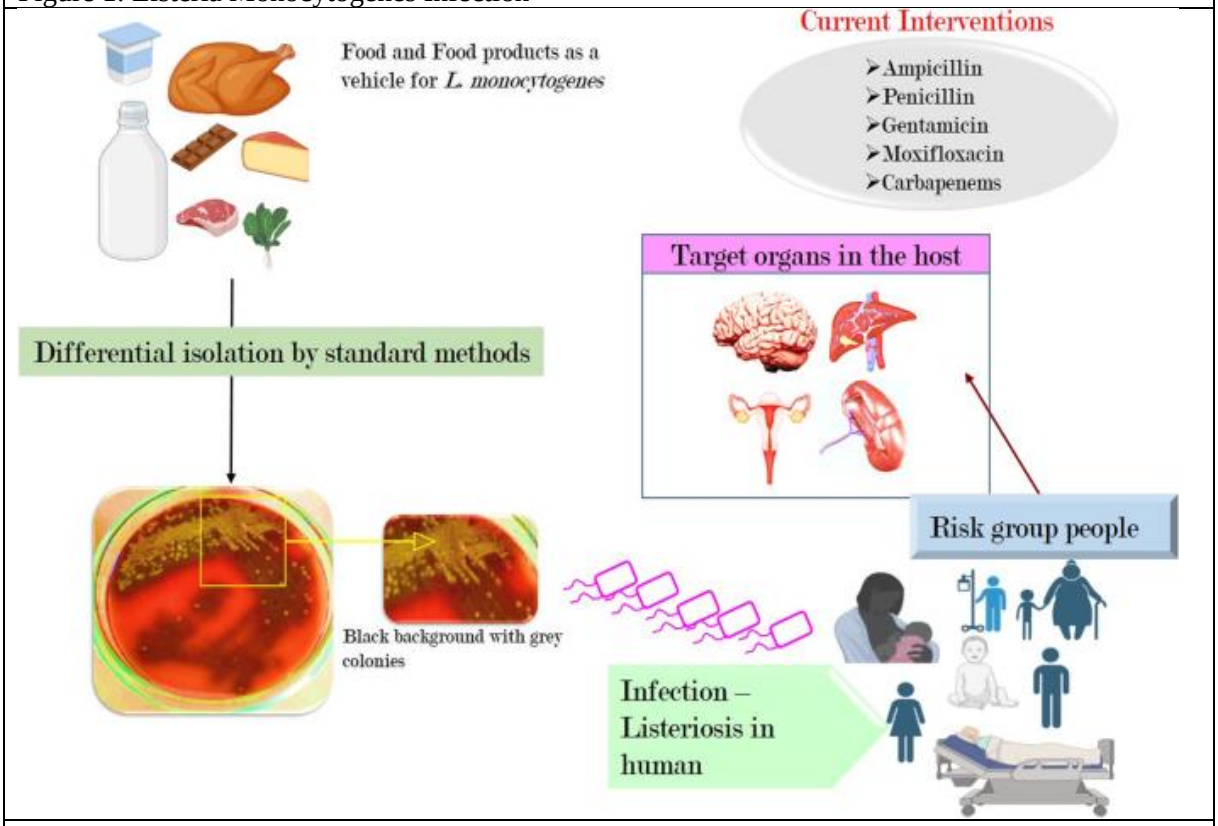
The clinical spectrum of L. monocytogenes infection is broad, ranging from mild, self-limiting gastroenteritis to severe invasive diseases such as meningoencephalitis and sepsis, which can pose life-threatening risks, but bacteremia and meningitis are most common. In immunocompromised patients, listeriosis predominantly presents as bacteremia (52%), while central nervous system (CNS) involvement, including meningitis and encephalitis, is observed in 64% of previously healthy individuals. The clinical presentation of listerial sepsis can mimic that of other bacterial sepsis syndromes, with diagnosis dependent on a positive blood culture. In immunosuppressed patients, sepsis without a localized focus is common, with reported incidence rates ranging from 21% to 43% (Yildiz et al., 2007). Affected patients typically present with non-specific symptoms such as fever, nausea,

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vomiting, and malaise, which may rapidly progress to disseminated intravascular coagulation, acute respiratory distress syndrome, and multi-organ failure (Doganay, 2003). Meningitis caused by L. monocytogenes often manifests with encephalitic features, including altered mental status (87%), nuchal rigidity (65%), aphasia (19%), seizures (18%), and spinal cord involvement (17%) (Singh et al., 2007). Additional clinical features may include cranial nerve deficits, stroke-like symptoms such as hemiplegia, reduced incidence of nuchal rigidity, and movement disorders including tremors, monoclonus, and ataxia (Johns Hopkins ABX Guide, 2022; Yildiz et al., 2007). In the case of our patient, who was immunocompromised, she presented with the full spectrum of sepsis-related clinical manifestations.

Antimicrobial therapy remains the cornerstone of listeriosis treatment. However, despite appropriate antibiotic management, listeriosis carries a high mortality rate, with approximately one-third of cases resulting in death (Nieman & Lorber, 1990). Early recognition of the clinical characteristics of L. monocytogenes infection is crucial for timely and appropriate treatment, particularly in neutropenic patients, to mitigate the elevated mortality risk associated with this pathogen (Nahid et al., n.d.). This case report aims to illustrate a L. monocytogenes infection in an immunocompromised female patient undergoing chemotherapy for diffuse infiltrative carcinoma of the gastric fundus.

Figure 1: Listeria Monocytogenes Infection



Source: Ravindhiran (2023)

Case report

A 60-year-old female patient with a medical history of diffuse infiltrative carcinoma of the gastric fundus, who was undergoing chemotherapy, presented to the Infectious Diseases Emergency Department at UHC "Mother Theresa" in January 2024. She reported a five-day history of high fever (up to 40°C), headache, nausea, watery diarrhea, fatigue, and myalgia.

The patient's past medical history included a partial gastrectomy performed 5 years prior. Following the second cycle of chemotherapy for infiltrative peritoneal carcinomatosis, she developed the aforementioned symptoms. Consequently, the planned subsequent chemotherapy cycle could not be administered due to leukopenia identified in her blood tests.

Upon admission, her laboratory tests revealed: White Blood Cell (WBC) count: 1.0 × 10^9/L with neutrophils at 90.8%, C-reactive Protein (CRP): 51.63 mg/dL, ferritin: 14,989.15 ng/dL, fibrinogen: 816 mg/dL, Blood Urea Nitrogen (BUN): 46.6 mg/dL, creatinine: 1.37 mg/dL.

She was promptly started on empirical antibiotic therapy with ciprofloxacin (400 mg i.v. every 12 hours) and metronidazole (500 mg i.v. every 8 hours) for presumed gastroenteritis. On the third day of hospitalization, the empirical regimen was revised based on sensitivity testing from blood cultures, which isolated *Listeria monocytogenes*. The updated treatment protocol included imipenem (1.0 g i.v. every 8 hours), levofloxacin (500 mg i.v. every 24 hours), and metronidazole (500 mg i.v. every 8 hours).

On the fourth day, the patient experienced convulsive episodes with eye fixation and limb rigidity, approximately 3-4 episodes. She was subsequently transferred to the Intensive Care Unit (ICU), where her seizures, which were a new onset, were managed. Neurological evaluation included a head CT scan and lumbar puncture (LP). The cerebrospinal fluid (CSF) analysis was notable for acellular fluid, and the CT scan showed no abnormalities.

During her ICU stay, in addition to anti-seizure medications, anti-inflammatory agents, diuretics, antibiotics, vitamins, and electrolytes, the patient received filgrastim (Neupogen) at a dose of 5 μg/kg/day to address severe neutropenia.

Despite comprehensive multidisciplinary management, the patient's condition worsened. Her laboratory results indicated: WBC count: 0.2 × 10^9/L, neutrophils: 59.2%, CRP: 0.86 mg/dL, ferritin: 15,231 ng/dL, fibrinogen: 914 mg/dL, BUN: 17.3 mg/dL, creatinine: 0.58 mg/dL. Despite aggressive treatment, the patient succumbed to her illness on the seventh day of hospitalization.

Table 1: Laboratory tests of the patient

	On admission	On the 7-th day	Unit
WBC	1.0	0.2	K/μL
Neutrophils	90.8	59.2	%
CRP	51.63	0.86	mg/dl
Ferritin	14989.15	15231	ng/dl
Fibrinogen	816	914	mg/dl
BUN	46.6	17.3	mg/dL
Creatinine	1.37	0.58	mg/dL

Source: Authors

Discussion

The association between malignancies and Listeria monocytogenes infections has been established for several decades, as documented by (Khardori et al., 1989; Louria et al., 1967). Despite this, recent extensive studies on listeriosis in oncological patients remain limited (Rivero et al., 2003). Immunosuppressive therapy, including chemotherapy and other cytotoxic treatments, is a prominent predisposing factor for listeriosis. Among patients undergoing immunosuppressive regimens, listerial sepsis and meningitis are notably prevalent and associated with the highest case-fatality rates among foodborne infections (Yildiz et al., 2007). Our patient was considered immunocompromised due to recent administration of cytotoxic agents, which likely contributed to the onset of listeriosis.

Recent evidence suggests that chemotherapy-induced intestinal paralysis, malnutrition, and myeloablation may enhance the risk of bacterial translocation and sepsis, thereby affecting the severity and prognosis of listeriosis (Singh et al., 2007). The primary clinical syndromes associated with L. monocytogenes infection include febrile gastroenteritis, perinatal infection, and systemic infections with central nervous system (CNS) involvement, with or without bacteremia (Drevets & Bronze, 2008). Therefore, in elderly or immunocompromised patients presenting with these clinical features, L. monocytogenes should be a differential consideration (Pasquier & Chuard, 2017).

Accurate diagnosis and microbiological confirmation are critical for effective management of listeriosis. The identification of L. monocytogenes can be challenging due to its resemblance to other Gram-positive pathogens, particularly streptococci. Comprehensive patient medical histories, including clinical symptoms and pertinent host factors, are essential for guiding suspicion and diagnosis (Nahid et al., 2015). Initially, Listeria spp. isolation methods relied on direct culture of clinical samples on simple agar media. However, advances in selective and enrichment media have improved the isolation and detection rates of L. monocytogenes (Beumer & Hazeleger, 2003). In our case, successful isolation of L. monocytogenes from the blood culture demonstrated the efficacy of modern diagnostic techniques in detecting pathogenic microorganisms.

Antimicrobial treatment remains the cornerstone for managing listeriosis. Penicillin, amoxicillin, and ampicillin are the antibiotics most frequently recommended by current guidelines due to their high affinity for penicillin-binding proteins (PBPs) and retention within the cytosol. Although amoxicillin has superior in vitro activity compared to ampicillin, ampicillin is the current first-line treatment for listeriosis. While quinolones exhibit excellent tissue and cellular penetration and are bactericidal, their clinical efficacy is sometimes less predictable (Charpentier & Courvalin, 1999). Combined antimicrobial therapies have been proposed to enhance penicillin activity against L. monocytogenes, aiming for complete eradication and reduced mortality. Despite sensitivity to imipenem in the strain from our case, empirical treatment did not improve the patient's condition. Multi-drug resistant L. monocytogenes strains have been reported, with the potential for acquiring antibiotic resistance genes (Charpentier & Courvalin, 1999).

Listeria monocytogenes infections, although infrequent, are severe, particularly in high-risk populations. Stringent sanitary controls throughout food production are essential to prevent outbreaks. Recent years have seen an increase in reported outbreaks and sporadic cases linked to contaminated meat products in developing countries (Matle et al., 2020). Factors independently associated with increased mortality in listerial bacteremia and neurolisteriosis include ongoing malignancy, multi-organ failure, decompensated comorbidities, monocytopenia, and the presence of concomitant bacteremia (Charlier et al., 2017; Huang et al., 2023).

Research indicates that primary bacteremia caused by L. monocytogenes is associated with higher mortality compared to listeriosis with CNS involvement (Huang et al., 2023). Invasive syndromes induced by L. monocytogenes can have a case-fatality rate up to 30%, especially in vulnerable populations such as the elderly, immunocompromised individuals, and neonates (Lomonaco et al., 2015). Mortality rates in patients with malignancy and bacteremia can approach 40% (Safdar & Armstrong, 2003). In our case, clinical deterioration and poor prognosis were primarily due to underlying malignancies and recent toxic chemotherapy.

The prevalence of listeriosis acquired through contaminated food in hospitalized patients is well-documented globally. Implementing rigorous hospital protocols for safe food handling and avoiding high-risk foods for immunocompromised patients could significantly reduce listeriosis cases (Benjamin et al., 2014). Effective listeria control involves stringent food hygiene practices. Patients should avoid high-risk foods, particularly when there is uncertainty about adherence to proper hygiene. Specialized diets for neutropenic and immunocompromised patients vary widely in implementation and adherence (Benjamin et al., 2014).

Table 2: Foods that are usually implicated in foodborne listeriosis.

Dairy Products	**Fruits and Vegetables**	**Meat Products**	**Fish Products**
Pasteurized whole milk	Coleslaw(cabbage)	Delicatessen foods (deli meats)	Shrimp salad
Chocolate milk	Lettuce	Pâté	Smoked fish
Soft cheese (different types)	Corn	Foie gras	Tuna salad
Hard cheese	Rice salad	Uncooked hot dogs	
Mexican-style cheese	Salted mushrooms	"Rillettes"	
Goat cheese	Sprouts	Pork tongue in aspic	
Ice cream	Strawberries	Pork pie	
Fresh cream	Nectarines	Beef	
	Apples	Turkey franks	
	Cantaloupes	Jellied pork	
	Blueberries	Cooked ham	
	Stone fruit	Ox tongue	
		Undercooked chicken	

Source: Bongiovanni (2024)

Conclusion

This case underscores the critical importance of early recognition and aggressive management of listeriosis, particularly in immunocompromised patients undergoing chemotherapy. The initial empiric treatment should invariably include an anti-listeriosis agent. Delay in the initiation of treatment increases

the likelihood of a poor prognosis, even though its onset (as in our case) does not completely exclude the possibility of fatalities. Moving forward, continued efforts to enhance awareness, prompt diagnosis, and targeted treatment strategies are paramount in improving outcomes and minimizing morbidity and mortality associated with listeriosis.

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