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BACTERAEMIA WITH MENINGITIS CAUSED BY LISTERIA INNOCUA OF UNKNOWN SOURCE IN AN ELDERLY PATIENT WITH TYPE 2 DIABETES MELLITUS: A CASE REPORT AND LITERATURE REVIEW

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ABSTRACT

Background: Listeria innocua is widely distributed in the natural environment and food products. Human infections caused by *L. innocua* are extremely rare, with only approximately 5 cases reported globally over the past three decades (1990-2025).

Case report: We report a case of a 74-year-old female with a history of poorly controlled type 2 diabetes mellitus (HbA1c 9.88%) and hypertension, who was admitted with headache, low-grade fever, and progressive altered mental status over 5 days. Cerebrospinal fluid analysis revealed pleocytosis. Both blood cultures (two sets) and the cerebrospinal fluid culture were positive for *L. innocua*, identified by matrix-assisted laser desorption/ionization-time of flight mass spectrometry. Despite an epidemiological investigation, the source of infection could not be determined. Initial treatment with ceftriaxone for 3 days failed with no clinical improvement. The patient was successfully treated with ampicillin for 49 days after culture results and antibiotic susceptibility testing became available. Cerebrospinal fluid parameters were normalized, and the patient was discharged after a 49-day treatment.

Conclusion: This is a rare case of bacteraemia with meningitis caused by *L. innocua* in an elderly diabetic patient. The case emphasizes the importance of awareness of the pathogenic potential of *L. innocua* in immunocompromised patients, and the need to add ampicillin to empiric antibiotic regimens for meningitis in high-risk groups (age >65, diabetes mellitus, cancer, or immunosuppression).

KEYWORDS

Listeria innocua, bacteraemia, meningitis, diabetes mellitus, elderly

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LEARNING POINTS

- *Listeria innocua*, although considered non-pathogenic in healthy individuals, can cause severe bacteraemia and meningitis in elderly patients with poorly controlled diabetes mellitus.
- Third-generation cephalosporins are not effective against all Listeria species; empiric treatment in patients >65 years with diabetes mellitus and meningitis must include ampicillin.
- Recent molecular studies have identified some atypical *L. innocua* strains carrying virulence genes, challenging the traditional view of the harmlessness of this species.

INTRODUCTION

The genus *Listeria* comprises at least 28 species, among which *Listeria* monocytogenes is the primary pathogen causing human disease[1]. Listeriosis predominantly affects the elderly (>65 years), pregnant women, neonates, and immunocompromised patients. Diabetes mellitus, cancer, cirrhosis, and immunosuppressive therapy are some of the most important risk factors[2-4].

Listeria innocua was first described in 1981 with the species name 'innocua' (harmless) because it did not cause disease in experimental animals[5]. This species lacks the *Listeria* pathogenicity island-1 (LIPI-1) which contains genes essential for the intracellular cycle of *Listeria*, including cell invasion, phagosome escape, and intracellular spread[2]. Therefore, *L. innocua* is commonly used as an indicator of environmental quality in food safety control.

To our knowledge, from 1990 to 2025, only 5 cases have been documented: meningitis (2 cases), prosthetic joint infection (1 case), meningoencephalitis (1 case), and bacteraemia (1 case)[6-10]. Recent studies have shown that atypical/haemolytic *L. innocua* strains may possess pathogenic potential due to their possession of complete or partial LIPI-1 (prfA cluster), which supports the intracellular cycle. The inlA/inlB genes enhance epithelial cell invasion, and the haemolytic phenotype is observed on blood agar. Additionally, LIPI-3 encodes listeriolysin S.

We report the first case of bacteraemia with meningitis caused by *L. innocua* in Vietnam and the sixth case worldwide with both blood and cerebrospinal fluid cultures yielding positive results, thereby contributing to the medical literature on the pathogenic potential of *L. innocua*.

CASE DESCRIPTION

The patient was a 74-year-old female living in Bac Ninh province, Vietnam with hypertension and type 2 diabetes mellitus treated regularly with medications (metformin 500 mg/day and amlodipine 5 mg/day). She had no history of surgery, or corticosteroid or immunosuppressive drug use. She lived independently with self-care abilities. Epidemiological investigation could not identify a clear source of infection.

The patient initially presented with headache and a low-grade fever of 37.5-38.5°C (mainly in the evening), without vomiting. No cough, dyspnoea, abdominal pain, or urinary/bowel dysfunction. After 2 days at home, progressive mental obtundation led family members to bring her to the provincial hospital.

At the provincial hospital, cerebrospinal fluid examination showed 100 white blood cells/µl (55% lymphocytes, 45% neutrophils). A computed tomography (CT) scan of the brain was normal. The patient was diagnosed with meningitis and treated with ceftriaxone and dexamethasone for 3 days. However, her clinical condition did not improve. She remained febrile at 38°C with headache and altered consciousness (Glasgow coma scale 13). The patient was transferred to our hospital, the National Hospital for Tropical Diseases (NHTD).

Upon admission to our hospital, physical examination revealed: Altered consciousness with a Glasgow coma scale score of 13, no focal neurological deficits, temperature of 38°C, pulse of 82 beats/minute, and blood pressure of 120/70 mmHg. Meningeal signs were present.

At NHTD, the patient underwent a lumbar puncture for cerebrospinal fluid analysis, including culture, to assess the condition. Two sets of blood cultures were obtained. Laboratory tests at admission included a white blood cell count of 12,500/ml, C-reactive protein of 121 mg/l, blood glucose of 12.5 mmol/l, and HbA1c of 9.88%. The brain CT scan was routine.

After 3 days of admission, both cerebrospinal fluid culture (1 specimen) and blood cultures (2 sets) were positive for *L. innocua*, identified by matrix-assisted laser desorption/ionization-time of flight mass spectrometry. Antimicrobial susceptibility testing revealed susceptibility to ampicillin and trimethoprim-sulfamethoxazole. Follow-up cerebrospinal fluid examinations showed progressive improvement, as shown in *Table 1*.

Normal reference values: cells <5/µl, protein 0.15-0.45 g/l, glucose 2.5-4.4 mmol/l (50-80% of plasma glucose), chloride 118-132 mmol/l.

The patient was initially treated with empiric antibiotics consisting of ampicillin 12 g/day (2 g IV every 4 hours) in combination with linezolid and dexamethasone. Blood glucose is controlled with insulin. After culture results confirmed *L. innocua* susceptibility to ampicillin, linezolid was discontinued, and treatment continued with ampicillin monotherapy for a total duration of 49 days. Blood glucose levels were maintained in the range of 7–10 mmol/l throughout the hospitalization.

After 49 days of treatment, a repeat lumbar puncture

Day	Day 1	Day 14	Day 40	Day 48
Cells (/µl)	1467	191	94	3
Neutrophils (%)	90	2	15	-
Lymphocytes (%)	10	96	80	-
Protein (g/l)	1.4	1.7	0.9	0.35
Glucose (mmol/l)	4.89	4.3	4.15	3.61
Chloride (mmol/l)	112.8	112.5	125.1	123
Culture	*L. innocua*	Negative	-	Negative

Table 1. *Cerebrospinal fluid laboratory results evolution.*

Reference	Age/sex	Specimen	Comorbidity	Diagnosis	Outcome
Perrin et al.[6]	62/F	Blood	Hypertension, asthma, gout, and osteoarthritis	Cholangitis with severe septic shock	Died 40 h after admission
Favaro et al.[7]	72/F	CSF	Etanercept and corticosteroid for rheumatoid arthritis	Meningitis	Death in ~10 days
Karli et al.[8]	9 months/M	CSF	None	Ventriculoperitoneal shunt infection	Unknown
Liao et al.[9]	3/M	Blood	None	Meningoencephalitis	Complications (hydrocephalus)
Gupta et al.[10]	Elderly/F	Knee joint fluid	Total knee replacement 12 years prior, diabetes mellitus	Prosthetic joint infection	Recovered
Present case	74/F	Blood and CSF	Diabetes mellitus	Bacteraemia with meningitis	Recovered

Table 2. *Global cases of L. innocua infection.*
Abbreviations: CSF, Cerebrospinal fluid.

revealed that the cerebrospinal fluid parameters had normalized, and the patient was discharged in satisfactory condition. The patient was transferred to a local hospital for specialized management of diabetes mellitus.

DISCUSSION

Listeria innocua infections in humans are considered extremely rare. The medical literature only documents a few sporadic cases (bacteraemia, meningitis/meningoencephalitis), mainly in the elderly, immunocompromised patients, or neonates *(Table 2)*. According to data from food and clinical surveillance by the World Health Organization Collaborating Center for Listeria (Institut Pasteur, France), 7,236 *L. innocua* strains were isolated over 30 years (1987-2018) without detecting any atypical haemolytic *L. innocua* strains[2]. This indicates that human exposure to pathogenic *Listeria innocua* strains is exceptionally low.

This patient had two major risk factors for listeriosis:

Advanced age of 74 years: Studies consistently show that individuals over 65 years constitute the most susceptible group for listeriosis, with a mortality rate of approximately 17% in the European Union (EU). The incidence of listeriosis in humans in the EU from 2014 to 2018 remained at 0.43 to 0.48 cases per 100,000 population. In Spain in 2018, the incidence of listeriosis was reported as 0.89 cases per 100,000 population[4].

Poorly controlled type 2 diabetes mellitus (HbA1c 9.88%): Hyperglycaemia creates a favourable environment for bacterial growth. It impairs the function of polymorphonuclear leukocytes, their chemotactic capacity, and T-cell-mediated immunity[3], which are the primary mechanisms against *Listeria* infection.

Previously, *L. innocua* was considered non-pathogenic in humans due to the absence of LIPI-1 - the virulence gene cluster that encodes six major factors (prfA, plcA, hly, mpl, actA, and plcB) regulated by prfA—necessary for the intracellular cycle of Listeria. Only rare, atypical haemolytic *L. innocua* strains possess LIPI-1 and cause human disease, albeit less severe than L. monocytogenes[2,11,12]. Additionally, studies have shown that atypical/haemolytic *L. innocua* strains possess pathogenic potential due to the presence of complete/partial LIPI-1 (prfA cluster), which supports the intracellular cycle; the inlA/inlB genes enhance epithelial

cell invasion; a haemolytic phenotype on blood agar[2]; and LIPI-3, which encodes listeriolysin S[12]. However, virulence depends not only on the presence or absence of virulence genes but also on the expression levels of these genes. This explains why some *L. innocua* strains can cause severe disease in vulnerable hosts (elderly, diabetics, pregnant women, and neonates).

The patient's lack of response to ceftriaxone at the provincial hospital was predictable. All Listeria species exhibit intrinsic resistance to cephalosporins due to the lack of appropriate penicillin-binding proteins. Current guidelines recommend adding ampicillin (2 g IV every 4 hours) to empiric regimens for meningitis in patients with advanced age (over 65 years); diabetes, cancer, or chronic disease; current corticosteroid or immunosuppressive therapy; or pregnancy. Optimal treatment is ampicillin or penicillin G combined with gentamicin (synergistic effect), prolonged for at least 3 weeks for meningitis. For patients allergic to beta-lactams, trimethoprim-sulfamethoxazole is an alternative option.

A limitation of this case is the absence of genetic sequencing to determine whether this strain carries virulence genes. Whole genome sequencing to identify the presence and expression levels of LIPI-1, LIPI-3, and other virulence genes would help us to better understand the pathogenic mechanisms of *L. innocua*.

CONCLUSION

We report the first case of bacteraemia with meningitis caused *by L. innocua* in Vietnam, the sixth case worldwide with both blood and cerebrospinal fluid cultures positive, successfully treated with ampicillin for 49 days. This case emphasizes three important points:

L. innocua can cause severe disease in immunocompromised patients, challenging the traditional notion of the harmlessness of this species;

Cephalosporins are ineffective against *Listeria*—ampicillin or penicillin G must be added to empiric regimens for meningitis in elderly patients and those with risk factors;

Molecular research (whole genome sequencing) is needed to identify pathogenic mechanisms and antimicrobial resistance of disease-causing *L. innocua* strains.

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