Listeria monocytogenes meningoencephalitis in an immunocompetent adult patient

João D Melo, Sara Ventura, Paula Coutinho, Adriano Rodrigues

Centro Hospitalar e Universitário de Coimbra

Abstract

Listeria monocytogenes infections may lead to a severe and potentially lethal disease. This occurs mainly in risk groups (elderly, immunocompromised and newborns). Severe infections in people without any of these factors are rare. Here is reported the case of a 24-year old previously healthy female patient, who presented with altered mental status (Glasgow Coma Scale score of 11, with worsening to 6 within a few hours), fever and meningeal signs. The cerebrospinal fluid analysis was compatible with lymphocytic meningitis. Empirical therapy with Ceftriaxone and Acyclovir had been started. There was clinical worsening, with rhombencephalitis viewed in MRI. Ampicilin was associated and Listeria was actively searched, turning out positive. Despite all measures, the patient died in the Intensive Care Unit.

This report of a *Listeria monocytogenes* infection in a patient without risk factors reinforces the need of an early detection and effective treatment.

Keywords: *Listeria monocytogenes,* Meningoencephalitis, Rhombencephalitis.

Palabras clave: *Listeria monocytogenes,* Meningoencefalitis, Rombencefalitis.

Introduction

Listeria monocytogenes (L. monocytogenes) is a Gram-positive, facultative anaerobic intracelular bacillus. It has an ubiquitous distribution, being fully adapted to living either in soil or inside the cytosol of eukaryotic cells. This pathogen can cause severe foodborne infections, within a spectrum that goes from febrile gastroenteritis to life-threatening central nervous system (CNS) infections[1].

L. monocytogenes infections show a variable incidence between 0.39 and 0.73 cases per 100,000 inhabitants[2,3]. In Portugal, this incidence is lower, with 0.14 to 0.23 cases per 100,000 inhabitants[4]. These infections affect mainly some well defined risk groups, including neonates, pregnant women, the immunocompromised (including alcoholics) and the elderly. This makes such infections extremely rare in immunocompetent adults[5].

The abilities to survive gastric acid environment and cross intestinal, blood-brain and placental barriers contributes to *L. monocytogenes's* virulence[6]. Infections caused by this pathogen can take two forms: non-invasive gastrointestinal listeriosis or invasive listeriosis. Most listeriosis in immunocompetent patients are non-invasive, and these infections are mainly febrile uncomplicated gastroenteritis. On the other hand, the invasive form, more frequent in risk groups, develops as severe sepsis or, even more frequently, CNS infections. Rarely, this form can present as endocharditis, peritonitis, or even myopericarditis, arthritis or osteomyelitis[6, 7]. The CNS infection can be meningoencephalitis, rhombencephalitis, brain abscess or any combination of these manifestations. All these have in common the fact that they are severe life-threatening infections. Rhombencephalitis appears in about 10% of CNS listeriosis, and usually is a biphasic disease. It is characterized by an inicial prodromic period of 4-5 days of headache, náusea, vomiting and fever, followed by cerebellar and brainstem damage[8].

Despite being a life-threatening infection, its well known epidemiological profile makes it less likely for doctor to include *L. monocytogenes* empiric antibiotic therapy in patients without risk factors[9]. Thus, it takes a high degree of suspicion to make timely diagnosis and start effective therapy.

Case presentation

A 24-year-old Portuguese woman, previously healthy, with no history of recent travels or sick contacts, was admitted in the emergency room, having had altered mental status for a few hours. She had suffered vomiting and headache the day before. Five days prior to admission, she went to her doctor, complaining with fever and sore throat. Being diagnosed as acute tonsillitis, she was treated with penicillin.

On physical examination, she was sub-febrile with an axilar temperature of 37.8ºC, blood pressure of 107/63 mmHg, heart rate of 89 beats/min and respiratory rate of 24 breaths/min. There were no rashes or other mucocutaneous signs. She had altered consciousness (Glasgow Coma Scale score 11/15, E4V2M5), with right hemifacial fasciculations and neck stiffness. The remainder of the systemic examination was unremarkable. The initial laboratory studies were as follows: haemoglobin 12.9g/dL leukocytes 13300 cell/mm^3 (83.6% neutrophils, 9.8% lymphocytes, 6.36% monocytes, 0.13% eosinophils and 0.07% basophils), platelets 399000 cell/mm^3, glucose 6.6mmol/L, and C-reactive protein 41mg/L; the rest of her biochemistry values were within normal range. The brain computed tomography (CT) scan showed no parenchymal abnormalities (Figure 1-A). A lumbar puncture was performed, and the results of cerebrospinal fluid (CSF) analysis were the following: glucose 3.7mmol/L, protein 1.4 g/L, leukocytes 60 cell/mm^3 with 95% lymphocytes.

At first, the empirical treatment was intravenous ceftriaxone, 2g bid. There was a fast worsening of the patient's mental status, with a Glasgow Coma Scale score 6/15 (E1V2M3) three hours after admission. In this context, a magnetic resonance imaging (MRI) was performed (Figure 2-A), and there were some hypersignal ar-

Correspondencia: joaodgmelo@gmail.com

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Figure 1. Brain CT evolution.
A / Brain CT at admission,with no relevant findings.

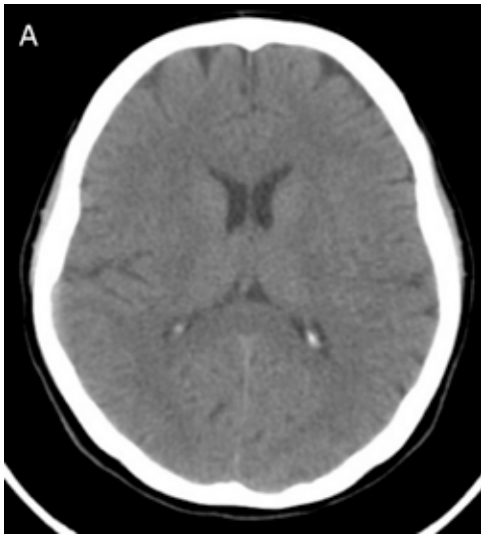


Figure 1. Brain CT evolution.
B / Brain CT at 4th day, with widespread parenchymal edema.

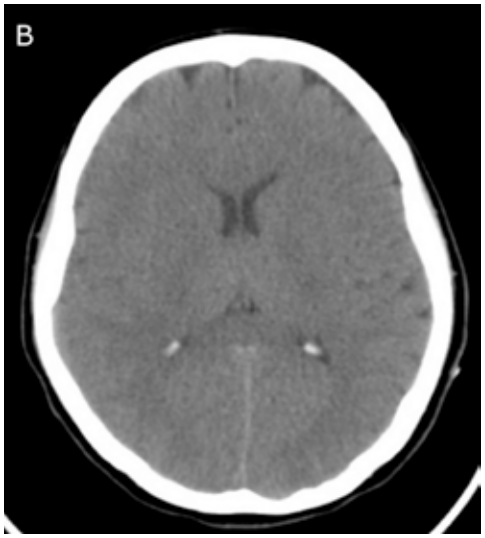


Figure 2.
Brain MRI evolution (*left* – T2; *right* – FLAIR).
A / Brain MRI at admission, with few hypersignal areas, probably related with viral encephalitis.

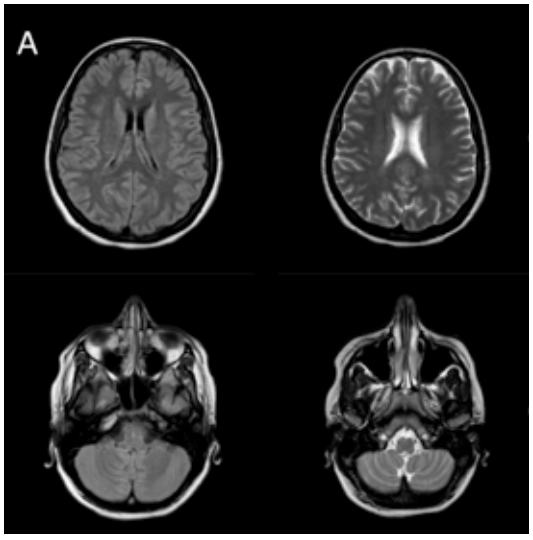
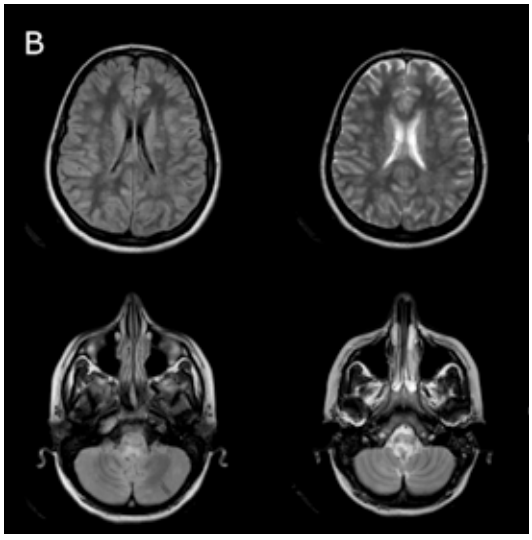


Figure 2.
Brain MRI evolution (*left* – T2; *right* – FLAIR).
B / Brain MRI at 4th day, with widespread encephalitis and rhombencephalitis.



eas that could not exclude the inicial phase of a viral encephalitis. Thus, intravenous acyclovir, 10m/kg q8h, was associated in order to achieve antiviral coverage. She was then admitted to the intensive care unit (ICU).

Indirect immunofluorescence serological tests for Rickettsia were negative, and so were complement-fixing serological tests for *Chlamydia* and *Coxiella.* Polymerase chain reaction for Herpes simplex virus and Varicella-Zoster virus were also negative. Syphilis testing (rapid plasma reagin) was negative. Adenovirus, Echovirus and Coxsakie virus were also negative, and the same result was observed for autoantibodies.

It is also noteworthy that serology for Human Immunodeficiency Virus (HIV) was also negative. Quantiferon and tuberculin test were also negative. The patient was not pregnant and there was no evidence of any contamined food or water source.

The patient's clinical condition kept deteriorating, with a sustained Glasgow Coma Scale 3/11 even after stopping sedation. On the fourth day of hospitalization, the complementary studies were repeated, with a lumbar puncture which was similar to the first one. The CT (Figure 1-B) and the MRI (Figure 2-B) were also repeated, and by now both of the exams demonstrated generalized encephalitis with rhombencephalitis. At this moment, the culture of CSF was negative. Nevertheless, intravenous ampicilin, 2g q4h, was associated with the previous antimicrobial therapy, as rhombencephalitis was a typical sign of *L. monocytogenes* infection. Four days later, serological complement-fixing test for *L. mono-*

cytogenes were positive, confirming the diagnosis of *L. monocytogenes* meningoencephalitis. Despite all treatments, the patient died on the fifteenth day of hospitalization.

Discussion

In the reported case, the patient was a young adult without known risk factors for *L. monocytogenes* infection. Also, the prior history of acute tonsillitis and active herpes reduced the clinical suspicion of *L. monocytogenes* infection, which delayed the diagnosis and the institution of effective treatment. The differential diagnosis of this case includes all infectious causes of lymphocytic meningitis, such as *L. monocytogenes, Rickettsia, Chlamydia, Coxiella, Syphilis, Tuberculosis* and virus. Other bacteria, such as *Streptococcus pneumoniae,* can also be a rare cause of lymphocytic meningitis. Also, non-infectious causes of lymphocytic meningitis should be excluded, such as neoplastic disease or, more frequent in this age, autoimmune diseases.

This case demonstrates the need of an early diagnosis in order to start effective treatment in time to improve the patient's outcome. Since these infections have a very high mortality rate, *L. monocytogenes* must always be considered, even if the patient is an immunocompetent adult, especially in severe cases at presentation or when there is failure of empirical antibiotic therapy.

Even though it is rare in healthy adult patients, the absence of risk factors can not exclude the diagnosis of invasive Listeriosis. Since it is a severe and potentially lethal infection, empirical coverage for *L. monocytogenes* should be considered in patients with severe CNS infections. The failure to respond to empirical antibiotic therapy, with clinical worsening, should prompt active search for other severe causes of CNS infections, such as *L. monocytogenes.*

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