Visceral leishmaniasis in a patient with direct positive coombs hemolytic anemia: a public health alert

Leishmaniose visceral em paciente com anemia hemolítica de Coombs direta positiva: um alerta de saúde pública

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Keywords

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Visceral leishmaniasis (VL) is a zoonosis with high morbidity and mortality. Endemic in tropical and subtropical regions. Autoimmune Hemolytic Anemia (AIHA) is a clinical condition in which autoantibodies bind to antigens located on the erythrocyte surface. The coexistence of the hematological picture of AIHA is rarely observed in patients with VL. The symptomatic manifestation of the case can become a dilemma, as the evolution to a more severecondition, due to intrinsic factors of the patient. In this report, we present the case of a patient with VL infection associated with a hematological picture of AIHA, with clinical manifestations of asthenia, weight loss, pyrexia, night sweats, jaundice, choluria, faecal acholia, nausea, vomiting, pancytopenia and hepatosplenomegaly. This article aims to present a case report, as a form of alert to health authorities, about the clinical-epidemiological impact of theVL-AIHA association in the area of circulation of the VL transmitting vector.

Palavras-Chave

Calazar
Infecção Parasitária
Doenças Hematológicas
Doenças autoimunes

A leishmaniose visceral (VL) é uma zoonose com alta morbidade e mortalidade. Endêmico em regiões tropicais e subtropicais. A Anemia Hemolítica Autoimune (AIHA) é uma condição clínica na qual autoanticorpos se ligam a antígenos localizados na superfície eritrocitária. A coexistência do quadro hematológico de AIHA raramente é observada em pacientes com VL. A manifestação sintomática do caso pode se tornar um dilema, como a evolução para um quadro mais grave, devido a fatores intrínsecos do paciente. Neste relato, apresentamos o caso de um paciente com infecção por VL associada a quadro hematológico de AIHA, com manifestações clínicas de astenia, emagrecimento, pirexia, sudorese noturna, icterícia, colúria, acolia fecal, náuseas, vômitos, pancitopenia e hepatoesplenomegalia . Este artigo tem como objetivo apresentar um relato de caso, como forma de alerta às autoridades sanitárias, sobre o impacto clínico-epidemiológico da associação VL -AIHA na área de circulação do vetor transmissor da VL.

INTRODUCTION

Leishmaniasis is a zoonotic disease, transmitted by endemic vectors in Brazil, which carry the etiological agents, flagellated protozoa of the genus Leishmania. The disease can present in the clinical form of cutaneous leishmaniasis (CL), developing scars and disfigurement, and systemic or visceral leishmaniasis (VL), with a higher risk of lethality if left untreated in more than 95% of cases (ADAM *et al.,* 2014; CUNHA *et al.,* 2020; WHO, 2021).

Also called Calazar, in Brazil, VL is caused by the species Leishmania (Leishmania) *infantum chagasi* (MONGE-MAILLO *et al.,* 2014; CUNHA *et al.,* 2020). The transmission to humans occurs during the blood meal of infected female sandflies of the genus Lutzomyia (*Lutzomyia longipalpis*). In the urban environment, VL has dogs as a reservoir and main source of infection (MONGE-MAILLO *et al.,* 2014).

VL is considered one of the main parasitic diseases with potential for outbreak and mortality. Most cases occur in Brazil, East Africa and India. The World Health Organization (WHO) estimates that 50,000 to 90,000 new cases of VL occur annually worldwide, with 25 to45% being reported to the WHO. In 2020, more than 90% of new cases reported to the WHO occurred in 10 countries: Brazil, China, Ethiopia, Eritrea, India, Kenya, Somalia, South Sudan,Sudan and Yemen (WHO, 2021).

In Brazil, a rare case of LV-AIHA association is recorded in the scientific literature at that time, demonstrating the unprecedented nature of the case report. Visceral leishmaniasis can progress to severe forms with significant hematological disorders including: pancytopenia (anemia,

thrombocytopenia and leukopenia with neutropenia, marked eosinopenia and relative lymphocytosis and monocytosis), hemolysis, fibrinolysis, among others (MAHAJAN; MARWAHA, 2007).

Unusual manifestations with non-specific signs and symptoms can make diagnosis difficult and delay treatment, increasing the risk of severity and death, especially in endemic areas of the vector species. There are few studies with patients with these characteristics of VL-AIHA in Brazil (MAHAJAN; MARWAHA, 2007; LEAL *et al.,* 2008).

The LV-AIHA association should be considered an important factor of attention,whether in the surveillance and management of patients, mainly due to risk factors that determine the severity of clinical manifestations, including nutritional status and the immunogenetic characteristics of the affected person.

CASE REPORT

A twenty-two-year-old man, preliminarily asthenic and in the process of losing weight,for five months, was admitted to the emergency department of a state hospital with a clinical picture of intermittent fever, chills, night sweats, choluria, faecal acholia, nausea, vomiting, hepatosplenomegaly, pancytopenia and palpable cervical lymph nodes. On admission, he was jaundiced, pale and had a hippocratic facies. Physical examination revealed painful peripheral (cervical) lymphadenopathy and moderate hepatomegaly by palpating the liver 4 cm from the right costal margin. Vital signs were: heart rate 96 bpm, blood pressure 100/60 mmHg, oxygensaturation 99% and body temperature 37.5°C. Serological, biochemical, microbiological, hematological, parasitological and imaging tests were requested for diagnostic investigation.

The patient was transferred to a referral hospital for clinical surveillance. Serology wasnegative for HBV, HCV, HIV I/II, Dengue, Chagas disease, Malaria and positive for *Leishmania* (anti-*Leishmania* antibodies were detected in the patient's serum by immunochromatography). A complete blood count revealed pancytopenia [Erythrogram (RBCs 2.68 million/mm3, Hemoglobin 7.2 g/dL, Hematocrit 21.3%, Mean Corpuscular Volume 79.5 fL, Mean Corpuscular Hemoglobin 26.9 pg, Erythroblasts 1.4% , RDW 21.1%), Leukogram (Leukocytes 7,300/mm3, Segmented 16.4%, Lymphocytes 74%), Platelet count (platelets130,000/mm3, MPV 10.4 fL)]. The patient had Transferrin Saturation around 54%, Iron Binding Capacity (TIBC) of 170 ug/dL and positive direct Coombs 3+. Liver function tests were abnormal: Aspartate aminotransferase (AST) 1128 U/L, Alanine aminotransferase (ALT)513 U/L; Gamma glutamyl transferase (Gamma GT) 102 U/L; Alkaline Phosphatase 951 mg/dL; Total Bilirubin 27.05 md/dL, Direct 13.26 mg/dL and Indirect 13.79 mg/dL fractions; Total proteins 8.9 g/dL, Albumin 2.5 g/dL, Globulins 6.4 g/dL, alb/glob ratio 0.39. Altered Coagulation Tests: Prothrombin Activity Time 34 seconds, Prothrombin Activity 19.55%, INR:3.38% and Partial Thromboplastin Time 67.00 sec. Inflammatory Activity: C-Reactive Protein 6.72 mg/dL, Cell and Tissue Damage: Lactic Dehydrogenase (DHL) Dosage 1,166 U/L. Ultrasound examination of the entire abdomen revealed moderate hepatomegaly, marked splenomegaly, and ascites. Computed tomography of the chest showed no changes. The transthoracic echocardiogram showed a slight pericardial effusion. Total abdomen computed tomography examination reiterated ultrasound examination, demonstrating hepatomegaly and marked splenomegaly. Magnetic resonance cholangiography showed luminal gallbladder collapse, splenomegaly, and laminar ascites. After medical evaluation, antibiotic therapy basedon beta-lactam of the carbapenem subclass (meropenem trihydrate) was prescribed for 15 days;an antimicrobial from the glycopeptide group (teicoplanin) for 10 days; conventional amphotericin B, for 14 days; 5 days of a lipid formulation of the polyene class produced by actinomycete culture (liposomal amphotericin B); vitamin K and folic acid replacement; plus dexamethasone-based pulse therapy for 4 days.

DISCUSSION

In the present case report, a man presented with hepatosplenomegaly, jaundice, fatigue and intermittent fever. In the context of the severity of the clinical manifestations presented bythe patient, the health team that assisted the clinical case requested tests for diagnostic investigation and patient management. The clinical picture was an association between VL andAIHA, although it is rarely observed, there are some reports in the literature of VL-AIHA. Themarked symptomatic manifestations and the determining risk factors for the emergence of newcases, led the health team to report the present case, as a form of alert to the health authorities,due to the proven circulation of the vector transmitting VL in the region, as well as the previous occurrence of death from complications of liver cirrhosis, caused by VL, in a riversideindividual, 82 years old, infected in the municipality of Mazagão-Amapá-Brazil (ALMEIDA *et al.,* 2020).

VL is an anthropozoonosis endemic in tropical areas, it is a neglected disease that has shown expansion and global increase in lethality. The World Health Organization (WHO) considers VL as a priority among tropical diseases, mainly due to the increase in incidence and transmission areas, the disease mainly affects low-income populations in developing countries(MARTINS-MELO *et al.,* 2018; WHO, 2021).

The VL case presented, when investigated, was an imported case, however, the state of Amapá harbors the vector species. Demonstrating, therefore, the need for integrated actions andeffective monitoring of the disease to complement curative practices and minimize the risk of

epidemics, as already evidenced in other states in northern Brazil (PRESTES-CARNEIRO *et al.,* 2019).

VL presents a wide spectrum of clinical manifestations, from asymptomatic forms(positive serology without clinical manifestations) to the classic form, such as the presence of febrile hepatosplenomegaly, weight loss, pancytopenia, hypergammaglobulinemia, in addition to a significant decrease in general condition (FERREIRA *et al.,* 2020), manifestations these were also observed inthe present study, plus AIHA, a rare hematological condition seen in adult patients with VL (MAHAJAN; MARWAHA, 2007). Several unusual manifestations with non-specific signs and symptoms can make diagnosis difficult and delay treatment, increasing the risk of severity and death, especially innew endemic areas (PRESTES-CARNEIRO *et al.,* 2019).

The positive Direct Coombs, in the laboratory findings of the patient,confirmed the picture of AIHA, a cytopenia with the formation of autoantibodies linked toantigens of the erythrocyte membrane, whose dominant pathophysiological mechanism is thefailure to maintain self-tolerance (FERREIRA *et al.,* 2020). VL can progress to severe forms with significant hematological disorders. The factors that determine the severity of clinical manifestations may be related to age, nutritional status and immunogenetic characteristics of the affected individual. Its progressive worsening can lead to death (MAHAJAN; MARWAHA, 2007).

The detection of LV-AIHA in this case reaffirms the need for rapid diagnosis and immediate treatment that the case requires, ensuring an efficient prognosis for the patient and improvement of the anemic condition.

CONCLUSIONS

More studies are needed to clarify the broad clinical spectrum of the LV-AIHAassociation in the adult population. However, in view of the rare reports in the literature and the present finding, it is necessary for health professionals to consider the association between VLand AIHA within their diagnostic hypotheses, when dealing with adult patients with hepatosplenomegaly, jaundice, fatigue and intermittent fever.

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All authors have participated equal.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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