



The rapidly progressing and fatal outcome of rhombencephalitis by listeriosis in a 61-year-old male

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A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Skrobas U, Zie WS, Bielewicz J, Rejdak K. The rapidly progressing and fatal outcome of rhombencephalitis by listeriosis in a 61-year-old male. *Ann Agric Environ Med.* 2024; 31(2): 311–314. doi: 10.26444/aaem/178178

Abstract

Listeria monocytogenes is a Gram-positive facultative anaerobic bacterium that is ubiquitous in the environment and can cause severe infections in immunocompromised individuals, pregnant women, and newborns. Listeriosis can manifest as meningitis, encephalitis, or sepsis, and its diagnosis requires a high index of suspicion. The case is reported of a rare presentation of rhombencephalitis by listeriosis in a 61-year-old male who initially suffered from subacute gastric disturbances and fever. Neurological consultation showed abnormal functions of cranial nerves and meningeal signs were observed. MRI revealed a poorly demarcated focus of approximately 45 × 16 × 15 mm, indicating possible inflammatory processes, necessitating a lumbar puncture. Assessment of the CSF indicated infection with the bacterium- *Listeria Monocytogenes*, with the final diagnosis of Listeriosis encephalitis. Despite antibiotic therapy of Ceftazidime and Ampicillin, the patient's condition deteriorated, followed by death.

Key words

listeriosis, neuroinfection, rhombencephalitis, foodborne illness, brainstem inflammation, listeriosis encephalitis

INTRODUCTION

Listeriosis is a relatively rare, foodborne disease with approximately 0.1–10 cases per 1 million people each year, depending on the countries and region of the world. Even though the number of cases of listeriosis is small, the high rate of death associated with this infection is of significant public health concern [1, 2].

CASE REPORT

A 61-year-old male was referred to the Emergency Department due to subacute nausea, abdominal pain, persistent biliary vomiting, dizziness, and general weakness. He had a fever for three days, reaching up to 40 degrees Celsius, and had been constipated for six days before admission. His past medical history revealed a gastric and duodenal ulcer, and he had undergone gastric subtotal resection. During that time, he was being treated for paroxysmal atrial fibrillation. He had no history of drug allergy or tick bite, and despite being the owner of a catering firm, he denied any contact with uncontrolled food. The patient was eventually admitted to the Gastroenterology Department for further investigation.

Shortly after admission to the Gastroenterology Department, the patient began experiencing headaches, vision disturbances, and difficulties with swallowing and speech. Additionally, nausea, vomiting, and an elevated body temperature of up to 40 degrees were noted, although the intensity of abdominal pain decreased. A gastroscopy was conducted which revealed no significant changes except

for inflammation of the gastric mucosa. Due to the rapid progression of swallowing issues, persistent headaches, and diplopia, an urgent neurological consultation was requested. The patient was conscious and properly oriented but exhibited prominent dysarthria and dysphagia. Abnormal functions of cranial nerves VI, VII, IX, X, and XII on the right and meningeal signs were observed during neurological examination, which suggested a brainstem lesion.

The patient was subsequently transferred to the Neurological Department for further examinations and management. A 1.5T MRI of the head was performed, which revealed a poorly demarcated focus measuring approximately 45 × 16 × 15 mm with a high signal intensity on T2-weighted images and in the sequence of Turbo Inversion Recovery Magnitude (TIRM) in the lower medulla. The focus did not show enhancement after intravenous paramagnetic administration and did not exhibit features of diffusion restriction. (Fig. 1, Fig. 2) A similar focus, measuring 8 mm in diameter, was also visible in the middle cerebellar branch. The MRI images suggested the possibility of various processes, such as inflammatory, demyelinating, or proliferative, because their radiological presentation can be similar. However, an ischemic process was excluded. The laboratory test results showed an increased level of inflammatory factors. Initial WBC count – 11.92 × 10³cell/ul, CRP level – 39.93 mg/l; the latter WBC count – 23.37 × 10³cell/ul, CRP level – 132.16 mg/l.

A lumbar puncture was performed due to suspicion of neuroinflammation. The cerebrospinal fluid (CSF) results confirmed the presence of an inflammatory process with a cytosis of 128 cell/ul. The smear showed 82% lymphocytes, 5% monocytes, and 13% neutrophils, while the protein level was 144 mg/dl, and the glucose level was 49 mg/dl. After 24 hours, *Listeria monocytogenes* (LM) culturing on agar

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Received: 08.08.2023; accepted: 02.01.2024; first published: 04.03.2024



Figure 1. T2 weighted MRI sagittal image. A hyperdense poorly-demarcated focus which was not enhanced after paramagnetic administration. Change is seen mostly in the lower medulla and higher

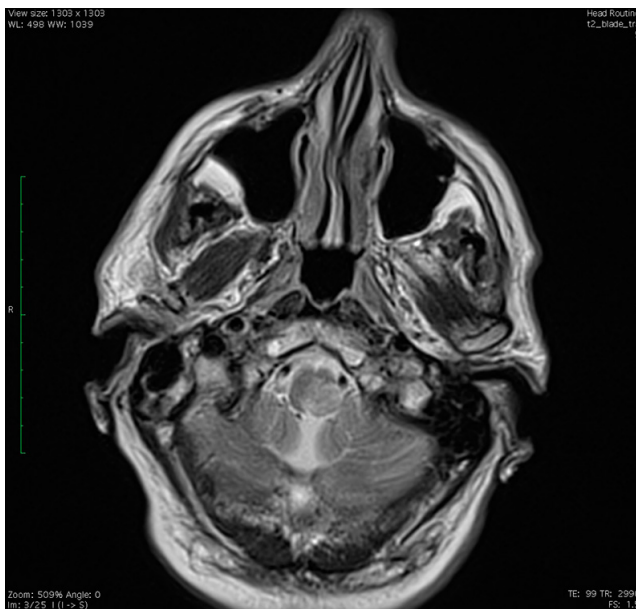


Figure 2. T2 weighted MRI axial image. A hyperdense poorly demarcated focus which was not enhanced after paramagnetic administration. Change is seen mostly in the pons infiltrating the right side of structures

medium in CSF was positive, leading to a final diagnosis of listeriosis encephalitis. Antibiotic treatment was initiated with Ceftriaxone 3x2 g i.v. and modified after antibiogram results were obtained, with the addition of Ampicillin 6x2 g i.v. The patient's condition rapidly deteriorated, with a notable escalation in signs of cranial nerve injury, resulting particularly in dysarthria and dysphagia. Enteral nutrition became mandatory. Progressive limb paresis manifested, starting with the left side and subsequently affecting the right. Simultaneously, disturbances in consciousness, marked by a decline in awareness, became apparent. Ultimately, respiratory insufficiency occurred, requiring artificial respiration. The patient died two days later.

DISCUSSION

Listeriosis, caused by the pathogen *LM*, is a severe foodborne disease if it is not prevented. The *LM* bacteria are ubiquitous in nature, and can be isolated from soil, water, and animal digestive tracts. This bacterium is found in high-risk foods, such as deli meat, ready-to-eat meat products, and soft cheeses. It is a rare disease, but can be more frequent in agricultural regions where untested food may be suspected. *LM* survives and thrives at low temperatures usually found in refrigerators [1, 3, 4]. After ingestion of *LM* via contaminated food, it usually causes gastrointestinal and/or flu-like symptoms. It can be life-threatening, often manifested as septicemia and/or neuroinfection, particularly among high-risk individuals, such as pregnant women, the elderly, or immunocompromised individuals. Neuroinfection can have a clinical picture of meningitis, abscess, or rhombencephalitis (brainstem inflammation). In the case of listeriosis associated with brainstem inflammation, it is thought to be caused by invasion of the nerves and subsequent axonal migration of *LM* to the base of the brain. The haematogenous spread of this bacterium via invasion of the blood-brain barrier likely leads to a more diffuse infection of the brain. The trigeminal nerve serves as a potential route for *LM* to access the brainstem after infiltrating compromised oropharyngeal mucosa or encountering periodontal problems. While in the majority of cases involving inflammation of the brainstem due to *LM* are observed in individuals previously enjoying good health, identifying the disease during its initial stages remains a formidable challenge [5]. Brainstem inflammation occurs in about 24% of listeriosis patients, with a distressing mortality rate of approximately 50% and a propensity for survivors to experience serious long-term consequences, affecting roughly 60% of cases.

The likelihood of surviving this condition is markedly associated with early detection, accurate diagnosis, and the prompt administration of appropriate antibiotics. Due to non-specific symptoms (fever, headache, nausea, and vomiting) and unusual meningeal signs, listeriosis in the course of brainstem inflammation is often misdiagnosed. Individuals with this condition eventually manifest symptoms that commonly involve lower cranial nerve palsies, manifesting dysphagia, dysarthria, and persistent hiccupping. Additionally, some patients may experience symptoms such as gaze disturbances, abnormal facial sensations, or vertigo.

The differential diagnosis should include other neuroinfections, such as herpes virus encephalitis, autoimmune inflammation like Bickerstaff inflammation or CLIPPERS (chronic lymphocytic inflammation with pontine perivascular enhancement), Miller Fisher syndrome, or vascular injury in the posterior circulation [5, 6, 7]. These entities may exhibit a comparable clinical presentation involving cranial nerves, similar brainstem localization, or a shared infection etiology. Due to this, the presented case necessitated a broad diagnostic approach.

To accurately diagnose brainstem inflammation in listeriosis, investigations should include an MRI of the head, cerebrospinal fluid (CSF) assessment, and blood cultures. Clinicians evaluating undifferentiated meningitis or encephalitis should simultaneously consider autoimmune, infectious, and neoplastic causes, using patient risk factors, clinical syndrome, and diagnostic results [8]. Results of MRI and CSF examinations have prominent values. In MRI,

lesions in the brain stem are seen with T1 presents hypo- to isointense, T2/flair hyperintense, diffusion-weighted imaging (DWI) to measure the motion of water molecules within the volume of the brain tissue, hyperintense/hypointense on the apparent diffusion coefficient (ADC) map to measure the magnitude of water diffusing within the brain tissue and linear cranial nerve enhancement. When analyzing cerebrospinal fluid, it may not always reveal the presence of LM, but it may exhibit signs such as pleocytosis, an increase in polymorphonuclear leukocytes, and elevated protein levels. Therefore, it is imperative to initiate empirical treatment with appropriate antibiotics as soon as possible, without delaying antimicrobial therapy [9]. The preferred initial treatment approach typically involves administering intravenous ampicillin or penicillin in combination with gentamicin for a minimum of six weeks, as this has demonstrated effectiveness. In situations where patients have allergies to ampicillin or penicillin, alternatives such as vancomycin, meropenem, or linezolid can be considered [5, 6].

As mentioned above, Listeriosis with invasion of the central nervous system primarily affects certain risk groups, including pregnant women, neonates, the elderly, and immunocompromised patients. In the elderly, cancer and diabetes mellitus are the debilitating comorbidities most often found [10]. In rare instances, Listeriosis is observed in immunocompetent adults and children, as shown in the presented case. The reason behind the development of this neuroinfection in this particular group remains unclear (genetic predisposition? subclinical immunodeficiencies?). Listeriosis is still difficult to diagnose, making continuous education important. Infectious disease with the insidious beginning of gastrointestinal disturbances signs, and subsequently signs of neurological involvement, should raise awareness of neuroinfection (Tab. 1). For these reasons, this case report can have educational value for specialists in neurology, infectious diseases, gastroenterology, or internal medicine.

The challenging aspect of quick diagnosis and the rapid progression with frequently fatal outcomes justifies introducing broad-spectrum antibiotic therapy with ampicillin and gentamicin, and early incentive intubation and ventilator therapy in suspected cases.

Next-generation sequencing (NGS) of CSF is an emerging technique for diagnosing infrequent causative pathogens which is promising for quick diagnosis of LM. This method involves extracting and purifying DNA from 200 µL of CSF supernatant. Subsequently, DNA libraries are constructed through end-repaired adaptation and polymerase chain reaction (PCR) application. Finally, the concentration and quality of the libraries are evaluated [11].

CONCLUSIONS

Many questions remain to be resolved to limit the impact human listeriosis. Listeriosis is a foodborne disease, hence

the reason for food safety regulations and educational programmes are crucial to reduce the incidence of human listeriosis. Additional research is necessary to identify predisposing risk factors, particularly among immunocompetent subjects. The usage of new tests, such as NGS, should be widely assessed as valuable methods for quick confirmation of LM. Furthermore, investigations into trials for more effective antibiotics are needed.

Listeriosis is still difficult to diagnose properly and quickly. However, because it can have fulminant and fatal results, the patient with signs of neuroinfection localized in the brainstem should be suspected of Listeriosis, especially in agricultural regions. The proper, available antibiotic therapy should be introduced empirically before and even with a lack of LM confirmation to minimize fatal outcomes. Education should be continued among doctors of many specializations to increase knowledge about listeriosis.

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Table 1. Differential diagnosis of neurolisteriosis with brainstem involvement.

Entity	Progression	General clinical presentation	Localization	MRI	CSF	Culturing	Other laboratory tests
Listeriosis with brainstem involvement	Insidious beginning with gastrointestinal disturbances and subacute progression	Meningeal signs, involvement of cranial nerves mostly of the lower group with dysarthria and dysphagia, diminished consciousness and central respiratory insufficiency	Lower medulla and pons	T2-weighted hyperdense area with no gadolinium enhancement	Pleocytosis with lymphocytes prevalence, elevated protein level, normal or decreased glucose level	Positive CSF or/blood with presence of LM lack of LM does not exclude listeriosis	Culturing of blood
Tuberculous meningitis	Subacute or chronic sometimes with history of tuberculosis	Fever, headache, decrease of consciousness involvement of cranial nerves and meninges	Different brain regions can be involved including basal meninges	T1- and T2- weighted with enhancement of basal meninges after gadolinium	Lymphocytic pleocytosis elevated protein level, decrease glucose level	Positive CSF for MT but negative MT does not exclude tuberculosis	Positive polymerase chain reaction for MT
Herpesvirus encephalitis	Subacute with prodromal symptoms of respiratory of general infection	Altered mental status, seizure, paresis, fever	Asymmetric mesiotemporal or orbitotemporal regions	T1- may show general edema in the affected region as low signal. T2-weighted hyperintensity if affected white matter and cortex.	Lymphocytic pleocytosis, elevated protein, normal glucose level	Positive PCR for HSV-1 and HSV-2	Abnormal findings in EEG
Bickerstaff inflammation	Insidious beginning preceded by infection often with <i>Campylobacter jejuni</i> Subacute progression	Impaired consciousness, bilateral ataxia, ophthalmople-gia pyramidal signs	Midbrain	T2-weighted hyperdense area with enhancement after gadolinium	Normal	Negative	Anti-ganglioside antibodies anti-GQ 1b IgG presented in 70%
Multiple Sclerosis	Sudden beginning of relapse sometimes preceded by infectious signs	Signs of injury of different, disseminated area of brain	Disseminated-periventricular and subtentorial changes	T2-weighted and Flair hyperdense area with enhancement after gadolinium of acute changes	Elevated protein level, normal pleocytosis, and glucose level	Negative	Oligoclonal bands present
CLIPPERS	Subacute	Ataxia, dysarthria, diplopia, facial sensory disturbances	Pons, cerebellum, spinal cord,	T2-patchy area with enhancement confined to the pons with enhancement after gadolinium	Sometimes mild pleocytosis or protein elevation	Negative	Occasionally oligoclonal bands present
Miller Fisher syndrome	Insidious beginning preceded by infection often with <i>Campylobacter jejuni</i> , subacute progression	Bilateral ataxia, ophthalmoplegia, areflexia,	N/A	Normal/multiple cranial nerves enhancement.	Elevated protein level with normal pleocytosis	Negative	Antiganglioside antibodies anti-GQ1b IGG
Stroke in posterior circulation	Acute beginning	Progressive decrease of consciousness with involvement of cranial nerves, ataxia, tetraparesis and sensory disturbances	Brainstem, and/or cerebellum and/ or thalamus uni- or bilateral	Positive diffusion weighted imaging DWI in acute state	Normal	Negative	Risk factors of vascular diseases

MRI – Magnetic Resonance Imaging; **CSF** – cerebrospinal fluid; **HSV** – Herpes Virus; **LM** – Listeria monocytogenes; **MT** – Mycobacterium Tuberculosis; **CLIPPERS** – chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids