Case report

Acute Lyme neuroborreliosis with transient aphasia – Case report and review of current knowledge

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**A B S T R A C T**

Lyme borreliosis (LB) is a tick-borne infectious disease, endemic in the Northern hemisphere, with a polymorphic clinical spectrum (cutaneous, articular, and neurologic involvement). The variability of clinical manifestations poses LB as a diagnostic challenge. We describe a case of acute Lyme neuroborreliosis (LNB) in an adult female with a history of recent travel in Europe. There are few reports of acute LNB presenting as encephalitis in the literature. Suspicion for the diagnosis and prompt treatment seems to have a positive impact on patient outcomes.

**Introduction**

Lyme disease, the most common human arthropod-borne infectious disease in the Northern hemisphere, is caused by the spirochete \textit{Borrelia burgdorferi} (Bb) sensu lato complex \cite{1,2}. In Europe, the highest incidences of Lyme disease are found in Scandinavian countries and central Europe (Austria, Slovenia, and Germany) \cite{2,3}. Lyme disease is spread by ticks infected with \textit{Borrelia}, but different species of bacteria are found in endemic areas. In North America, the only known species responsible for human disease is \textit{B. burgdorferi} sensu stricto, while in Europe at least five \textit{Borrelia} species (\textit{B. burgdorferi} sensu stricto, \textit{B. garinii}, \textit{B. bavariensis}, \textit{B. lusitaniae}, \textit{B. afzelii}, and \textit{B. spielmani}) can cause the disease \cite{2,3}.

Lyme disease is a multistage and multisystem disorder predominantly affecting the skin, but also involving the joints, heart, and peripheral and central nervous system (CNS) \cite{1,2}. Neurological manifestations are reported in 10–15% of patients with Lyme disease in both Europe and the USA \cite{4}. Early Lyme neuroborreliosis (LNB) generally develops within 2–18 weeks after infection and can be the presenting (or even the only) sign of Lyme disease. The most common manifestations of early LNB are painful meningoaradiculitis and lymphocytic meningitis \cite{5}. Other forms of CNS involvement, such as encephalitis and myelitis, are rare (below 5%) in patients with early LNB.

The diagnosis of LNB includes CSF study and serologic tests. Direct detection methods for \textit{B. burgdorferi} are of limited use for the diagnosis of LNB \cite{2}. The Centers for Disease Control and Prevention (CDC) recommend a two-test approach: screening test with enzyme-linked immunosorbent assay (ELISA), followed by a Western-blot \cite{4}.

**Case report**

A 44-year-old woman presented to the emergency department with transient aphasia, fluctuating level of consciousness, and fever in the last three days. She had also complained of headache with photophobia the week before. The patient was febrile at admission, alternating periods of aggressive behavior with prostration. Neurological examination revealed orofacial involuntary movements and global aphasia, but no motor deficits or pyramidal signs. Her past medical history was unremarkable, except for dyslipidemia, medicated. She lived in an urban area and had traveled to a village in Paris’ surroundings two months before, where she performed trails in forest areas with some insect bites. She also recalls another insect bite in the woods last year, in the central region of Portugal. She did not remember identifying a tick. The patient’s history was negative for erythema migrans.

Routine laboratory analysis showed lymphocytosis, elevated liver enzymes, and C-reactive protein (CRP). Blood and urine cultures were negative. Serological tests were positive for acute Bb infection.
Further studies excluded active infection with Epstein-Barr virus (EBV), Herpes simplex 1 and 2 viruses (HSV), cytomegalovirus (CMV), human immunodeficiency virus (HIV), Hepatitis E virus (HEV), Treponema pallidum, Toxoplasma gondii, Coxielia burnetii, Bartonella henselae, Rickettsia conorii. Autoimmune workup was negative for ANAs, ANCAs, anti-ds-DNA, anti-SS-A, anti-SS-B, RNP, Sm, Ro/RO52, JO1, C3, C4. Immunoglobulin levels were normal.

Cerebrospinal fluid (CSF) analysis showed a lymphocytic pleocytosis and elevated protein levels with no agent identification by culture or molecular method (Table 1). Magnetic resonance imaging (MRI) of the brain showed no acute vascular lesions or contrast enhancement of the meninges. Electroencephalography (EEG) showed an interhemispheric asymmetry with slow-wave activity in the left frontotemporal area, with no epileptiform activity. An acute lymphocytic meningoencephalitis was diagnosed and the patient was admitted to the Infectious Diseases department, under treatment with intravenous (IV) ceftriaxone 2 g bid, dexamethasone 10 mg QID, and acyclovir 750 mg tid.

CSF analysis was repeated forty-eight hours later, showing a decrease in lymphocyte cell count and a slightly elevated protein level (Table 1). Serological tests were performed in CSF second sample and revealed positive Bb-specific IgM antibodies. Polymerase chain reaction (PCR) for Bb in CSF was negative (Table 2). Oligoclonal bands were detected in the CSF. The diagnosis of acute neuroborreliosis was confirmed by a positive IgM Western-Blot (WB) in CSF, performed in the National Reference Laboratory, Instituto Nacional de Saúde Doutor Ricardo Jorge (Table 3).

Antibiotic treatment with iv ceftriaxone was carried out for 21 days. Neurological recovery of the patient was excellent since the first days of hospitalization. The patient maintains follow-up consultations in our outpatient clinic, with no symptoms of post-treatment Lyme disease syndrome.  

**Discussion**

Acute Lyme neuroborreliosis presenting as encephalitis is an unusual form of the disease. Very few cases have been reported in the literature [7]. The neurological symptoms at admission raised suspicion of a CNS infection. An extensive investigation was performed, including lumbar puncture, brain MRI, EEG, and serology for other arthropod-borne infections. Considering the epidemiology of our patient, we suspected *Borrelia burgdorferi* as a microorganism likely to be responsible for this episode, despite the absence of tick-bite lesions or erythema migrans. The time of infection was not clear at the beginning since there were two suspected possibilities for inoculation: (1) insect bite in summer about a year ago, in Portugal’s central region, (2) insect bite in the countryside, in France, about ten weeks before the symptoms. However, the absence of suspicious symptomatic episodes before the one here reported leads us to consider the epidemiological link with the patient’s stay in France.

The diagnosis of LNB should be based on a combination of patient history, clinical findings, CSF analysis, and serologic studies of serum and CSF. The presence of erythema migrans is not obligatory; cutaneous involvement is recalled in up to 50% of the cases [2]. The incubation period (eight weeks) is in the time interval usually considered in acute LNB [8,9]. The suspicion of LNB was supported by positive serology for *B. burgdorferi* sensu lato. An elevated IgM was detected in both serum and CSF, indicating an acute installation of the disease. These results were confirmed by a positive Western Blot in CSF, demonstrating an evolving humoral response in the CNS. A negative PCR does not exclude the presence of *B. burgdorferi* [2,10]; consequently, the use of a PCR assay to confirm LNB infection is not recommended [8]. Recently, a new diagnostic approach has been proposed by the Food and Drug Administration (FDA), named as the two-tier modified testing. This approach considers the use of a second sensitive enzyme immunoassay (EIA) in place of western immunoblot assay as an alternative for the serologic diagnosis of Lyme disease [11].

Treatment of LNB with antibiotics is recommended, to avert persistent neurological deficits [2,12]. Recommendations suggest the use of penicillin, ceftriaxone, cefotaxime, or doxycycline in LNB [9]. Recent studies showed non-inferiority of oral doxycycline compared to IV ceftriaxone [13,14]. Nevertheless, these studies include a reduced number of cases of LNB with CNS symptoms compared to LNB cases with peripheral nervous system (PNS) symptoms; the evidence is scarce in this topic, requiring further studies to better understand the effect of oral doxycycline-based regimens in LNB with CNS involvement. Recommended treatment duration is 14 days in acute

### Table 1

**CSF findings, at admission and 48 hours later.**

| Baseline examination | Post 48-hours |
|----------------------|---------------|
| Cells, mm³ | 75 (mononuclear) | 7 (mononuclear) |
| Proteins, mg/dL | 138 | 75 |
| Glucose, mg/dL | 52 | 76 |
| Lactate, U/L | 29 | – |
| Multiplex PCR testing for meningitis/encephalitis* | Negative | Negative |
| HSV-1 and HSV-2 DNA detection (by PCR) | Negative | Negative |
| RNA B. burgdorferi | – | Detected |
| Oligoclonal bands | – | – |

**Baseline examination Post 48-hours Reference values**

| Serum | Negative if < 10 UA/mL | Positive if > 15 UA/mL |
|-------|------------------------|-----------------------|
| IgG   | 50                     |                        |
| IgM   | 20.05                  | Positive if > 18 UA/mL |
| CSF   | –                      | –                     |

**Table 2**

**Serology results in serum and CSF.**

| Serum | Negative if < 2.5 UA/mL | Positive if > 3.5 UA/mL |
|-------|------------------------|------------------------|
| IgG   | 0.62                   |                        |
| IgM   | 4.59                   |                        |

**CSF: cerebrospinal fluid; Ig: immunoglobulin**

### Table 3

**Confirmatory tests for *Borrelia burgdorferi* in CSF.**

| Western Blot in CSF | B. burgdorferi |
|---------------------|----------------|
| Negative            | Positive       |

**CSF: cerebrospinal fluid; Ig: immunoglobulin**
LNB and 21 days in late LNB [9,15]. In our case, we were not certain of the inoculation moment and disease evolution until WB confirmation of an acute process, therefore a 3-week treatment was performed. There is no sufficient data on the usage of steroids in LNB [9]; however, we considered that the anti-inflammatory effect of dexamethasone over cerebral parenchyma has contributed to an earlier neurological improvement in our patient.

Antibody titters generally decline after antibiotic therapy. Nonetheless, both IgM and/or IgG can remain positive for months or years after treatment [12,16]. Borrelia-specific antibodies do not help monitor treatment response and disease evolution [2].

This case illustrates the importance of a careful history, considering the type of exposure (rural areas, forests), together with the inflammatory CSF findings as suspicions to the diagnosis. With the actual massive traveling phenomena, though Portugal is not considered an endemic country, we should ponder Lyme neuroborreliosis in a patient with recent travel history to endemic countries and suspicion of CNS infection.

Consent for publication

The patient gave written consent for the publication of this case report.

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CRediT authorship contribution statement

F.C. – Conception, and design of the study; acquisition of data; analysis and/or interpretation of data; drafting the manuscript; approval of the version of the manuscript to be published. J.A.D. – Conception, and design of the study; drafting the manuscript; approval of the version of the manuscript to be published. R.G. – revising the manuscript critically for important intellectual content; approval of the version of the manuscript to be published.

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Conflict of interest statement

The authors have no conflict of interest to declare.

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