Case report

Chronic lymphomonocytic meningoencephalitis, oligoarthritis and erythema nodosum: report of Baggio-Yoshinari syndrome of long and relapsing evolution

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Abstract

The Brazilian human borreliosis, also known as Baggio-Yoshinari Syndrome (BYS), is a tick-borne disease but whose ticks do not pertain to the Ixodes ricinus complex. It is caused by Borrelia burgdorferi sensu lato microorganisms and resembles clinical and laboratory features of Lyme disease (LD). BYS is also distinguished from LD by its prolonged clinical evolution, with relapsing episodes and autoimmune dysfunction. We describe the case of a young female who, over one year, progressively presented with oligoarthritis, cognitive impairment, meningoencephalitis and erythema nodosum. Diagnosis was established by means of the clinical history and a positive serology to Borrelia burgdorferi sensu strictu. The patient received Ceftriaxone 2 g IV/day during 30 days, followed by 2 months of doxycycline 100 mg bid. Symptoms remitted and the Borrelia serology tests returned to normality. BYS is a new disease described only in Brazil, which has a rising frequency and deserves the attention from the country’s medical board because of clinical, epidemiological and laboratory differences from LD. Despite the fact that it is a hard-to-diagnose zoonosis, it is important to pursue an early diagnosis because the symptoms respond well to antibiotics or it might be resistant to treatment and may evolve to a chronic phase with both articular and neurological sequelae.

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Meningoencefalite linfomonocitária crônica, oligoartrite e eritema nodoso: relato de síndrome de Baggio-Yoshinari de longa e recorrente evolução

RESUMO

A borreliose humana brasileira, também conhecida como Síndrome de Baggio-Yoshinari (SBY), é uma enfermidade infecciosa própria do território brasileiro, transmitida por carrapatos não pertencentes ao complexo Ixodes ricinus, causada por espiroqueta do gênero Borrelia e que apresenta semelhanças clínicas e laboratoriais com a Doença de Lyme (DL). A SBY distingue-se da DL por apresentar evolução clínica prolongada, com episódios de recorrência e importante disfunção autoimune. Descreveremos o caso de uma paciente jovem, que desenvolveu progressivamente durante cerca de um ano oligoartrite de grandes articulações, seguida de distúrbio do cognitivo, meningoencefalite e eritema nodoso. O diagnóstico foi firmado devido à concomitância de queixas articulares e neurológicas com sorologia positiva para Borrelia burgdorferi sensu stricto. A paciente foi medicada com ceftriaxone 2 g/EV/dia por 30 dias, seguido de dois meses de doxiciclina 100 mg duas vezes ao dia. Houve remissão dos sintomas e normalização dos exames sorológicos para a borreliose. A SBY é uma zoonose emergente descrita apenas no Brasil, cuja frequência tem crescido bastante, e que, em razão das importantes diferenças nos aspectos epidemiológicos, clínicos e laboratoriais em relação à DL, merece especial atenção da classe médica do país. Trata-se de zoonose camuflada e de difícil diagnóstico, mas este deve ser perseguido com tenacidade, pois a enfermidade responde aos antibióticos no estágio inicial, podendo evoluir com sequelas neurológicas e articulares nos casos reconhecidos tardivamente ou recorrentes.

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Introduction

Brazilian human borreliosis or Baggio-Yoshinari Syndrome (BYS) is an endemic anthropozoonosis proper to Brazil, caused by spirochetes of the genus Borrelia, transmitted by ticks of the genus Amblyomma and Rhipicephalus, which have clinical similarities with Lyme disease (LD). BYS can be distinguished from LD, since the transmission vectors for this latter disease belong to the Ixodes ricinus species. Furthermore, from a clinical standpoint, this Brazilian disease evolves with symptomatric and immunological disorder recurrence. Researchers at the Medical Research Laboratory, Medicine School, Universidade de São Paulo (LIM -17) suggest that the biodiversity conditions particular to the Brazilian territory, such as the presence of exotic vectors and favorable ecological conditions, have allowed for bacteria of the Borrelia burgdorferi complex sensu lato, to adapt to the country and develop a zoonosis with typical clinical and laboratory aspects.

The dissemination of clinical and laboratory knowledge about BYS has been a great challenge, because even with a different clinical and laboratory picture of LD, there is huge resistance from national and international scholars to admit the existence of this Brazilian zoonosis. Concepts such as prolonged latent infection caused by spirochetes in the form of cysts, clinical recurrence, different serologic diagnosis from standards adopted by the Centers for Disease Control and Prevention (CDC), and the therapeutic strategies for use of antibiotics during extended periods of time are not acceptable for certain countries of the northern hemisphere.

However, to deny its existence as an emerging clinical entity would be gross negligence, especially when there is evidence that the disease may progress to develop severe joint and neurological sequelae, if not treated properly. In this paper, we describe an illness of prolonged evolution and recurrent symptoms, in that the diagnosis of BYS was established after the onset of meningoencephalitis with positive serology for B. burgdorferi, according to LIM-17 adopted standards.

Case report

Female, 35 years old, white, coming from the city of Cotia, São Paulo, where she lives since childhood. At 23, the patient showed additive polyarthritis, affecting hands, elbows, shoulders, knees and ankles. She recounts being treated with benzathine penicillin after hypothesis of rheumatic fever; however, due to the persistence of symptoms, she sought a rheumatologist who diagnosed rheumatoid arthritis, being treated with sulfasalazine, with improvement. She ceased medication after five years of clinical remission. She denied having erythema migrans (EM) and an infectious or surgical history. In June 2006 the patient displayed arthritis in her knees and left ankle, with erythematous spots on her legs. The case evolved to slow logical reasoning, amnesia for recent events, nervousness, depression and difficulty planning activities, dysgraphia, loss of balance and appearance of intermittent diplopia episodes with an increasing visual impairment. She reported febrile episodes (unmeasured). The patient lives in an urban area with dogs at home, but always goes to a farm in Ibiuna, Sao Paulo, where horses and cows are raised. The patient did not recall tick bites in the past 12 months, but relates that it had occurred several times before.
In December 2006 the patient was admitted for evaluation of cerebellar ataxia and neuritis of the 2nd cranial nerve. On admission, she was in good general condition, pale, normocytic and normochromic anemia, without lymphadenomegalgy. Upon inspection, the patient had hyperchromic macules, with palpable nodules in the anterior region of both legs, with no other mucocutaneous lesions. Cardiopulmonary and abdominal workup revealed no changes.

Arthritis showed up on her knees and left ankle, with preservation of small joints, without joint limitation or deformities. The patient was lucid and oriented in time and space, alert and cooperative, amnesic to recent events, but with remote memory preserved. A nontoxic march with grade V driving force in all members was observed, with a mild dysmetria of the left arm. Sensitivity and reflexes were preserved and there was no sign of meningeal irritation.

Laboratory tests revealed normocytic and normochromic anemia, erythrocyte sedimentation rate = 85 mm/1st hour and C-reactive protein = 99 mg/L. The tuberculin test was negative, as well as antinuclear and rheumatoid factors. A CSF analysis revealed pleocytosis at the expense of lymphocytes, with 250 mg of chloroquine diphosphate. The serology for B. burgdorferi became negative during the evolution, according to data from Table 2.

Currently, the patient is asymptomatic, without changes in the brain resonance, but with some memory impairment.

### Table 1 – Evolutionary analysis of the cerebrospinal fluid (CSF).

<table>
<thead>
<tr>
<th>Date</th>
<th>Leukocytes (/mm³)</th>
<th>Neutrophils</th>
<th>Lymphocytes</th>
<th>Monocytes</th>
<th>Glucose (mg/dL)</th>
<th>Proteins (mg/dL)</th>
<th>ELISA IgM</th>
<th>ELISA IgG</th>
<th>Neurology ward</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dec 13, 06</td>
<td>0 - 5</td>
<td>960</td>
<td>1</td>
<td>3</td>
<td>50 - 90</td>
<td>&lt; 40</td>
<td>-</td>
<td>-</td>
<td>July 13, 07</td>
</tr>
<tr>
<td>Dec 15, 06</td>
<td>1</td>
<td>160</td>
<td>3</td>
<td>6</td>
<td>41</td>
<td>62</td>
<td>-</td>
<td>-</td>
<td>July 30, 07</td>
</tr>
<tr>
<td>Mar 19, 07</td>
<td>65</td>
<td>7</td>
<td>76</td>
<td>17</td>
<td>55</td>
<td>38</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Apr 04, 07</td>
<td>81</td>
<td>42</td>
<td>41</td>
<td>15</td>
<td>48</td>
<td>43</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>July 13, 07</td>
<td>190</td>
<td>6</td>
<td>73</td>
<td>19</td>
<td>63</td>
<td>32</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>July 30, 07</td>
<td>18</td>
<td>0</td>
<td>67</td>
<td>21</td>
<td>80</td>
<td>30</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

Ref, reference value.
areas, socialized with domestic animals and had episodes of tick bites. The BYS vectors often infest animals living close to man.16

The fact that the patient denied recent tick bites is not surprising, as the contagion may have occurred months or years before the current symptoms.

The concomitant occurrence of meningencephalitis and the involvement of the second cranial nerve, associated with the joint manifestation, is a relevant aspect. Shinjo et al.,20 studied 30 patients with BYS neuroborreliosis, and found that 73.6% had recurrence episodes, 56.7% had concomitant neurologic complaints with arthritis, and meningencephalitis was identified in 33.3% of cases.

The encephalomyelitis of human borreliosis may be confused with multiple sclerosis (EM).12,13 In this report, the exuberance of the inflammatory symptoms, the multiplicity of systemic complaints, a positive serology for B. burgdorferi and the good response to antibiotics excluded this diagnostic option. Other causes of infectious and autoimmune encephalomyelitis were also excluded.

There is no mention about MS in our patient’s history, but it should be noted that this initial injury, which arises at the point of inoculation of spirochetes, occurs in less than 50% of cases in Brazil.14 Interestingly, other atypical cutaneous presentations of inoculation of spirochetes, occurs in less than 50% of cases should be noted that this initial injury, which arises at the point of inoculation of spirochetes, occurs in less than 50% of cases.6,8 Interestingly, other atypical cutaneous presentations of inoculation of spirochetes, occurs in less than 50% of cases.6,8

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This paper confirms the existence of recurring outbreaks in BYS patients. This finding is highly relevant, since the current symptoms are not always associated with epidemiological and clinical data of the past. However, due to the severity of illness, a good response of the condition to the treatment with antibiotics in its early stages, and the possibility of preventing progression to chronicity, physicians of different specialties should be vigilant for suspected cases of Brazilian human borreliosis.

Conflicts of interest
The authors declare no conflicts of interest.

REFERENCES


Table 2 – Evolutive analysis of serology for Borrelia burgdorferi.

<table>
<thead>
<tr>
<th>B. burgdorferi Serology</th>
<th>Ref</th>
<th>Outpatient’s unit</th>
<th>Outpatient’s unit</th>
<th>Neurology ward</th>
<th>Outpatient’s unit</th>
<th>Outpatient’s unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELISA IgM</td>
<td>1/100</td>
<td>Neg</td>
<td>1/100</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>ELISA IgG</td>
<td>1/400</td>
<td>1/800</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>WB IgM</td>
<td>a</td>
<td>1 b</td>
<td>2 b</td>
<td>2 b</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>WB IgG</td>
<td>a</td>
<td>3 b</td>
<td>3 b</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
</tr>
</tbody>
</table>

Neg, negative; Ref, reference value.

WB is considered positive with presence of at least 4 IgG bands, or at least 2 IgM bands; or at least 2 IgG bands and 1 IgM band simultaneously.

Ceftriaxone was initiated on June 29, 2007.

A WB is considered positive with presence of at least 4 IgG bands, or at least 2 IgM bands; or at least 2 IgG bands and 1 IgM band simultaneously.