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Neuro-ophthalmological manifestations associated with Lyme disease

Manifestações neuroftalmológicas associadas a doença de Lyme

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Abstract

Lyme disease is a systemic infection caused by the spirochete Borrelia burgdorferi and transmitted by the tick of the genus Ixodes sp. and species Amblyomma cajennense. The disease usually manifests itself in three distinct clinical stages, which may vary according to the characteristics of each host. The objective of this paper is to report the case of a 33-year-old patient with Lyme disease who presented as neuro-ophthalmological manifestations diplopia, paralytic lagophthalmos and punctate keratitis, with negative laboratory tests. Although the spirochete Borrelia burgdorferi has a greater tropism in the tissues of the skin, nervous system and joints, the ocular involvement should not be diminished, being described in this case report, which approached the most pertinent aspects to the disease to aid its diagnosis and treatment.

Keywords: *Lyme disease, Facial paralysis; Diplopia*

Resumo

A doença de Lyme é uma infecção sistêmica causada pela espiroqueta Borrelia burgdorferi e transmitida pelo carrapato do gênero Ixodes sp. e espécie Amblyomma cajennense. A doença costuma se manifestar em três estágios clínicos distintos, que podem variar de acordo com as características de cada hospedeiro. O objetivo deste trabalho é relatar o caso de uma paciente de 33 anos com doença de Lyme que apresentou como manifestações neuroftalmológicas diplopia, lagoftalmo paralítico e ceratite punctata, com exames laboratoriais negativos. Embora a espiroqueta Borrelia burgdorferi tenha maior tropismo pelos tecidos da pele, sistema nervoso e articulações, o acometimento ocular não deve ter sua importância diminuída, sendo descrito neste relato de caso, que abordou os aspectos mais pertinentes à doença para auxiliar seu diagnóstico e tratamento.

Descritores: Doença de Lyme; Paralisia facial; Diplopia

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Introduction

Lyme disease, also known as Lyme borreliosis and chronic erythema migrans (CEM), is a systemic infection caused by the spirochete Borrelia burgdorferi[1] transmitted by the tick of the Ixodes ricinus complex (in the Northern Hemisphere) and by the species Amblyomma cajennense (lone star tick) in Brazil.[2]

Although it is endemic in regions of North America, Europe and Asia, the disease is little reported in Brazil. In this country, the disease is called Lyme simile disease (Borreliosis Humana Brasileira or Baggio-Yoshinari Syndrome), because its clinical and laboratory conditions, as well as its etiology, are different from those found in the United States and Europe.[3]

The incubation period varies from 4 to 18 days10, and since the organism does not maintain natural immunity to the disease, the person may be reinfected from a new tick bite.[4] The disease usually manifests in three distinct clinical stages, and they may vary according to the tissues or organs affected, the patient immunity, and the duration of infection. [5]

After the arthropod bite, 60-80% of patients present an annular cutaneous lesion (chronic erythema migrans), which may be followed by constitutional symptoms (such as malaise, fatigue, fever, headache and myalgia), and it corresponds to stage 1 (early infection). Stage 2 (disseminated infection) starts after a few days to months, and may present neurological (e.g., cranial nerve paralysis), cardiac (eg arrhythmia), or ocular manifestations, among others. Stage 3 (late infection) usually includes chronic complications such as arthritis of large joints, polyneuropathy and encephalopathy, and may manifest years after the onset of the disease.[3]

Among the most frequent neurophthalmological manifestations, we can mention early transient conjunctivitis, episcleritis and scleritis, stromal keratitis, multifocal choroiditis, vasculitis and retinal detachment, neuroretinitis, optic neuritis, papilledema, orbital myositis, and cranial neuropathies. They may appear in any period of the disease, although they are more frequent in stages 2 and 3.[3] Diplopia and keratitis have also been documented, as in the case report described.

Case Report

A 33-year-old white female patient from Brazil and of Swedish origin. She sought medical care in this country referring to migratory erythema in the left scapular region, which in two weeks progressed to paraesthesia in the lips and tongue and peripheral facial paralysis on the right of grade IV (moderate to severe dysfunction). Cerebrospinal fluid (CSF) and serologic tests (including Elisa for antibodies to Borrelia burgdorferi) were carried out, both with negative results. The patient remained in the hospital for 12 hours, and was managed symptomatically with ocular lubricant gel and buffer in the right eye.

One month after the onset of symptoms, there was worsening of the facial paralysis on the right to grade V (severe dysfunction), and empiric treatment started with acyclovir 40 mg orally every 6 hours for 10 days, in addition to facial physiotherapy, with discrete clinical improvement.

In Brazil, three months later, she developed myalgia, lumbar and knee arthralgia, meningeal signs, intense irritability, binocular diplopia, amnesia, paralytic lagophthalmos on the right (Figure 1), and punctate keratitis in the lower third of the cornea. She was medicated with oral prednisolone 20 mg every 8 hours for 12 days, and liquid and gel ocular lubricants. A new Elisa test for antibodies to Borrelia burgdorferi was requested because of high diagnostic suspicion, and although it showed a negative result, empiric treatment with ceftriaxone 1g intravenous was started every 12 hours for 5 days due to the high suspicion of Lyme disease. After one week, there was improvement of the general clinical condition, and partial regression of facial paralysis was observed, with peripheral facial paralysis grade III (moderate dysfunction) remaining as sequel.

Discussion

Some of the earliest case reports of Lyme disease were made in Sweden in 1910 and in Austria in 1914.[6] It is a disease causing systemic inflammatory alteration caused by the activation of the immune system and hypersensitivity to Borrelia burgdoferi antigens, as well as virulence and aggression factors of the same[7] Transmission of the spirochetes occurs during the inoculation of the tick saliva, and its infection can evolve to spontaneous cure or disease, being classified in three stages:[8]

- Stage 1 (early/limited infection): characterized by migrating erythema annulare present in about 60-80% of patients infected a few days after the bite, with or without constitutional symptoms (such as fever, headache, and myalgia);
- Stage 2 (disseminated infection): weeks to months after stage 1, with predominantly neurological, cardiovascular and rheumatologic involvement, and less frequent, ocular nvolvement. Examples are paresthesias, cranial neuropathy, meningitis, behavioral alterations, Bell's paralysis, imprecise encephalitis, cerebellar ataxia, arrhythmias, angina, atrioventricular block, myocarditis and pancarditis, arthritis, myositis, osteomyelitis, conjunctivitis, episcleritis and scleritis, iridia, keratitis, choroiditis, vasculitis, retinal detachment, pannophthalmus, neuroretinitis, optic neuritis, diplopia and papilledema;
- Stage 3 (late/persistent infection): months to years after stage 2, characterized by chronic arthritis, periostitis, polyneuropathies, chronic atrophic acrodermatitis, mental disorder, dementia, spastic paraparesis, ataxic gait, and encephalomyelitis.[9]

Cranial nerve palsies are the most common neurological manifestations, affecting mainly the facial nerve (it is estimated that Lyme disease accounts for about 25% of cases of peripheral facial paralysis). Other abnormalities of the cranial nerves described are diplopia, paresthesia, muscle pain and weakness.[10] Other clinical presentations vary with geographic regions, with cutaneous and articular manifestations being predominant in North America, cutaneous and neurological in Europe, and mainly cutaneous in Asia.[11]

Ophthalmologic manifestations are more frequent in Europeans and some of the most common are conjunctivitis, episcleritis and scleritis, papilledema, optic nerve neuropathy, iridocyclitis, choroiditis, vasculitis, retinal detachment, pan-ophthalmitis, diplopia with paralysis of V and VI pairs of cranial nerves, and altered ocular mobility.[12] Fewer cases were reported of pupillary abnormalities such as the Argyll-Robertson pupil, and Claude Bernard Horner's syndrome. Chronic ophthalmologic alterations are often associated with neurological impairment.[13]

In Brazil, this disease started having other denominations such as Lyme-like disease, Brazilian Lyme-like Disease, Infectious-Reactive Lyme-like syndrome (SIRLS), Baggio-Yoshinari

Syndrome (SBY), and Brazilian Human Borreliosis, since there are some differences between it and the classic Lyme disease of the Northern Hemisphere. In our country, despite the similar clinical condition, there are larger recurrences of signs and symptoms, the bacteria of the complex Borrelia burgdorferi Sensu Lato have never been isolated in patients, and the spirochete vector is usually ticks of the genus Amblyomma sp.[14]

The diagnosis of Lyme disease is essentially clinical. In the early stages, it is based mainly on the suggestive clinical condition and epidemiological data on the exposure to tick, since the serology has variable sensitivity and specificity generating a considerable number of false positives and false negatives. In the later stages, serology is more reliable, although it may still reveal nonspecific results.[9]

The Enzyme-linked Immunosorbent Assay (ELISA) is the most widely used, and is less sensitive than WB (Western Blotting), but is also subject to errors.[9] Culture and histopathological examination may be carried out but are not widely used because they have an even lower sensitivity. It is also possible to identify spirochetes by PCR (Polymerase Chain Reaction).[15] Thus, although serological tests remain preferred for the complementary diagnosis of Lyme disease,[9] in high-risk patients (symptomatic and from endemic areas) laboratory confirmation is not necessary for the disease,[16] since the search for antibodies against Borrelia burgdorferi results in low and oscillating values rapidly denying biological fluids and being able to remain negative at all stages of the disease.[14]

According to the American Centers for Disease Control and Prevention (CDC), the diagnostic criteria for Lyme disease encompass:

• erythema migrans (of at least 5 cm) within 30 days after exposure in an endemic area of the disease;

• in the absence of erythema migrans, history of exposure in endemic area with signs of involvement of one or more organs and positive laboratory;

• in the absence of exposure in endemic area, presence of erythema migrans and two or more organs involved;

• in the absence of exposure in endemic area, presence of erythema migrans and positive serology for the disease.[17]

The patient is treated with systemic antibiotic according to the stage of the disease. The drug of first choice for early infections is doxycycline 100 mg twice a day from 14 to 21 days, or amoxicillin 500 mg 3 times a day from 14 to 21 days; allergy patients may use erythromycin or tetracycline. For advanced and late infections such as in neurological and ocular manifestations, ceftriaxone 2g once daily for 14 to 28 days or crystalline penicillin is preferred.[18, 19] Vaccination against Lyme disease may be useful in endemic areas, although it does not bring complete protection. Therefore, the best preventive measure remains to avoid exposure in risk areas.[20]

Regarding the management of peripheral facial paralysis, besides the therapy directed to the underlying disease, there are indications that steroids may be beneficial, in addition to physiotherapy, acupuncture, botulinum toxin, surgery in selected cases, and psychological support.[21] Prevention of ophthalmic complications such as corneal ulcer is made with general measures such as the use of ocular lubricants and ocular occlusion.[22, 23]

Therefore, Lyme disease should comprise a multidisciplinary approach. Ophthalmologists should be aware of their clinical manifestations in order to handle early ocular complications and thus avoid compromising the patient's visual acuity. Ophthalmic resources such as lagophthalmos correction should be used according to the severity of each case, but the priority is always to preserve visual abilility.

The objective of the present study was to reveal and discuss the aspects of a case report with peripheral facial paralysis and consecutive paralytic lagophthalmos, diplopia and punctate keratitis associated with the history of exposure to endemic areas for ticks, previous chronic erythema migrans, and neurological manifestations. Although laboratory tests (serology and cerebrospinal fluid) were negative, Lyme disease was diagnosed because of highly suggestive clinical and epidemiological data. Thus, we could conclude that knowledge of this disease by all health professionals, including the ophthalmologist, is mandatory for its early treatment and consequent improvement of the patient's prognosis.

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