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Case report

Listeria monocytogenes and *Staphylococcus aureus* coinfection in a patient with multiple myeloma: Case report

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ABSTRACT

Introduction: Listeria monocytogenes is a formidable pathogen that poses a significant threat to immunocompromised and might cause rare atypical forms of the disease especially complicated with *Staphylococcus aureus* coinfection.

Case: We present a case of a patient with *L. monocytogenes* meningoencephalitis, endocarditis, sepsis, and *S. aureus* osteomyelitis, highlighting the complexities of managing disseminated polymicrobial infection. A 64-year-old female with multiple myeloma treated with chemotherapy presented with fever, altered mental status, nausea, and diarrhea to the emergency department. During the physical examination, the patient was feverish, had a hemorrhagic rash and an abscess on the right thumb. Neurologically – nuchal rigidity was seen and the finger-nose test was abnormal. Blood tests and cerebrospinal fluid analysis were consistent with bacterial meningitis. The roentgenogram revealed osteomyelitis involving the right thumb. Later L. *monocytogenes* was identified in blood and cerebrospinal fluid cultures. The abscess was drained, and pus culture identified *S. aureus*. Echocardiography revealed vegetation on the aortic valve. The patient was initially treated with ceftriaxone, ampicillin, gentamicin, with clindamycin and ciprofloxacin for osteomyelitis and later with ampicillin/sulbactam and ciprofloxacin to cover both pathogens and pathologies. Due to an allergic reaction to ampicillin, treatment was changed to vancomycin. After 4 weeks of antibiotic therapy patient fully recovered and continued chemotherapy for multiple myeloma.

Conclusion: In conclusion, this case emphasizes the intersection of hematological malignancy, chemotherapy-related immunosuppression, and subsequent severe disseminated bacterial infections and coinfections. Prompt diagnosis and adequate treatment of the disease and its complications is key to the successful recovery.

1. Introduction

Listeria monocytogenes is a Gram-positive facultative intracellular bacterium that can cause severe invasive infections, particularly in individuals over 65 years old, pregnant women, infants or people with compromised immune systems, such as those with chronic illnesses, HIV/AIDS, malignancies, undergoing chemotherapy or immunosuppressive treatment. *L. monocytogenes* is a foodborne pathogen, that causes febrile gastroenteritis but also can manifest as mild or severe invasive listeriosis, primarily as meningitis, sepsis,

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or localized infections [1]. The incidence of listeriosis is underestimated because more serious cases are being reported. People in high-risk groups should be advised to avoid foods with long shelf lives that are stored in the refrigerator, as well as ready-to-eat meats and fish (like ham, sausages, spreads, and cold smoked seafood) and unpasteurized dairy products. Concurrent infections with other pathogens, particularly *Staphylococcus aureus*, can further complicate the clinical picture. We report a case of disseminated listeriosis and *S. aureus* coinfection in a patient with multiple myeloma, highlighting the challenges in managing polymicrobial infections.

2. Case presentation

A 64-year-old female presented to the emergency department (ED) with a one-week history of febrile fever, altered mental status, nausea, and non-bloody diarrhea 3–4 times per day. Before coming to ED, the patient fainted. The symptoms were getting worse. Prior the disease, the patient did not have any contact with sick people, no insect bites or any travel history. No specific food questionnaire for the patient was administered, but the patient actively was questioned about the dietary choices for the last few days. The patient denied eating processed foods, dairy products but ate some raw unwashed fruits. From comorbidities, the patient had multiple myeloma treated with chemotherapy (the last course was 10 days ago), no specific dietary recommendations were given to the patient. Upon arrival to ED, she was lethargic, febrile, with a temperature of 37.3 °C, and appeared acutely ill. Physical examination revealed a hemorrhagic rash on her right leg, hand and left shoulder, an abscess on her right thumb. Neurological examination revealed nuchal rigidity, and the finger-nose test was abnormal, suggestive of neurological involvement. Her vital signs were normal (pulse 90 b./min., BP 160/68 mmHg).

Laboratory investigations showed leukopenia, thrombocytopenia and elevated C-reactive protein (CRP 205.5 mg/L), and electrolyte imbalance (see Table 1). Cerebrospinal fluid (CSF) analysis revealed pleocytosis with a predominance of lymphocytes, elevated protein levels, and decreased glucose levels, consistent with bacterial meningitis (Table 1). Blood, CSF and stool cultures (MacConkey agar and Hektoen enteric agar) were obtained. The roentgenogram of the right hand, demonstrated evidence of osteomyelitis involving the distal phalanx of the right thumb. The abscess was drained, and pus sample was sent for culture.

Empiric antibiotic therapy was initiated with intravenous ceftriaxone 2 g BID and ampicillin 2 g 6 times per day to cover for possible bacterial meningitis, pending culture results. Gentamicin's 240 mg qd 5-day course was added for a synergistic effect. For osteomyelitis, the treatment was supplemented with ciprofloxacin 500 mg TID and clindamycin 600 mg TID. The patient was also started on intravenous fluids and supportive treatment with dexamethasone, mannitol and antipyretics. The patient was hospitalised to the Infectious diseases department (see Fig. 1 for case timeline).

The patient had some additional tests done because she started to feel dyspnoea. Transthoracic echocardiography revealed insufficiency of the aortic valve and mobile vegetations up to 1 cm on it. The patient was also diagnosed with endocarditis and, therefore consulted by the cardiologist, and additional treatment for heart failure was recommended with beta-blockers and diuretics.

Blood and CSF cultures subsequently grew *L. monocytogenes,*[1] confirming the diagnosis of *L. monocytogenes* sepsis and meningoencephalitis. The stool culture was negative, the patient was negative for *Clostridium difficile* infection also. Pus culture yielded *S. aureus*.[2] It was believed that endocarditis was caused by *L. monocytogenes*, because of the growth in the blood culture, although *S. aureus* is a more common causative agent for endocarditis. According to the susceptibility reports for both pathogens, antibiotic therapy was changed to ampicillin/sulbactam 2g/1g QID and ciprofloxacin. However, the patient developed an allergic reaction to ampicillin, necessitating a switch to intravenous vancomycin 1g BID. The patient tolerated the prescribed treatment, no other adverse events were seen.

Throughout her hospitalization, the patient's condition gradually improved with antibiotic therapy and supportive care. The drained abscess needed local treatment and a necrectomy. The patient completed a 30-day course of intravenous antibiotics and showed significant clinical improvement. Signs of acute infection, and neurological impairment resided in the first week of therapy. Repeat imaging studies demonstrated the resolution of the osteomyelitis, and follow-up echocardiography showed a decrease in the vegetation size. The patient was discharged home in stable condition with recommendations to repeat echocardiography and take prescribed medication for heart failure.

The patient was followed up on a phone call, she claimed to be using prescribed medication but did not repeat the echocardiography. The patient needed an additional visit to the surgeon, for the ulcer on the right thumb, but with local treatment the ulcer healed. The severe disseminated infections were healed, she did not have any sequelae and she continued her chemotherapy regimen for multiple myeloma as an outpatient with no complications.

3. Discussion

Listeria monocytogenes is an uncommon but serious cause of bacterial meningoencephalitis in adults, particularly in immunocompromised individuals [1]. Risk factors for listeriosis include advanced age, pregnancy, immunosuppression, and underlying medical conditions such as malignancy and diabetes mellitus. In patients with hematological malignancies, chemotherapy-induced immunosuppression further increases the risk of invasive listeriosis but does not necessarily boost the mortality rate [2,3].

[1] *L.monocytogenes* susceptible to ampicillin, meropenem, erythromycin, trimethoprim/sulfamethoxazole. Susceptibility report done according to EUCAST standardised disk diffusion method.

[2] *S.aureus* susceptible to oxacillin, cefoxitin, erythromycin, ciprofloxacine, clindamycin, tetracycline, trimethoprim/sulfamethoxazole; resistant to penicillin. Susceptibility report done according to EUCAST standardised disk diffusion method.

Table 1
Blood and CSF analysis results.

		1st day	5th day	29th day
Blood analysis	Leucocytes (x10^9/L)	3.3	3.1	4.1
	Platelet count (x10^9/L)	69	65	164
	CRP (mg/l)	205.8	32.8	3.3
	Potassium (mmol/l)	2.7	3.9	4.9
	Glucose (mmol/l)	4	–	–
CSF analysis	Pleocytosis (x10^6/l)	353		
	Lymphocytes (%)	70		
	Neutrophils (%)	30		
	Total protein (g/l)	1.2		
	Lactate (mmol/l)	2.4		
	Glucose (mmol/l)	1.89		

Fig. 1. Timeline of the events. CSF – cerebrospinal fluid; AoV – Aortic valve.

Meta-analysis on mortality risk factors related to listeriosis found that there was no significant difference in mortality between patients with hematological malignancy and those without hematological malignancies [2]. The mortality rate for patients with hematological malignancies was 26.7 % and the overall case-fatality rate described in the literature is 23.6–26 % [4,5].

The presentation of listeriosis can be nonspecific and variable, ranging from mild febrile illness to severe systemic infection involving multiple organ systems. Most commonly the disease manifests as septicemia, central nervous system (CNS) infections (meningoencephalitis, rhombencephalitis, cerebritis, brain abscesses) and pregnancy-associated infection [1,5]. Due to tissue penetration across the gastrointestinal tract or hematogenous spread, bacteremia, pathogens can spread to sterile sites and cause rare manifestations such as endocarditis, peritonitis, bone and joint infections [1,6]. *L. monocytogenes* caused endocarditis, as described in our case, is a rare occurrence, it is believed that the incidence is about 8 % [7,8]. *L. monocytogenes* can cause native, prosthetic valve and device endocarditis [9]. However, it is atypical to have a case with CNS and heart involvement together, it was found by *Shoai-Tehrani* et al. that 17 % of endocarditis had concomitant neurolisteriosis [9] and these occurrences in the literature are described more as case reports. Any cases of CNS involvement, endocarditis and osteomyelitis all together were not found.

The management of listeriosis involves prompt initiation of appropriate antibiotic therapy, usually with ampicillin alone or in combination with an aminoglycoside, depending on the severity of the infection and the patient's clinical status [1]. In case of penicillin allergy, alternative agents such as trimethoprim-sulfamethoxazole or vancomycin may be used instead of ampicillin. In the literature, there is some data on increasing antibiotic resistance to ampicillin, trimethoprim-sulfamethoxazole and other antimicrobials [1,10]. Furthermore, *L. monocytogenes* is intrinsically resistant to cephalosporins, therefore using empiric treatment with cephalosporins alone on nonspecific sepsis, meningitis might delay proper treatment for listeriosis. Consequently, it is recommended that patients with meningitis who are immunocompromised or older than 50 y.o. would also get ampicillin as part of empiric treatment [11]. Listeriosis cases emphasize the importance of timely microbiological cultures because if empirical antibiotics do not cover the pathogen, delays in obtaining the microbiological culture results could severely impact the patient's prognosis due to inadequate treatment. The duration of the treatment depends on the form of the disease, although the proper duration for listeriosis has not been studied. Usually, 2–3 weeks of therapy with ampicillin and gentamicin for invasive listeriosis is enough, however rhombencephalitis with abscess formation in the CNS requires prolonged treatment – 4 weeks [1]. For forms of infections that require long treatment (e.g. endocarditis, osteomyelitis, abscesses, or other), treatment depends on the general recommendations for that form of the disease and on the clinical response [6,9,12]. Some forms might require surgical treatment.

In our case, the patient presented with a disseminated polymicrobial infection involving both *L. monocytogenes* and *S. aureus*. It is believed that endocarditis was caused by *L. monocytogenes* because just one pathogen grew in the blood, although *S. aureus* is a more typical cause of endocarditis. Luckily both pathogens are similar in their susceptibility and require similar treatment duration. By reviewing the literature one other case with *L. monocytogenes* and *S. aureus* coinfection was found in a prosthetic joint infection [13], the patient received surgical treatment and antibiotic treatment and made their recovery.

This case has some limitations, it was not possible to confirm if the endocarditis was caused just by *L. monocytogenes*. The patient did not need surgical treatment, and molecular testing of the blood was not possible in the hospital. However, due to prompt adequate management, the patient fully healed and could continue the chemotherapy.

In conclusion, *Listeria monocytogenes* remains a significant concern, particularly in immunocompromised individuals, pregnant women, and the elderly. Despite its uncommon occurrence, the severity of listeriosis warrants prompt recognition and initiation of appropriate antibiotic therapy. Physicians should be wary of the possible uncommon and rare presentations of listeriosis, such as rhombencephalitis, endocarditis, prosthetic bone/joint infections and others. Further research in rare manifestation management is essential to enhance the management of this *L. monocytogenes* infection, to lower the mortality rate.

4. Conclusion

We presented a rare case of disseminated *Listeria monocytogenes* infection with concomitant *Staphylococcus aureus* osteomyelitis in a patient with multiple myeloma undergoing chemotherapy. Prompt diagnosis and management, including appropriate antibiotic therapy and supportive care, were crucial in achieving successful recovery. This case shows that listeriosis can have different than expected manifestations and that one patient can have a few important infections with different causative agents.

CRediT authorship contribution statement

Roberta Vaikutyte-Ramanauskiene: Writing – original draft, Conceptualization. **Danguole Vaznaisiene:** Writing – review & editing, Supervision.

Ethics statement

Review or approval by an ethics committee was not needed for this case report, because data was gathered retrospectively and the case highlights a rare coinfection and presentation of the disease. This case report does not present new investigation tactics or treatment methods.

The patient signed a written informed consent to publish this case. All patient-identifying information was excluded from the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

AoV	Aortic valve
BID	two times a day
CNS	central nervous system
CSF	Cerebrospinal fluid
ED	emergency department
qd	once a day
QID	four times a day
TID	three times a day

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