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Listeria monocytogenes bacteremia in a centenarian and pathogen traceability: A case report

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Abstract

BACKGROUND

Early diagnosis and appropriate antibiotic treatment are important to survival of *Listeria monocytogenes* (*L. monocytogenes*) bacteremia. Penicillin tends to be the most commonly used antibiotic. However, there are limited data on antibiotic use in elderly patients with serious complications. We describe the clinical presentation, antibiotic therapy, and traceability of *L. monocytogenes* in a centenarian with a history of eating frozen food.

CASE SUMMARY

A 102-year-old man suffered from high fever with chill after hematochezia. Tentative diagnoses were lower gastrointestinal hemorrhage and localized peritonitis. Meropenem and ornidazole were the empirical therapy. The patient did not respond and developed multiple system dysfunction even after teicoplanin was added to the therapy. *L. monocytogenes* was identified from blood cultures on day 5 of admission. The patient had a history of consuming frozen dumplings. Meropenem/ornidazole/teicoplanin were replaced with meropenem/linezolid. The patient gradually became afebrile. He received meropenem/linezolid for 10 d, and piperacillin/tazobactam was applied as step-down treatment for 2 wk with good clinical results. There was no sign of relapse during follow-up after discharge. *L. monocytogenes* isolates from the patient and frozen dumplings belonged to different serotypes and sequence types (STs): 1/2b and ST5 from the patient and 1/2c and ST9 from the dumplings.

CONCLUSION

More awareness of listeriosis should be raised. Linezolid might be an option for

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listeriosis in elderly people with serious complications.

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Core Tip: Appropriate antibiotic treatment is important to survival of *Listeria monocytogenes* bacteremia. Penicillin tends to be the most commonly used antibiotic. However, there are limited data on antibiotic use in elderly patients with serious complications. Linezolid might be valuable for treatment of the *L. monocytogenes* bacteremia. Geriatricians should be suspicious of listeriosis when patients do not respond to broad-spectrum antibiotics, and when patients have a history of frozen food consumption. Healthy eating habits and food processing methods should be prioritized in elderly people.

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INTRODUCTION

Listeria monocytogenes (*L. monocytogenes*) is a facultative anaerobic, Gram-positive pathogenic bacterium[1]. *L. monocytogenes* can present in extreme conditions, which make it possible to infect people *via* ingestion of contaminated food and cause listeriosis[2]. Listeriosis is a potentially fatal foodborne infection including gastrointestinal infection, meningitis, bacteremia, and abortion[3,4]. High-risk populations are pregnant women and very old people[5].

The incidence of human listeriosis is low[6] but the mortality rate is high, especially in elderly people[5]. The rareness and long incubation period[7] of listeriosis make prompt diagnosis and tracing the source difficult. Appropriate antibiotic treatment and early diagnosis are of importance to survival[8]. Penicillin tends to be the most commonly used antibiotic[5]. However, there are limited data on antibiotic use in elderly patients with serious complications.

To raise awareness of early diagnosis and antibiotic therapy of listeriosis, we report a case of *L. monocytogenes* bacteremia in a 102-year-old man with serious conditions who did not respond to initial broad-spectrum antibiotic therapy. An extensive source tracing of the *L. monocytogenes* infection was performed by Beijing Centers for Disease Control and Prevention (CDC). We searched PubMed from 2012 to 2019 for articles with key words "*Listeria monocytogenes*," "bacteremia," and "septicemia." The articles were limited to human infection. Fourteen case reports are summarized in [Supplementary Table 1](#).

CASE PRESENTATION

Chief complaints

A 102-year-old man was admitted with hematochezia, high fever of 39.4 °C, chills, and stupor.

History of present illness

Patient's symptoms started 7 d before admission and worsened over the last 24 h. He suffered from dark red bloody stool three episodes for 7 d. The total amount of stool was about 400 g. He also had symptoms of fatigue and anepithymia with subsequent stupor. Other symptoms such as amaurosis, syncope, nausea, vomiting, and abdominal pain were unrepresented. Five days prior to onset, he had consumed quick-

frozen dumplings stored in the refrigerator.

History of past illness

His medical history included hypertension and stage 3 chronic kidney disease, which were well controlled. The patient took amlodipine 5 mg once a day until hematochezia. No medications for chronic renal disease. There was no history of antiplatelet/anticoagulation, glucocorticoid, or immunosuppressant therapy.

Personal and family history

There was no history of hereditary disease. No family members had similar symptoms.

Physical examination

The patient was febrile with a temperature of 39.4 °C, blood pressure was 149/65 mmHg, and pulse 94 beats/min. He became stuporous with Glasgow Coma Scale score 7/15. There was no nuchal rigidity, rash, and lymphadenectasis. The abdomen was distended in the right lower quadrant.

Laboratory examinations

White blood count was 13270/ μ L with 89.8% neutrophils, hemoglobin 8.4 g/dL, and platelet count 243000/ μ L. Fecal occult blood was positive and there were no white blood cells in the stools. C-reactive protein and procalcitonin level were 173 mg/L (normal range, 1-8 mg/L) and 0.734 ng/mL (normal range, 0-0.5 ng/mL), respectively. Biochemical examination upon admission, and days 5 and 28 is summarized in [Table 1](#), indicating deterioration of liver, kidney and myocardial damage and coagulation within 1 wk of admission.

Imaging examinations

Echocardiography showed a depressed left ventricular ejection fraction (41%) and no evidence of vegetation or endocarditis. Abdominal ultrasound examination showed a tubular hypoechoic structure approximately 8.7 cm \times 3.3 cm with unclear boundary, and uneven internal echo in the right lower quadrant. Computed tomography scan of the abdomen and pelvis without contrast was performed, which showed mural thickening and exudation surrounding the ascending colon, suggesting that inflammation might be present ([Figure 1](#)).

Microbiological identification of the causative agent and traceability

Four sets of blood cultures were taken using BD BACTEC 92F aerobic and 93F anaerobic media on admission. Blood culture was performed by a BACTEC system (Becton Dickinson, Sparks, MD, United States). On day 5 of admission, *L. monocytogenes* was identified from blood cultures. Antimicrobial susceptibility testing was performed using the dilution method. The isolate was susceptible to erythromycin (32 mm inhibition zone), gentamicin (24 mm inhibition zone), levofloxacin (25 mm inhibition zone), linezolid (32 mm inhibition zone), penicillin (30 mm inhibition zone), trimethoprim/sulfamethoxazole (29 mm inhibition zone), and vancomycin (21 mm inhibition zone) was intermediate to ampicillin/sulbactam and there was resistance to clindamycin and oxacillin. Meropenem was not tested.

Food and environmental samples from the patient's home were collected by the CDC. One deep-frozen dumpling sample from the refrigerator was positive for *L. monocytogenes*. The *L. monocytogenes* isolate identified by the hospital was also sent to the CDC laboratory in Beijing. The strain was serotyped using multiplex polymerase chain reaction. Multilocus sequence typing was performed on the isolate by amplification and sequencing of internal fragments of seven housekeeping genes[9]. Sequencing was performed on the ABI 3770 automatic sequencer. *L. monocytogenes* isolates from the patient and dumpling sample revealed different serotype and sequence types (STs): 1/2b and ST5 from the patient and 1/2c and ST9 from the dumpling.

FINAL DIAGNOSIS

The patient was finally diagnosed with *L. monocytogenes* bacteremia, localized peritonitis, sepsis, multiple system dysfunction (respiration, liver, central nervous system, renal, and heart), and disseminated intravascular coagulation.

Table 1 Laboratory findings across disease duration upon admission, on days 5 and 28

	Upon admission	On day 5	On day 28
WBC (/μL)	13270	18350	6130
Neut (%)	89.8	90.1	71.6
CRP (mg/L)	173	180	14
PCT (ng/mL)	0.734	0.905	0.042
AST (IU/L)	25	93	36
T-Bil (μmol/L)	14.22	20.43	15.53
ALT (IU/L)	35	51	38
CRE (μmol/L)	92	121	82
BUN (mmol/L)	12.45	19.48	9.68
TnI (ng/mL)	0.001	0.253	0.003
NTproBNP (pg/mL)	10031	11560	5642
INR	1.12	1.33	1.15
PT (s)	13.2	16.8	14.9
APTT (s)	45.1	54.2	45.9
Fib (g/L)	4.61	5.41	3.17
D-dimmer (μg/mL)	4.62	5.63	3.15

ALT: Alanine aminotransferase; APTT: Activated partial thromboplastin time; AST: Aspartate aminotransferase; BUN: Blood urea nitrogen; CRE: Creatinine; CRP: C-reactive protein; Fib: Fibrinogen; INR: International normalized ratio; Neut: Neutrophile granulocyte; NTproBNP: N-Terminal pro-brain natriuretic peptide; PCT: Procalcitonin; PT: Prothrombin time; T-Bil: Total bilirubin; TnI: Phosphorylation of troponin I; WBC: White blood cell.



Figure 1 Abdominal and pelvis computed tomography. Computed tomography scan of abdomen and pelvis showed mural thickening and exudation surrounding the ascending colon (orange arrow).

TREATMENT

As the patient was in critical condition and had abdominal infection commonly caused by Gram-negative or anaerobic bacteria, he was treated empirically with intravenous meropenem (0.5 g every 8 h), teicoplanin (0.4 g every 12 h), and ornidazole (0.5 g every 12 h). The patient did not respond to the initial antibiotic treatment as high fever and stupor persisted. On day 2, a Gram-positive bacterium was detected in one of the anaerobic blood cultures (time to positivity 27.92 h). On day 3, the patient presented with Biot's breathing and oxygen saturation on room air of 88% (partial pressure of oxygen/fraction of inspired oxygen ratio: 276 mmHg). Oxygen therapy was administered by Venturi Mask and respiratory stimulant drugs were given. He responded subsequently with resolution of hypoxemia. During the disease course, the patient presented with myocardial damage, acute progression of chronic renal disease, liver injury, and disseminated intravascular coagulation. Disseminated intravascular

coagulation score was 6. The sequential organ failure assessment (SOFA)[10] and SOFA of elderly[11] score was 7 and 10, respectively. Glutathione and plasma were infused.

On day 5, *L. monocytogenes* was identified from the blood cultures. We did not choose penicillin to replace meropenem to avoid antibiotic step-down in a critical condition. Vancomycin or sulfamethoxazole/trimethoprim was not administered for serious complications and renal insufficiency. Gram-positive *L. monocytogenes* was susceptible to linezolid (32 mm inhibition zone); thus, intravenous teicoplanin and ornidazole were stopped and subsequently meropenem and linezolid (0.6 g every 12 h) were initiated.

The temperature gradually returned to normal. Starting from day 8, the patient was afebrile and conscious. He could answer questions correctly and no neurological sequelae developed. The abdominal signs relieved gradually. The patient received meropenem and linezolid for 10 d, and then piperacillin/tazobactam (4.5 g, every 8 h) as step-down therapy was administered for a total of 2 wk. The patient received intravenous antibiotic treatment for 4 wk upon discharge, and blood cultures were negative. Antibiotics used are summarized in Figure 2.

OUTCOME AND FOLLOW-UP

Abdominal ultrasound performed before discharge showed normal findings. Fecal occult blood was negative and liver, kidney, and coagulation functions were normal (Table 1). The patient was discharged in fair condition and there was no sign of relapse during follow-up after discharge. No family members suffered from listeriosis. He eventually died of *Klebsiella pneumoniae* after 8 mo.

DISCUSSION

We report a case of *L. monocytogenes* bacteremia in a 102-year-old man with serious complications that was successfully treated by meropenem, linezolid, and piperacillin/tazobactam. Geriatricians should be suspicious of listeriosis when infected patients do not respond to broad-spectrum antibiotics and when the patients have history of frozen food consumption. Linezolid might be valuable for the treatment of *L. monocytogenes* bacteremia. *L. monocytogenes* strains from the patient and refrigerated dumpling belonged to different serotype and STs. Thus, the *L. monocytogenes*-contaminated dumpling was not the source of the patient's infection. To the best of our knowledge, this is the oldest patient with *L. monocytogenes* bacteremia.

Listeriosis has an estimated incidence of 2-15 cases per million per year in developed countries[6]. There is currently no accurate incidence of listeriosis in China. The number of patients in Mainland China is higher than that reported in the previous decade[1]. A systematic review[1] extracted 136 articles about listeriosis in Mainland China. A total of 562 listeriosis patients were reported during 2011-2017 including 227 (40.4%) nonperinatal patients, 231 (41.1%) perinatal patients, and 104 (18.5%) nonclustered patients. Beijing CDC received 49 clinical *L. monocytogenes* infectious case reports (27 pregnancy-associated and 22 nonpregnancy-associated infections) between 2014 and 2016[9]. *L. monocytogenes* causes severe and life-threatening diseases such as meningitis and bacteremia, with an estimated lethality of 10%-30%[2,5,12]. Mortality rates increase among those reporting a delay in diagnosis and treatment and in those with severe comorbidity[5].

In this study, our patient's advanced age, nonresponse to broad-spectrum antibiotics, poor dietary history and mucosal injury caused by localized peritonitis, were the clues to suspicion of *L. monocytogenes* infection. As described in Supplementary Table 1, 7 of 14 case reports were patients aged > 65 years. Three cases were suspected to have come from possibly contaminated food sources, but none was traced by further analysis. *L. monocytogenes* is naturally and intrinsically resistant to first-generation quinolones, fosfomycin and cephalosporins[13]. Penicillin, amoxicillin and ampicillin are recommended as first-line drugs for *L. monocytogenes* infection by current expert opinions[5]. Cotrimoxazole can be administered as an alternative treatment for listeriosis. Linezolid and vancomycin are valuable drugs in the treatment of listeriosis. Linezolid is an oxazolidinone with *in vitro* activity against *L. monocytogenes*. Its elevated cerebrospinal fluid and intracellular concentrations seem adequate for the treatment of neurolisteriosis and bacteremia in animal models[14]. The Multicentric Observational National Study on Listeriosis and Listeria

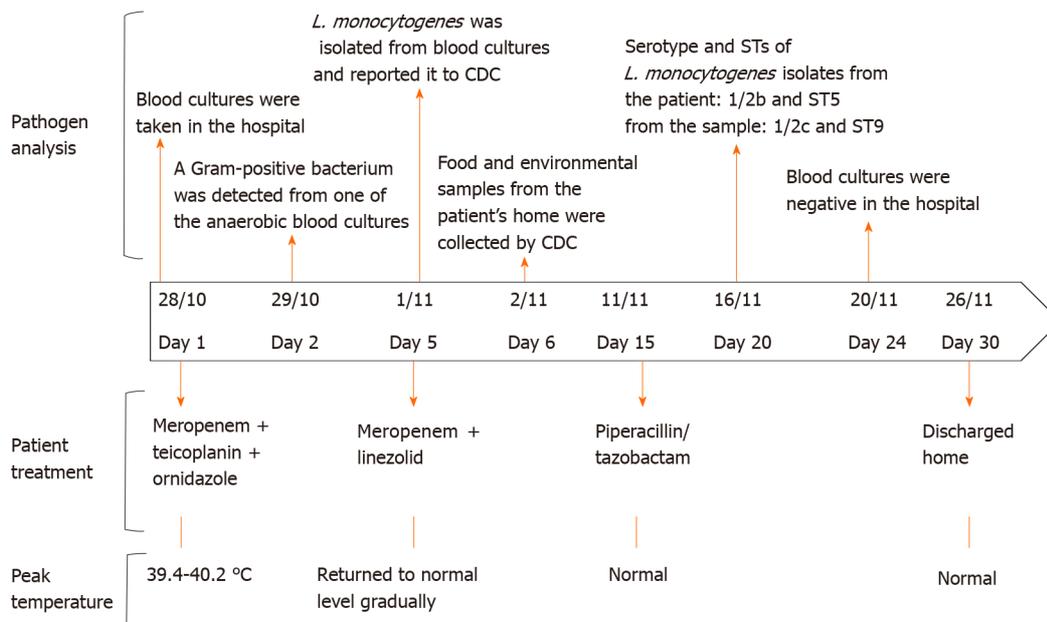


Figure 2 The *Listeria monocytogenes* bacteraemia patient treatment, peak temperature and pathogen analysis. CDC: Beijing Centers for Disease Control and Prevention; *L. monocytogenes*: *Listeria monocytogenes*; STs: Sequence types.

(MONALISA) study reported five cases (1%) treated with linezolid for a median duration of 10-15 d[8]. Meropenem in the treatment of listeriosis is still a matter of current debate. Meropenem displays a markedly low minimum inhibitory concentration *in vitro*, even lower than that of ampicillin against *L. monocytogenes*[15]. However, data on the efficacy of meropenem in clinical cases of listeriosis are scarce. Meropenem therapy failure in *L. monocytogenes* infection was reported on the basis of case reports[16]. A Danish retrospective study showed that definitive therapy with meropenem was associated with significantly higher 30-d mortality[17]. The current patient failed to respond to initial meropenem therapy until linezolid was added, indicating that linezolid is a valuable antibiotic for the treatment of the *L. monocytogenes* bacteremia. Meropenem, a broad-spectrum antibiotic, in combination therapy plays a role for the treatment of abdominal infection in the current patient. To avoid the long-term use of watch and reserve group antibiotics[18], piperacillin/tazobactam was administered as step-down therapy.

Pre-existing gastrointestinal disease was reported as a risk factor for *L. monocytogenes* infection of the gastrointestinal tract[19]. *L. monocytogenes* possesses different virulence factors such as internalin (InI) B, InIC, InIJ and the *Listeria*-mucin-binding invasion A that binds mucins[20-22]. The binding of *L. monocytogenes* to mucins *via* virulence factors may allow the bacterium to penetrate the mucus and facilitate bacterial adhesion or invasion of the host cells. *L. monocytogenes* evolved sophisticated mechanisms to cross the intestinal epithelial cells by different routes[23]: *Listeria* adhesion protein-mediated *L. monocytogenes* translocation, InIA/E-cadherin-mediated *L. monocytogenes* transcytosis, and M cell-mediated *L. monocytogenes* translocation occurs in the Peyer's patches. Within the host cell, *L. monocytogenes* destroys the phagolysosome membrane and gains access to the cytoplasm by listeriolysin O[24]. After invasion through the gastrointestinal tract, *L. monocytogenes* spread from cell to cell and may disseminate hematogenously. In the current patient, we speculate that the infection was probably acquired from mucosal injury caused by inflammation, which led to bacteremia and subsequent septicemia.

The long incubation period and food diversity make it difficult to trace the source of listeriosis. In this study, *L. monocytogenes* isolate from deep-frozen dumplings in the patient's home and blood cultures had different serotype and STs and was ruled out as the cause of infection. Mandatory declaration and surveillance of *L. monocytogenes* is urgently needed. From May 2015 to March 2016 in Italy, the source of an outbreak due to *L. monocytogenes* was identified as cheese through epidemiological and microbiological surveillance[25]. In England, crab meat was identified as the most plausible vehicle of infection by retrospective whole genome sequencing and epidemiological information[26].

This case report had some limitations. First, *L. monocytogenes* was identified after 5 d. We did not use characteristic tumbling motility of *L. monocytogenes* microscopically as a cheap test to obtain a presumptive diagnosis. Second, lumbar puncture was not performed, thus neuroinfection could not be ruled out. Third, the endoscopy was not performed for the advanced age of the patient and refusal of the relatives. Normal findings from abdominal ultrasound before discharge and relieved abdominal signs indicated the increased likelihood of abdominal infection. However, the exact cause of lower gastrointestinal bleeding is not clear. Finally, meropenem and piperacillin/tazobactam were applied as initial and step-down treatment but not narrower-spectrum antibiotics. Advanced age, serious complications, and *L. monocytogenes* bacteremia with localized peritonitis should be taken into account when we choose the antibiotics in clinical practice.

CONCLUSION

Although clinical data are currently limited, our patient seemed to benefit from linezolid therapy without linezolid-associated thrombocytopenia during 10 d of treatment. Linezolid might be a reasonable treatment option for *L. monocytogenes* bacteremia in elderly patients with serious complications. More suspicion of invasive listeriosis should be raised when infected elderly patients have a history of frozen food consumption history and do not respond to broad-spectrum antibiotics. Healthy eating habits and food processing methods should be prioritized in elderly people.

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