Revista da Sociedade Brasileira de Medicina Tropical
Journal of the Brazilian Society of Tropical Medicine
Vol.:52:e20180208: 2019
doi: 10.1590/0037-8682-0208-2018

Case Report

Visceral leishmaniasis mimicking systemic lupus erythematosus

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Abstract

Visceral leishmaniasis (VL), or kala-azar, a serious disease resulting from a systemic infection caused by a protozoan of the genus *Leishmania,* is potentially fatal to humans. According to data from Sistema de Informação de Agravos de Notificação (Brazil's Information System for Notifiable Diseases) from 2015 to 2016, 6,489 new cases were recorded in Brazil in 22 of the 27 federative units. In addition to typical clinical findings, VL may be associated with autoimmune phenomena, including simulating systemic lupus erythematosus (SLE). We present the first case of autochthonous VL mimicking SLE in Santa Catarina in southern Brazil.

Keywords: Leishmaniasis. Kala-azar. Systemic lupus erythematosus.

INTRODUCTION

Visceral leishmaniasis (VL), or kala-azar, a serious disease that is potentially fatal to humans, results from a systemic infection caused by a protozoan of the genus *Leishmania,* which, if left untreated, leads to death in 95% of the cases[1]. These protozoa are obligate intracellular parasites of lymphoid organs such as spleen, lymph nodes, bone marrow, and liver[2]. The disease manifests as intermittent fever, weight loss, hepatomegaly, major splenomegaly, and anemia[1]. Some laboratory findings of VL indicate that it is characterized by cytopenia and positive antibodies resembling an autoimmune rheumatic disease, especially systemic lupus erythematosus (SLE)[3,4], a chronic disease characterized by multisystem inflammation of unknown cause[5].

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Received 7 June 2018
Accepted 13 October 2018

It is estimated that there are 50,000 to 90,000 cases annually of VL worldwide, of which 90% occur in seven countries, including Brazil[1]. According to data from Sistema de Informação de Agravos de Notificação (Brazil's Information System for Notifiable Diseases; SINAN) from 2015 to 2016, 6,489 new cases were registered in the country in 22 of the 27 federative units. Santa Catarina was one of the five units without an autochthonous case recorded[6].

CASE REPORT

This case involves a 53-year-old male patient from Florianópolis, Santa Catarina, residing in the Saco dos Limões neighborhood, who worked as a painter and went fishing as a leisure activity. In his house, he had two dogs without veterinary supervision. He denied traveling in recent years and making any trip out of state.

He visited the Emergency Service of the Hospital Universitário Professor Polydoro Ernani de São Thiago (Professor Polydoro Ernani University Hospital of São Thiago) in June 2017, owing to a 2-week period of having a nightly

fever of up to 38°C, myalgia, asthenia, productive cough with yellowish mucus, and weight loss of approximately 10 kg. He also reported knee and elbow arthralgia.

At the physical examination, he was emaciated and pale, with a flat, flaccid, and painful abdomen on palpation of the epigastrium. He had hepatosplenomegaly (14 cm hepatometry and palpable spleen 3 cm from the left costal border). He had no lymphadenopathy or skin lesions. The most frequent diseases in Santa Catarina were eliminated, including leptospirosis, tuberculosis, HIV, and viral hepatitis B and C. Serology was repeated after a period of a possible immunological window.

Abdominal tomography confirmed hepatosplenomegaly, with the spleen on its largest axis measuring 19.6 cm. Laboratory tests revealed pancytopenia and elevated levels of C-reactive protein, lactate dehydrogenase, and hepatic markers (**Table 1**). The patient was discharged and followed up as an outpatient.

On his first follow-up visit, he presented worsening of asthenia, weight loss, and night fever. He reported a new episode of abdominal pain in the epigastric region. The examination showed hepatosplenomegaly, hepatometry of 16 cm, and palpable spleen 9.5 cm from the costal border. Laboratory results showed antinuclear factor (ANF) at 1:160 dilution with dense fine speckling and a cytoplasmic pattern, polyclonal hypergammaglobulinemia, pancytopenia with lymphopenia, and significant complement consumption and were positive for rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP) antibody, and cryoglobulins; a direct Coombs test was also positive (**Table 1**).

The diagnostic hypotheses at that time were autoimmune disease or lymphoma. Therefore, bone marrow aspiration was performed in the presence of persistent pancytopenia, with visualization of the amastigote form of *Leishmania*, confirming the diagnosis of VL via myelogram. In addition, test results showed a positive polymerase chain reaction for *Leishmania infantum*, reactive indirect immunofluorescence reaction at 1:640 dilution, and a positive culture.

TABLE 1: Laboratory exams.

Exam	Reference value	Results
Hemoglobin, g/dl	13.2-18	9.1
Hematocrit	39-51%	28.5%
Leukocytes, /mm^3	3800-11,000	2550
Segmented, /mm^3	1700-7500	1453.5
Lymphocytes, /µl	1000-3500	561
Monocytes, /µl	200-920	127.5
Eosinophils, /µl	20-670	0
Basophils, /µl	0-130	25.5
Bands	0-5%	11%
Platelets, /mm^3	150,000-440,000	86,000
C-reactive protein, mg/L	≤3	685
Lactate dehydrogenase, µ/L	81-234	845
Aspartate aminotransferase, µ/L	10-40	789
Alanine aminotransferase, µ/L	12-78	196
Rheumatoid factor, IU/ml	<15	292
Anti-CCP, U	Negative (<20)	46
Complement proteins		
C3, mg/dl	90-180	62
C4, mg/dl	10-40	7.8
IgG, mg/dl	694-1618	3600
β_2-Microglobulin, ng/ml	609-2164	7367
Protein electrophoresis	10.3-18.2%	Hypergammaglobulinemia (44.2%)

CCP: anti-cyclic citrullinated peptide.

Considering the absence of previous autochthonous visceral leishmaniasis in Santa Catarina, and since the patient denied recent trips, this is the first reported case of autochthonous VL in Santa Catarina according to the Municipal Health Secretariat and the State Epidemiological Surveillance Department. In addition to the epidemiological importance, this is a lupus-like condition, presenting with consumption of complement, pancytopenia with lymphopenia, hypergammaglobulinemia, a positive direct Coombs test, and ANF.

From the time of diagnosis, treatment with liposomal amphotericin B at 4 mg/kg/day was initiated owing to the age of the patient and the clinical and laboratory findings, which reduced the hepatomegaly and splenomegaly, improved the patient's general state, and reduced the inflammatory markers. He was discharged in August 2017 with an afebrile disposition and was asymptomatic.

DISCUSSION

There are reports in the literature that leishmaniasis can mimic or trigger an autoimmune disease such as autoimmune hepatitis, systemic lupus erythematosus and rheumatoid arthritis (RA)[7]. The present case involves a patient with VL who presented with clinical and laboratory characteristics of SLE and some particularities of RA.

Autoimmune phenomena in VL have been described for a long time. In 1983, a prospective study was conducted in Rio de Janeiro to evaluate immunological phenomena of VL. Serum samples from 17 patients with a diagnosis of kala-azar were collected, in which were observed a significant increase in serum IgG and IgM, high levels of RF, anti-DNA positivity, ANF, anti-basal membrane antibodies, and anti-Sm antibodies[8].

The mechanisms involved in the pathophysiology of this autoantibody production are not yet fully understood[9]. There is evidence that they are related to the activation of polyclonal B cells due to a decrease in regulatory T cell activity. Another possible mechanism would be the production of autoantigens in response to a cross-reaction between the parasite and host tissue antigens[7,8]. Notably, the patient had high titers of serum IgG, hypergammaglobulinemia, and increased β_2-microglobulin, suggesting extensive activation of B cells.

The patient in this report was positive for RF and anti-CCP. RF has already been described in VL, but anti-CCP is not commonly reported. It should be noted that anti-CCP has 95% specificity for RA. A 2007 Brazilian study investigated the prevalence of anti-CCP in 10 patients with VL, demonstrating positive results in three of them. The study concluded that sporadic production of anti-CCP is an autoimmune feature of VL that may be caused by citrullination of host proteins during *Leishmania* infection[9].

Consumption of C3 and C4, as observed in the patient in this study (**Table 1**), is seen in 50% of the cases[10]. However, in a review of the literature analyzing seven articles on VL mimicking SLE conducted by Santana et al. in 2015, only one described complement consumption in patients with VL[11].

Clinical manifestations such as decreased general status, asthenia, weight loss, fever, splenomegaly, and pericardial effusion associated with laboratory data such as complement consumption, ANF positivity, a positive direct Coombs test, hypergammaglobulinemia, and pancytopenia are clinical and immunological changes related to SLE; however, as described above, they may also be present in patients with VL. Therefore, these data indicate that, in addition to SLE, VL should also be considered even in cases with negative epidemiology. In addition, although less frequently reported, VL may present as an opportunistic disease in immunocompromised patients with SLE, and thus, this differential diagnosis should be considered[12].

Differentiating VL from autoimmune diseases can be challenging, especially when there is no positive epidemiology; however, it is of paramount importance as a misdiagnosis in patients who receive immunosuppressive treatments can lead to fatal consequences.[11] Therefore, after this first described case of VL in the Santa Catarina, Brazil, it is suggested that the possibility of VL be considered in patients with lupus-like symptoms, especially before administering immunosuppressive drugs.

Conflict of Interest: The authors declare that there is no conflict of interest.

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