Case Report/Relato de Caso

Listeria monocytogenes meningitis in an immunocompetent adult: a case report

Listeria monocytogenes meningite em um adulto imunocompetente: relato de caso

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ABSTRACT

Listeria monocytogenes (*L. monocytogenes*) is an uncommon cause of bacterial meningitis in immunocompetent adults. Patients with immunosuppression are at increased risk of developing serious invasive diseases, particularly meningitis. We describe a case of meningitis caused by *L. monocytogenes* in an immunocompetent and previously healthy 34-year-old adult. The patient received treatment with intravenous ampicillin plus amikacin and made a full recovery. *L. monocytogenes* should be suspected in immunocompetent adults with bacterial meningitis who fail to respond to empirical antibiotic treatment.

Keywords: *Listeria monocytogenes*. Meningitis. Immunocompetent adults.

RESUMO

Listeria monocytogenes (*L. monocytogenes*) é uma causa rara de meningite bacteriana em adultos imunocompetentes. Pacientes com imunossupressão têm maior risco de desenvolver graves doenças invasivas, especialmente a meningite. Descrevemos um caso de meningite por *L. monocytogenes* em um adulto imunocompetente e previamente sadio com idade de 34 anos. O paciente recebeu tratamento com ampicilina intravenosa mais amicacina e fez uma recuperação completa. *L. monocytogenes* deve ser suspeitada em imunocompetentes adultos com meningite bacteriana que não respondem ao tratamento antibiótico empírico.

Palavras-chaves: *Listeria monocytogenes*. Meningite. Adultos imunocompetentes.

INTRODUCTION

Listeria monocytogenes (*L. monocytogenes*) is a Gram-positive, facultative anaerobic, non-sporulating, and intracellular bacillus that has a characteristic tumbling motility at 20°C to 25°C. It is a well-recognized opportunistic pathogen that predominantly affects certain well-defined high-risk groups, including neonates, pregnant women, the elderly, and the immunocompromised[1]. The meningitis caused by *L. monocytogenes* differs from other types of bacterial meningitis, especially in treatment and prognosis. *L. monocytogenes* meningitis has been mostly reported at the extremes of life. It does occur in immunocompetent adults, although this is extremely rare.

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CASE REPORT

A previously healthy 34-year-old male engineer was admitted to our hospital, having had altered consciousness for one day. He had suffered fever (up to 39.2°C), headache, nausea, and vomiting for three days prior to admission. He had no history of recent travel and sick contacts. His past medical history was non-significant.

On physical examination, he appeared acute ill-looking and had altered consciousness (Glasgow Coma Scale score 11/15). His vital signs included body temperature of 39°C, blood pressure of 124/82mmHg, respiratory rate of 17 breaths/min, and pulse rate of 109 beats/min. There was marked neck stiffness with positive Brudzinski's sign. The remainder of the systemic examination was unremarkable.

Results of the initial laboratory studies were as follows results: leucocytes 15.0×10^9/L (90% neutrophils, 10% lymphocytes), erythrocyte sedimentation rate 89mm/h, and C-reactive protein 166mg/L; the rest of his serum biochemistry values were normal. A brain computed tomography scan demonstrated no parenchymal abnormality. For further assessment, a lumbar puncture was performed. Analysis of his cerebrospinal fluid (CSF) showed leucocytosis, high protein concentration, and low glucose level with a decreased CSF/serum glucose ratio **(Table 1)**. No organisms were seen on Gram, India ink, and acid-fast stains.

TABLE 1 - CSF findings of the patient with *Listeria monocytogenes* meningitis during hospitalization.

	On admission	The 13th hospital day	Normal range
Opening pressure (cm H_2O)	22.5	13.0	7.0-18.0
Leucocytes (10^6/L)	627	242	< 10
Neutrophils (%)	66.0	51.0	-
Lymphocytes (%)	34.0	49.0	-
Protein (g/L)	2.53	0.96	< 0.45
Glucose (mmol/L)	1.76	3.34	2.20-3.80
CSF/serum glucose ratio	0.38	0.76	> 0.50

CSF: cerebrospinal fluid.

Because an initial diagnosis of bacterial meningitis was made, the patient was treated empirically with intravenous vancomycin (1g every 12h) and ceftriaxone (2g every 12h) after cultures of blood and CSF were obtained. However, the high fever persisted and his clinical condition deteriorated. On the 4th hospital day, the culture of CSF grew short Gram-positive rods later identified as serotype 4b of *L. monocytogenes* which was susceptible to ampicillin, amikacin, erythromycin, trimethoprim-sulfamethoxazole

(TMP-SMZ), rifampin, levofloxacin, and vancomycin, and resistant to penicillin, fosfomycin, and ceftriaxone. Purified protein derivative tuberculin skin test was negative. Polymerase chain reaction of CSF for *Mycobacterium tuberculosis* was negative, as was latex agglutination test for *Cryptococcus neoformans*. A final diagnosis of *L. monocytogenes* meningitis was made.

Consequently, the treatment was changed to ampicillin (4g every 8h) combined with amikacin (0.4g daily) intravenously. The cultures of blood yielded no organisms. The patient responded well to the above-mentioned therapy. On the 11th hospital day, he was fully conscious and well oriented, the headache was alleviated, and the fever subsided. A second lumbar puncture was performed on the 13th hospital day and the CSF findings improved significantly **(Table 1)**. Comprehensive immunological investigations, including autoantibody tests, serum immunoglobulin and complement levels, human immunodeficiency virus test, and cell-mediated immunity tests (CD_3, CD_4, CD_8, CD_4/CD_8, and CD_{19}), were normal. Repeat cultures of CSF were sterile. Amikacin was discontinued after 2-week treatment was completed and ampicillin was discontinued after 3-week treatment was completed. The patient was then discharged home with normal CSF findings. On follow-up, he remained in good clinical condition.

DISCUSSION

L. monocytogenes is ubiquitous in the environment worldwide. The main route of transmission is believed to be through consumption of contaminated food. Ready-to-eat (RTE) foods and unpasteurized dairy products are especially associated with listerial infection. Unlike most other food-borne pathogens that primarily cause febrile gastroenteritis, *L. monocytogenes* can cause more serious invasive diseases, including sepsis, central nervous system (CNS) infection, and endocarditis. Serotypes 1/2a, 1/2b, and 4b are responsible for most human cases[2]. Listerial infection rarely occurs in healthy adults. Immunocompromised individuals, such as those with cancer or leukemia, those with liver cirrhosis or chronic renal failure, those with organ transplants, those with acquired immunodeficiency syndrome, and those receiving immunosuppressive therapy or corticosteroid drugs, are at increased risk. Receiving treatment to reduce stomach acid secretion may also facilitate listerial infection[3]. To the best of our knowledge, the patient was a previously healthy and immunocompetent adult without any underlying diseases or risk factors. He had no history of ingestion of dubiously preserved RTE foods or dairy products during the days immediately before admission. It was difficult to pinpoint the source of his infection.

Because of changes in diet and food processing, long life expectancy, and the large number and long survival of immunocompromised people, *L. monocytogenes* has become an important cause of community-acquired acute meningitis in developed countries. The incidence of *L. monocytogenes* meningitis among all episodes of community-acquired acute meningitis among adults in North America and Europe was reported at 5% to 10% or more[4]. It is characterized by a high case fatality rate of 24% to 62% even with appropriate antibiotic therapy[5].

The clinical manifestations of *L. monocytogenes* meningitis are not different from those of community-acquired bacterial meningitis caused by the more common etiologic agents[6]. However, some clinical differences exist. Patients with *L. monocytogenes* meningitis have a significantly lower incidence of meningeal signs compared with patients with acute meningitis due to other bacterial pathogens[4]. *L. monocytogenes* may cause other forms of CNS infection, including meningoencephalitis, cerebritis, rhombencephalitis, and intracranial abscess.

It is important to emphasize the difficulty in diagnosing *L. monocytogenes* meningitis. CSF findings of *L. monocytogenes* meningitis are similar to those of other bacterial meningitis. Microscopy and culture of CSF can distinguish the different causes of bacterial meningitis. However, Gram stain usually has a low yield[7] and the diagnosis is approved only after *L. monocytogenes* is isolated from culture of CSF. The total time for identification is about 5 to 7 days because of its slow growth. In addition, the sensitivity of microscopy and culture for bacteria in China is limited because of widespread preadmission use of antibiotics either administered in primary hospitals or self-prescribed over the counter. Therefore, the initiation of suitable antibiotic therapy for the patient with *L. monocytogenes* meningitis was delayed.

Vancomycin combined with a third-generation cephalosporin is advocated as an empirical antibiotic treatment of community-acquired bacterial meningitis in adult patients under 50 years of age[8]. However, *L. monocytogenes* is inherently resistant to third-generation cephalosporins and vancomycin has limited antimicrobial activity. An animal study has strongly suggested that intravenous vancomycin is likely to be ineffective in patients with CNS infection due to *L. monocytogenes*[9]. Although the optimal antibiotic treatment of *L. monocytogenes* meningitis is still uncertain, ampicillin and a synergistic aminoglycoside in combination are generally considered the drugs of choice. In patients with β-lactams allergy, TMP-SMZ may be the best alternative. Rifampicin and meropenem are reported to have some antimicrobial effects on *L. monocytogenes*[10]. Antibiotic treatment of *L. monocytogenes* meningitis for at least 3 weeks is recommended[8]. In case of intracranial abscess, the duration should be even longer.

Because of the high case mortality rate, it is important that *L. monocytogenes* should be considered among the possible causes of community-acquired bacterial meningitis in any patient, even an immunocompetent adult, who fails to respond to empirical antibiotic therapy.

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