A Peculiar Case of Neuroborreliosis
Um Caso Peculiar de Neuroborreliose

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Resumo:

A doença de Lyme é uma zoonose endémica em algumas regiões do hemisfério norte, como o continente europeu. Trata-se de uma doença multissistémica com manifestações cutâneas, articulares, cardíacas e neurológicas, variáveis, de acordo com o estadio da doença. O envolvimento do sistema nervoso designa-se por neuroborreliose de Lyme. É dividida em precoce e tardia. A neuroborreliose precoce apresenta uma tríade clássica com meningite linfocítica, neuropatia craniana e radiculonevrite. Apresentamos um caso de neuroborreliose precoce num homem com perturbação do uso do álcool a quem foi diagnosticada uma encefalopatia metabólica. Discutimos a importância do diagnóstico diferencial amplo, os critérios de diagnóstico e a gestão de uma doença extremamente heterogénea como é a doença de Lyme, particularmente no seu espectro neurológico.

Palavras-chave: Neuroborreliose de Lyme/complicação; Neuroborreliose de Lyme/diagnóstico.

Abstract:

Lyme disease is an endemic zoonosis in temperate regions of the northern hemisphere, such as the European continent. It is a multisystemic disease with cutaneous, articular, cardiac, and neurological manifestations that vary according to its stage. The nervous system's involvement is called neuroborreliosis and can be classified as an early or late disease, according to its progression.

A classic triad of lymphocytic meningitis, cranial neuropathy, and painful radiculoneuritis characterizes early neuroborreliosis. We present a case of neuroborreliosis in a man with chronic alcohol use disorder who was diagnosed with metabolic encephalopathy. We discuss the importance of broadening the differential diagnosis and the diagnostic criteria and managing an extremely heterogeneous disease such as Lyme disease, particularly in its neurological involvement.

Keywords: Lyme Neuroborreliosis/complications; Lyme Neuroborreliosis/diagnosis.

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Learning Points

1. Lyme neuroborreliosis (NBL) is a rare disease and for its diagnosis a detailed history is essential.
2. The absence of an established definition for NBL also increases the diagnostic challenge.
3. NBL should be suspected in the presence of neurologic symptoms and pleocytosis in the cerebrospinal fluid (CSF).
4. Treatment of Lyme disease (LD) is based on antibiotherapy and depends on the disease's stage and extent. Its early introduction is crucial to prognosis.

Introduction

Lyme disease (LD) is a multisystemic inflammatory disease caused in most cases by the spirochete *Borrelia burgdorferi* transmitted through the bite of the arthropod Ixodes ricinus complex.

There are stages of infection in LD: localized acute infection corresponding to *erythema migrans*, early disseminated infection (stage II), and late disseminated infection. Involvement of the nervous system, called Lyme neuroborreliosis (NBL), begins during stage II and occurs in 10% to 40% of cases of disseminated LD. NBL is divided into early and late disease (depending on whether the signs and symptoms appear before or after six months, respectively).[1,2] However, it is most commonly an acute disease with manifestations that develop within a few weeks of infection. The classic triad of early NBL includes lymphocytic meningitis, cranial neuropathy, with the facial nerve being the most severely involved, and painful radiculoneuritis (Bannwarth syndrome).[3] The last one is the most common manifestation of the European NBL, after erythema migrans. The diagnosis of NBL is based on clinical suspicion and cerebrospinal fluid (CSF) characteristics and serology. Other probable etiologies (infectious, vascular, and metabolic) should always be excluded since NBL is uncommon and presents with unspecific symptoms. To confirm the diagnosis a two-step investigation is recommended: a screening test with enzyme immunoadsorption assay (enzyme-linked immunosorbent assay - ELISA) followed by a Western-blot confirmatory test.[4]

Case Report

We present the case of a 64-year-old man who worked in cattle ranching and as a forest cutter. He had a personal history of benign prostatic hyperplasia, type 2 diabetes

mellitus and chronic alcohol use disorder (alcohol consumption of 85 g/day).

The patient was first observed in the emergency department of another hospital, presenting with a three-day history of asthenia, myalgias, chills and cold sweats and he was discharged after clinical evaluation. He returned to the hospital less than 12 hours later, complaining of headache, diplopia, vertigo, and gait imbalance, resulting in multiple falls. On readmission, his physical examination was reported as normal, though gait evaluation was not performed. He was admitted for further evaluation and monitoring of alarming symptoms. He received amoxicillin/clavulanic acid, oxazepam, and intravenous thiamine (200 mg QD). His lab results were similar to the initial evaluation: leukocytes 3760/mm^3, normal C-reactive protein 1.07 mg/L, platelets 47 000/mm^3, sodium 133 mEq/L, and gamma-glutamyl transferase 109 U/L. A brain computed tomography (CT) scan showed no significant abnormalities.

On the second day of admission, gait imbalance, mental confusion, and disorientation were also noted, followed by the development of dysarthria and horizontal nystagmus. A brain CT scan was repeated and remained normal.

On the eleventh day of admission, the patient was transferred to our hospital, at a family's request.

At our first observation, he presented fluctuating attention, bilateral ophthalmoplegia, and ataxic gait. He also showed central left facial palsy, scanted dysarthria, finger--nose-left dysmetria, and a positive Romberg test with decreased cutaneous-plantar reflexes. There were no other changes at the neurological examination, namely meningeal signs, visual acuity alterations, or motor and sensory modifications of the limbs. The remainder of the physical examination was unremarkable, and the patient remained hemodynamically stable and apyretic.

Given the history of alcohol abuse and pronounced ophthalmoplegia and ataxia, the hypothesis of a Wernicke encephalopathy (EW) was considered at initial observation. Therefore, thiamine supplementation was enhanced and magnetic resonance imaging (MRI) was requested. The MRI showed extensive T2/FLAIR hypersignal in the posterior aspect of the inner capsule's, thalamus, corona radiata (Fig. 1), midbrain, and pons (Figs. 2 and 3).

These findings were incompatible with EW, suggesting an infectious/inflammatory etiology.

After a multidisciplinary discussion with Neurology and Infectiology, given the pattern of rhomboencephalitis and integrating the patient's history of chronic alcoholism, the primary etiological presumption fell upon listeriosis. A lumbar puncture (LP) was performed. The analysis of the CSF revealed lymphocytic pleocytosis (198 cells/µL) and slight proteinorrhaquia (62 mg/dL). Molecular research for *Listeria monocytogenes*, other bacteria (*Haemophilus influenzae, Neisseria meningitidis, Streptococcus agalactiae,*

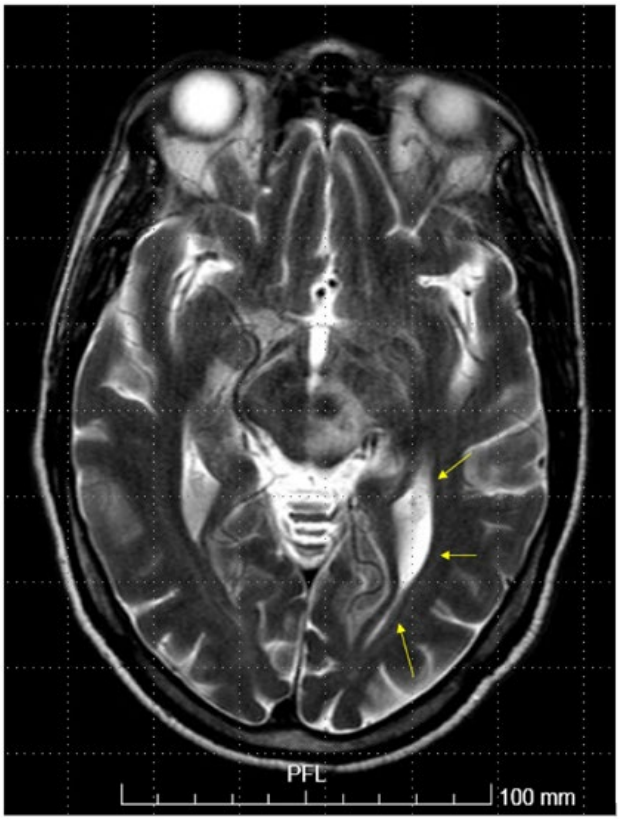

Figure 1: Extensive T2/FLAIR hypersignal in the posterior aspect of the inner capsule, thalamus, corona radiata at brain MRI.

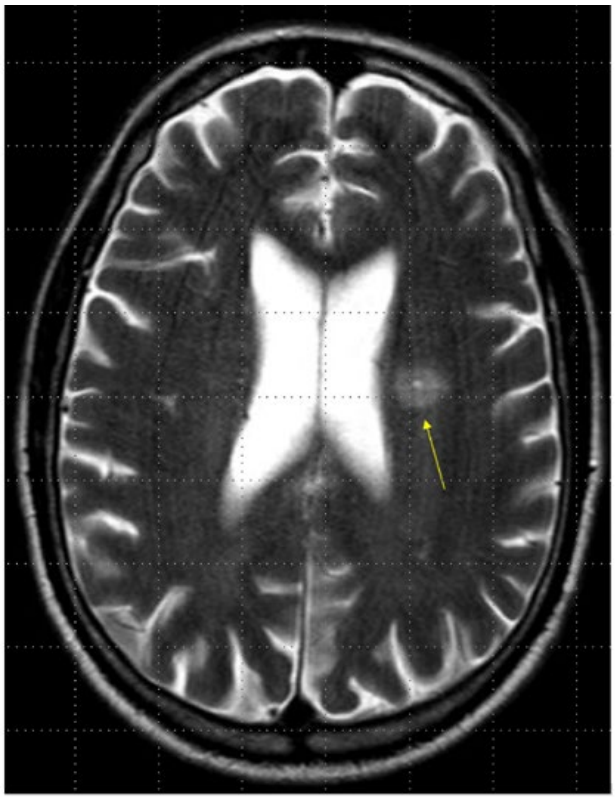

Figure 2: T2/FLAIR hypersignal at midbrain at brain MRI.

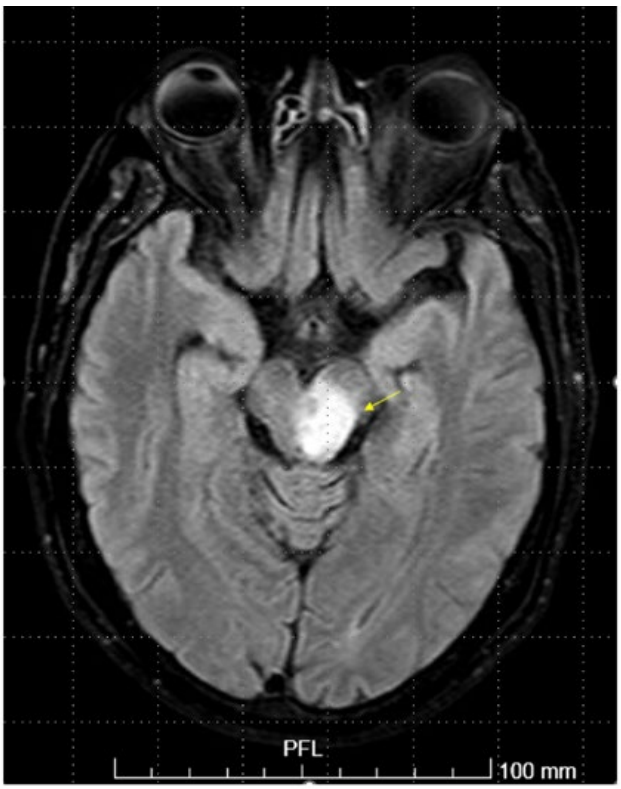

Figure 3: T2/FLAIR hypersignal at the pons at brain MRI.

Streptococcus pneumoniae), and viral (herpes simplex 1, 2 and 6, adenovirus, enterovirus, and parechovirus) agents was negative.

An ELISA and Western-Blot tests for Lyme disease were requested, which confirmed acute infection by *Borrelia* spp. In addition, a positive IgM title for *Borrelia burgdoferi*, at CSF and blood was obtained (respectively 8.70 AU/mL and 22.60 AU/mL). The patient was started on parenteral antibiotic therapy with ceftriaxone 2g qd/id for 14 days. The patient initiated a motor rehabilitation program and speech therapy, with complete resolution of diplopia, vertigo, and substantial gait improvement. Despite this, he maintained mild dysarthria, ataxia, and facial paralysis in the 3-month follow-up appointment after discharge.

Analysing the key points listed, we would like to highlight the fact that the wider differential diagnosis was kept open and that we remained on the diagnostic path for other diseases, with lumbar puncture and magnetic resonance imaging. We believe that the introduction of a meningeal dose of ceftriaxone had an impact on the patient's good evolution. The need for more uniform diagnostic criteria between the European and American schools, in addition to standardisation, could facilitate the recognition of this pathology; with regard to our patient, in addition to the diagnostic heterogeneity, we highlight the fact that the most common clinical manifestation on the European continent, radiculoneuritis, was absent, which represented an additional diagnostic difficulty.

Discussion

This case report emphasizes the heterogeneity of clinical presentations in LD, since there were no typical signs (such as radiculonevritis and lymphocytic meningitis), and there was a dominance of uncommon findings such as facial nerve involvement, ophthalmoplegia, and gait impairment. The involvement of the VII cranial nerve is unusual and is responsible for facial paralysis and dysarthria. When present, lymphocytic meningitis coexists in more than 60% of cases.[5]

The presence of ophthalmoplegia is presumed to be related to an increase in intracranial pressure, even if the initial CT scan is described as normal. Gait impairment, obvious through Roomberg's test alteration and ataxia, is associated with posterior chordal neuropathy". This clinical-symptomatologic atypia made the diagnosis of NBL unquestionably tricky and delayed. We believe that the patient´s area of residence and his profession constitute an increased risk factor for infection by *Borrelia* spp.

Treatment of LD is based on antibiotherapy and depends on the disease's stage and extent. Its early introduction is crucial to prognosis because it accelerates the resolution of symptoms and therefore allows full clinical recovery, avoiding progression to later stages of disease.[6-8]

The absence of an established definition for NBL also increases the diagnostic challenge. Some proposals have been made, like the one from the European Federation of Neurological Societies (EFNS),9 which establishes the NBL diagnosis as definite or possible, depending on the presence of the following three criteria:

i) Neurological symptoms suggestive of NBL without other obvious reasons;
ii) CSF pleocytosis;
iii) Intrathecal production of specific antibodies to *Borrelia* spp.[6]

Most patients present a full recovery within a few weeks to months after the onset of symptoms.[10-12]

In rare cases, as described, recovery may be incomplete with permanent neurological symptoms, which happens when NBL is recognized in later stages, and tissue damage is already established.

We describe an unusual presentation of a complex, heterogeneous, and underdiagnosed disease.

This case highlights the importance of a detailed clinical history and examination, as well as the need for a broader differential diagnosis when we have a patient with unspecific and persistent symptoms with an unclear diagnosis. Clinical suspicion and consensual NBL diagnostic criteria are crucial to an early and correct diagnosis and consequently better prognosis. ■

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SS, MC, IR, AFV, HM – Redação do manuscrito original

Todos os autores aprovaram a versão final a ser publicada.

Contributorship Statement

SS, MC, IR, AFV, HM - Writing the original manuscript
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REFERENCES

1. Omotosho YB, Sherchan R, Ying GW, Shayuk M. A Unique Case of Bannwarth Syndrome in Early Disseminated Lyme Disease. Cureus. 2021;13:e14680. doi: 10.7759/cureus.14680.
2. Oliveira R, Sotero F, Marques I. Neuropatia Ótica Anterior Como Manifestação Primária de Neuroborreliose. Sinapse. 2019; e107:90-1
3. Koedel U, Fingerle V, Pfister HW. Lyme neuroborreliosis-epidemiology, diagnosis and management. Nat Rev Neurol. 2015;11:446-56. doi: 10.1038/nrneurol.2015.121.
4. Rizzoli A, Hauffe H, Carpi G, Vourc H G, Neteler M, Rosa R. Lyme borreliosis in Europe. Euro Surveill. 2011;16:19906.
5. Logar M, Ruzic-Sabljic E, Maraspin V, Lotric-Furlan S, Cimperman J, Jurca T, et al. Comparison of erythema migrans caused by Borrelia afzelii and Borrelia garinii. Infection. 2004;32:15-9. doi: 10.1007/s15010-004-3042-z
6. Knudtzen FC, Andersen NS, Jensen TG, Skarphédinsson S. Characteristics and Clinical Outcome of Lyme Neuroborreliosis in a High Endemic Area, 1995-2014: A Retrospective Cohort Study in Denmark. Clin Infect Dis. 2017;65:1489-95. doi: 10.1093/cid/cix568.
7. Blanc F, Jaulhac B, Fleury M, de Seze J, de Martino SJ, Remy V, et al. Relevance of the antibody index to diagnose Lyme neuroborreliosis among seropositive patients. Neurology. 2007;69:953-8. doi: 10.1212/01.wnl.0000269672.17807.e0.
8. Pachner AR, Steiner I. Lyme neuroborreliosis: infection, immunity, and inflammation. Lancet Neurol. 2007;6:544-52. doi: 10.1016/S1474-4422(07)70128-X.
9. Mygland A, Ljøstad U, Fingerle V, Rupprecht T, Schmutzhard E, Steiner I, et al. EFNS guidelines on the diagnosis and management of European Lyme neuroborreliosis. Eur J Neurol. 2010;17:8-16:e1-4. doi: 10.1111/j.1468-1331.2009.02862.x.
10. Ljøstad U, Skarpaas T, Mygland A. Clinical usefulness of intrathecal antibody testing in acute Lyme neuroborreliosis. Eur J Neurol. 2007;14:873-6. doi: 10.1111/j.1468-1331.2007.01799.x.
11. Stanek G, Fingerle V, Hunfeld KP, Jaulhac B, Kaiser R, Krause A, et al. Lyme borreliosis: clinical case definitions for diagnosis and management in Europe. Clin Microbiol Infect. 2011;17:69-79. doi: 10.1111/j.1469-0691.2010.03175.x.
12. Lantos PM, Rumbaugh J, Bockenstedt LK, Falck-Ytter YT, Aguero-Rosenfeld ME, Auwaerter PG, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA), American Academy of Neurology (AAN), and American College of Rheumatology (ACR): 2020 Guidelines for the Prevention, Diagnosis and Treatment of Lyme Disease. Clin Infect Dis. 2021;72:1-8. doi: 10.1093/cid/ciab049.