Case Report

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Severe invasive *Listeria monocytogenes* rhombencephalitis mimicking facial neuritis in a healthy middle-aged man: a case report and literature review

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Abstract

Neurolisteriosis is a foodborne infection of the central nervous system that is easily misdiagnosed, especially in healthy adults with atypical symptoms. A 50-year-old man presented with a 3-day history of distortion of the oral commissure. Facial neuritis was diagnosed and treated with intravenous dexamethasone. His condition deteriorated rapidly, and he presented with a slow pharyngeal reflex, stiff neck, and signs of peripheral facial paralysis. Brain magnetic resonance imaging revealed multiple ring-enhanced foci in the brainstem. Routine and biochemical cerebrospinal fluid (CSF) analyses showed increased white blood cells and microproteins. Blood culture and high-throughput genome sequencing revealed *Listeria monocytogenes* DNA in the CSF. Ampicillin, amikacin, and meropenem were administered, and the patient was transferred from the intensive care unit to a standard medical ward after 2 months. The patient could walk and eat normally; however, he required intermittent mechanical ventilation at 11 months after discharge. Although *L. monocytogenes* meningitis is rare in healthy immunocompetent adults, it must be considered as a differential diagnosis, especially in adults whose conditions do not improve with cephalosporin antibiotic administration. *L. monocytogenes* rhombencephalitis mimics facial neuritis and develops quickly. Prompt diagnosis is essential for rapid initiation of antibiotic therapy to achieve the best outcome.

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Introduction

Listeriosis is a rare disease, with a reported annual incidence of 4.4 per 1 million individuals,[1] and typical symptoms include fever, body aches, and gastrointestinal symptoms such as diarrhea. Immunocompromised, elderly, and pregnant individuals, as well as newborns, are most susceptible. *Listeria monocytogenes* is a Gram-positive facultative intracellular bacillus, and its transmission occurs mainly through the consumption of contaminated food. *L. monocytogenes* causes one of the most life-threatening bacterial infections of the central nervous system (CNS). Manifestations include meningitis, meningoencephalitis, and rhombencephalitis, and it is the third most common cause of bacterial meningitis.[2] *L. monocytogenes* encephalitis has high mortality and neurological sequelae rates, at 20% and 68%, respectively.[3] At present, reports of *L. monocytogenes* meningitis in immunocompetent and healthy adults with atypical initial symptoms (similar to facial neuritis) are limited. Such cases are easily misdiagnosed, and use of steroid therapy can endanger the patient's life. Therefore, we report a case of severe, invasive *L. monocytogenes* rhombencephalitis mimicking facial neuritis in a healthy middle-aged man, and we present a comprehensive review of the literature to summarize similar reports.

Case report

In January 2018, a 50-year-old man was admitted to our hospital with a 3-day history of distortion of the oral commissure. He had dizziness, headache, malaise, and vomiting beginning 3 days before admission. A shallow nasolabial sulcus on the left side, distortion of the oral commissure, and weakness in closing the left eye subsequently appeared. The patient had no diplopia, dysdipsia, hemiplegia, or limb numbness, and he was lucid and alert. Diagnoses of acute upper respiratory tract infection and peripheral facial neuritis had been considered at another hospital. The patient was previously diagnosed with tuberculosis at 4 years old; he reported that the tuberculosis had long been cured, and he had no history of immunodeficiency. He had no history of major trauma, toxic exposure, smoking, alcoholism, drug abuse, or hereditary disease. His family denied any history of unpasteurized buttermilk consumption.

A physical examination on admission revealed a blood pressure of 135/85 mmHg, temperature of 36.5°C, and pulse rate of 85 bpm. He had no signs of meningismus or other neurological irregularities. The patient's white blood cell count (10.61×10^9/L), fasting blood glucose level (6.3 mmol/L), and glycosylated hemoglobin level (6.1%) were slightly increased, whereas his serum creatinine, cholesterol, C-reactive protein, creatine kinase, and procalcitonin levels were normal. The blood coagulation parameters were within normal limits. Tests for antibodies to human immunodeficiency virus and *Treponema pallidum* were negative. Emergency head computed tomography (CT) showed no apparent abnormalities

(Figure 1a). Chest CT showed chronic-appearing fibrotic streaks in both lungs. Peripheral facial neuritis was diagnosed; the patient was admitted, and dexamethasone (10 mg/day) was administered intravenously (iv) for 3 days.

The patient then developed a headache, dysdipsia, malaise, and fever (39.2°C) 3 days after hospitalization, and a physical examination at that time showed neck stiffness and slowness of the pharyngeal reflex, along with signs of peripheral facial paralysis. The facial nerve, glossopharyngeal nerve, and meninges were considered affected; however, the nature of the lesion was unknown. No apparent abnormality was found in a head CT re-examination (Figure 1b). The patient's condition

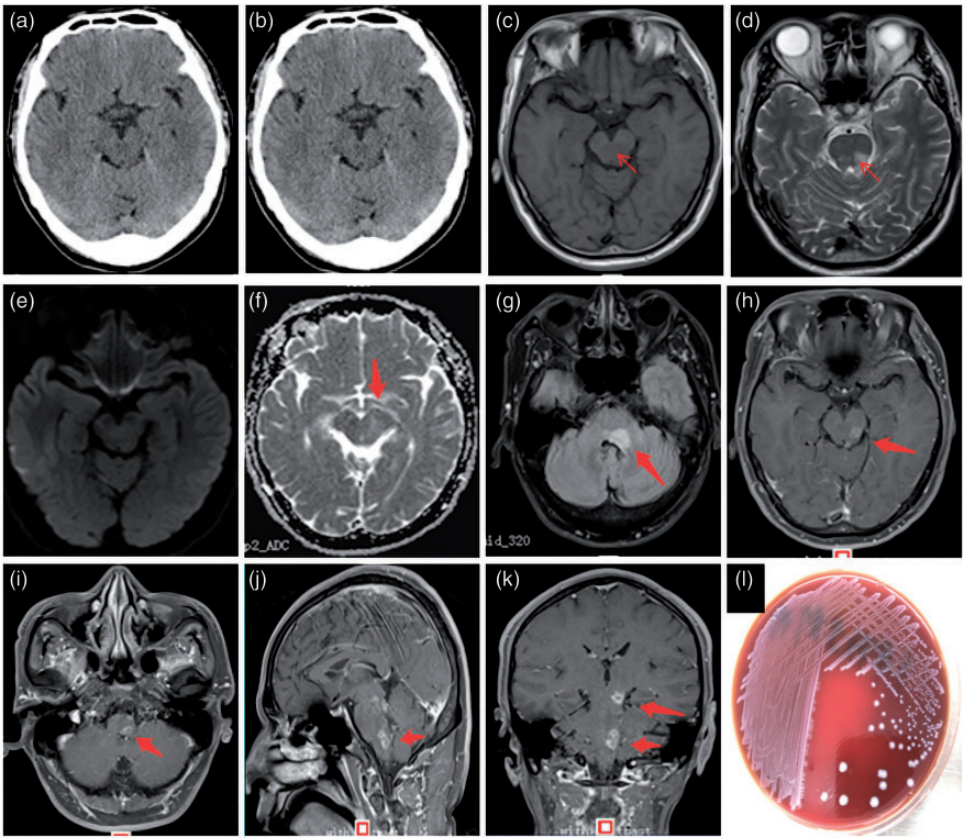

Figure 1. Computed tomography (CT), magnetic resonance imaging (MRI), and blood culture results. (a) Head CT showing no apparent abnormality after admission. (b) The patient's condition worsened; however, head CT re-examination showed no apparent abnormality on the third day after admission. (c) T1-weighted image (WI) showing low-signal midbrain lesions (arrow). (d) T2-WI showing a hyperintense dorsal pontine lesion (arrow). (e) Diffusion WI showing no abnormal signal in the midbrain. (f) A high apparent diffusion coefficient was observed in the midbrain lesions (arrow). (g) Fluid-attenuated inversion recovery sequence showing hyperintense lesions (arrow) in the dorsal lower pons. (h–k) Gadolinium-enhanced MRI showing multiple ring-enhanced lesions in the (h) left midbrain (arrow), (i) medulla oblongata, (j) dorsal upper medulla oblongata (arrow), and (k) dorsal lower pons (arrow). (l) *Listeria monocytogenes* was cultured from peripheral blood. The tryptone soy blood agar plate produced round bacterial colonies with neat edges and central uplifting; the surfaces were smooth and whitish gray.

worsened rapidly, and he developed somnolence, aphagia, and slurred speech. Brain magnetic resonance imaging (MRI) (Figure 1c–k) performed 4 days after admission showed multiple abnormal foci in the brainstem. The cerebrospinal fluid (CSF) opening pressure was 245 mmH_2O. Routine CSF testing showed a markedly increased white blood cell count (8.35×10^8/L). Biochemical CSF examination showed a potassium concentration of 2.5 mmol/L, chloride concentration of 144 mmol/L, glucose concentration of 3.0 mmol/L, and microprotein concentration of 2.19 g/L. No organisms were observed on Gram, India ink, or acid-fast staining.

The patient was considered to have a tuberculous or bacterial intracranial infection and was transferred to the intensive care unit (ICU). He underwent physical cooling using an ice blanket and ice cap and was given anti-infective and antiviral medications (ceftriaxone, 2 g iv every 12 hours; ganciclovir, 0.25 g iv every 12 hours). Furthermore, he underwent intracranial decompression using mannitol and symptomatic and supportive treatment in the ICU. Further examination revealed negative tests for influenza A and B viral antigens and anti-*Toxoplasma* antibodies. Two days later, *L. monocytogenes* (Figure 1l) was isolated from the blood culture and was identified by time-of-flight mass spectrometry, but no abnormality was found in the CSF culture. Genetic identification of CSF pathogens by high-throughput genome sequencing found only *L. monocytogenes* (sequence number 210).

The patient's condition quickly progressed to respiratory failure; thus, mechanical ventilation was initiated. Based on the sequencing and antimicrobial susceptibility testing results, anti-infectives (ampicillin, 1 g iv every 8 hours; amikacin, 0.4 g iv every 12 hours; and later, meropenem, 2 g iv every 8 hours) were administered, and the patient was transferred from the ICU to a standard medical ward after 2 months. The patient could walk and eat normally; however, damage to the respiratory center resulted in central respiratory insufficiency, and he required intermittent mechanical ventilation at the 11-month post-discharge follow-up visit. He was satisfied with his treatment and recovery.

Discussion

This case of severe, invasive *L. monocytogenes* rhombencephalitis mimicking facial neuritis in a healthy middle-aged man showed that the disease can be easily misdiagnosed in this population. Moreover, this case showed that observation of ring-enhanced brainstem lesions on MRI and high-throughput genome sequencing results are important for accurate diagnosis. Furthermore, this case showed that the choice of proper antimicrobials is key to a successful therapy.

L. monocytogenes is routinely described as an opportunistic bacterium, and it typically infects pregnant women, newborns, the immunocompromised, and older adults. As in healthy adults, it is very rare in healthy children[4] beyond the neonatal period. The cause of *L. monocytogenes* encephalitis in healthy adults may differ from that in patients with immunodeficiency.

The main transmission route of *L. monocytogenes* infection is the digestive tract, from which it is absorbed into the peripheral blood. From the peripheral blood, it can access the CNS by crossing the blood–brain barrier.[5] Most patients have gastrointestinal symptoms (Table 1);[6–10] however, as in this case, they often do not have a clear history of contaminated food ingestion.

Some patients with *L. monocytogenes* encephalitis show mild symptoms and have a good treatment response.[7] However, the disease can be aggressive, as in the case of our patient.

Table 1. Clinical features of healthy and immunocompetent young and middle-aged individuals with *Listeria* meningitis.

Author, year of publication	Age (years) and sex	Consumption of unpasteurized buttermilk	Symptoms and signs	Brain CT/MRI	CSF/CSF cultures for LM	Blood/CSF cultures for LM	Specific antibiotic treatment for LM and outcome
Zhang et al. [6], 2012	34, M	Not mentioned	Fever, headache, nausea, and vomiting for 3 days	Not mentioned	Leukocytosis and high protein levels	–/+	Initial treatment with vancomycin (1 g iv q12h) and ceftriaxone (2 g iv q12h); however, his condition deteriorated
			Altered consciousness for 1 day				Consequently, the patient was given a combination of ampicillin (4 g iv q8h) and amikacin (0.4 g iv daily), to which he responded well
			Meningeal irritation sign (+)				The patient remained in good clinical condition on follow-up
Callaghan et al. [7], 2012	35, F	Not mentioned	Headaches, nausea, vomiting, and malaise for 4 days, followed by hemianesthesia, facial weakness, nystagmus, and ataxia	MRI showed multiple ring-enhancing lesions in the brainstem	Leukocytosis and high protein levels	–/–	Amoxicillin (2 g six times daily) and gentamicin (80 mg iv three times daily) for 2 weeks, to which the patient responded well
						CSF PCR: +	She had recovered well on follow-up
Vrbiü et al. [8], 2013	18, M	Not mentioned	Fever, severe headache, and vomiting for 3 days	CT showed diffuse cerebral edema	Leucocytes ↑ and high proteins levels	–/+	Initial treatment with vancomycin and ceftriaxone, substituted with meropenem (2 g iv q8h), had no clinical effect
			Meningeal irritation sign (+)				Subsequently, ampicillin (2 g iv q4h) was administered after LM was isolated; the patient recovered completely.

(continued)

Table 1. Continued.

Author, year of publication	Age (years) and sex	Consumption of unpasteurized buttermilk	Symptoms and signs	Brain CT/MRI	CSF/CSF cultures for LM	Blood/CSF cultures for LM	Specific antibiotic treatment for LM and outcome
De´card et al. [9], 2017	31, F	Yes	Isolated right facial numbness, followed by dysphagia, nystagmus, diplopia, peripheral facial palsy, and hemiparesis	MRI showed multiple ring-enhancing lesions in the brainstem	Lymphocytic pleocytosis and slightly elevated protein levels	+/+	Ampicillin, ceftriaxone, and acyclovir were initiated and substituted with ampicillin and gentamicin after culturing of LM, followed by combination treatment with ampicillin, rifampicin, linezolid, and cotrimoxazole The patient had severe sequelae
Li et al. [10], 2019	37, M	Not mentioned	Fever for 2 days, with dysphoria, followed by coma and respiratory and circulatory failure	CT showed swelling of the brain and hydrocephalus	High CSF pressure, increased leucocytes, and normal protein levels	+/−	Vancomycin (0.5 g iv q8h) and meropenem (0.5 g iv q8h) The patient died 2 weeks after admission

CSF, cerebrospinal fluid; CT, computed tomography; F, female; iv, intravenously; LM, *Listeria monocytogenes*; MRI, magnetic resonance imaging; M, male; PCR, polymerase chain reaction; q4h, every 4 hours; q8h, every 8 hours; q12h, every 12 hours; −, negative; +, positive.

L. monocytogenes rhombencephalitis typically has a biphasic course, with nonspecific prodromal symptoms such as fever, malaise, fatigue, headache, nausea, and vomiting, followed by any combination of cranial nerve palsies, ataxia, hemiparesis, hypesthesia,[2] and altered consciousness. *L. monocytogenes* rhombencephalitis develops quickly and is often complicated by sepsis and respiratory failure.[11] Common clinical findings include fever (57%), headache (57%), and focal neurological signs (64%).[11] *L. monocytogenes* rhombencephalitis should be differentiated from tuberculous meningitis; both have similar CSF and brain MRI abnormalities, but *L. monocytogenes* rhombencephalitis often presents with high fever and progresses rapidly. *Listeria* may be identified in CSF cultures and much more rarely in blood cultures. *L. monocytogenes* rhombencephalitis should be distinguished from cryptococcal meningitis and other types of bacterial encephalitis. MRI usually shows multiple ring-enhanced lesions in the brainstem,[7,9] as was observed in this case. With its high resolution, high-throughput genome sequencing is a promising technique for pathogen identification.

In general, penicillin, ampicillin,[12] and amoxicillin are effective treatments for *L. monocytogenes* infection, but some strains are resistant. Thus, effective antibacterial agents, such as trimethoprim-sulfamethoxazole,[13] meropenem, linezolid, and aminoglycosides,[12] should be selected with the guidance of an antimicrobial sensitivity test. Guidelines recommend early steroid therapy for facial neuritis;[14] however, patients with neurolisteriosis receiving adjunctive dexamethasone have higher mortality,[15] and this treatment could aggravate conditions in patients without effective antibiotic treatment, as in this case. The treatment course with effective antibiotics should be at least 21 days. Because *L. monocytogenes* has a natural resistance to cephalosporin antibiotics, *L. monocytogenes* should be considered when third-generation cephalosporins are not effective against bacterial encephalitis. The empirical treatment of bacterial meningitis should include agents effective against listeriosis.[16] The survival rate is greater than 70% when appropriate antibiotic therapy is initiated early.[17] Younger, immunocompetent individuals with *L. monocytogenes* meningitis have favorable disease outcomes.[8] However, approximately 60% of survivors develop neurological sequelae.[17] Timely and effective antibacterial therapy is crucial to improving the prognosis.

We searched the PubMed database for the Medical Subject Heading terms "facial paralysis/cranial nerve injuries" and "*Listeria monocytogenes*/*Listeria*" in different combinations, but no case similar to ours was found. It is necessary to further study *L. monocytogenes* encephalitis with atypical initial symptoms to aid early identification.

In conclusion, although *Listeria* meningitis is rare in healthy, immunocompetent adults, it must be considered in the differential diagnosis, especially in those whose disease conditions do not improve with cephalosporin antibiotic treatment. *L. monocytogenes* rhombencephalitis develops quickly, and prompt diagnosis of *L. monocytogenes* encephalitis, which mimics facial neuritis, is essential so that adequate antibiotic treatment can be initiated and the best outcome is achieved.

Ethics Statement

The study design was approved by the ethics review board of the Third Affiliated Hospital of Shenzhen University (No. 2020-SZLH-LW-015). We obtained written consent for publication from the patient.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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