



# VISCERAL LEISHMANIASIS IN PEDIATRICS: A CLINICAL STUDY

LEISHMANIOSE VISCERAL NA PEDIATRIA: UM ESTUDO CLÍNICO LEISHMANIASIS VISCERAL EN PEDIATRÍA: UN ESTUDIO CLÍNICO

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#### ABSTRACT

To report a case of Visceral Leishmaniasis in a child from an endemic area in the Northeast, in Quixeramobim-Ceará. Case report on a pediatric patient, carried out by data collection, using medical record review, including clinical and epidemiological characteristics and analysis of diagnostic tests between October and December 2023, in a secondary hospital in Ceará. A 7-year-old male patient from Quixeramobim-CE was admitted with intermittent fever for a month, hypoactivity, drowsiness, increased abdominal volume, HCD pain, dry cough, weight loss, hyporexia and occasional nausea. With the initial hypothesis of VL, an rK39 test was performed, with a negative result and a myelogram with leishmania in the smear. The patient's clinical condition must be considered, even in the face of negative results from the initial methods chosen, and other tests must be sought to help confirm the initial diagnostic hypothesis or rule out differential diagnoses.

**Keywords:** *Pediatrics*; *Clinical Diagnosis*; *Visceral Leishmaniasis*; *Epidemiology*.

#### RESUMO

Relatar um caso de Leishmaniose Visceral em uma criança procedente de área endêmica no Nordeste, em Quixeramobim-Ceará. Relato de caso em paciente pediátrico, realizado por coleta de dados, sendo utilizada revisão de prontuário, incluindo as características clínicas, epidemiológicas e a análise dos testes diagnósticos entre outubro e dezembro de 2023, em hospital secundário do Ceará. Paciente masculino, 7 anos, procedente de Quixeramobim-CE, foi admitido apresentando febre intermitente há um mês, hipoatividade, sonolência, aumento de volume abdominal, dor em HCD, tosse seca, perda de peso, hiporexia e náuseas ocasionais. Com hipótese inicial de LV, foi realizado teste rK39, com resultado negativo e mielograma com leishmanias no esfregaço. O quadro clínico do paciente deverá ser considerado, mesmo diante de resultados negativos dos métodos iniciais escolhidos, devendo ser buscados outros exames que auxiliem a confirmar a hipótese diagnóstica inicial ou a descartar diagnósticos diferenciais.

Descritores: Pediatria; Diagnóstico Clínico; Leishmaniose Visceral; Epidemiologia.

#### RESUMEN

Reportar un caso de Leishmaniasis Visceral en un niño de una zona endémica del Nordeste, en Quixeramobim-Ceará. Reporte de caso de un paciente pediátrico, realizado mediante recolección de datos, mediante revisión de historias clínicas, incluyendo características clínicas y epidemiológicas y análisis de pruebas diagnósticas entre octubre y diciembre de 2023, en un hospital secundario de Ceará. Paciente masculino de 7 años del Quixeramobim-CE, ingresó con fiebre intermitente de un mes de evolución, hipoactividad, somnolencia, aumento de volumen abdominal, dolor de HCD, tos seca, pérdida de peso, hiporexia y náuseas ocasionales. Con la hipótesis inicial de LV se realizó prueba rK39, con resultado negativo y mielograma con leishmania en frotis. Se debe considerar la condición clínica del paciente, incluso ante resultados negativos de los métodos inicialmente elegidos, y buscar otras pruebas que ayuden a confirmar la hipótesis diagnóstica inicial o descartar diagnósticos diferenciales.

Descriptores: Pediatría; Diagnostico Clinico; Leishmaniasis Visceral; Epidemiología.

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## **INTRODUTION**

Visceral leishmaniasis (VL) is endemic in 76 countries. Regarding the cases registered in Latin America, 90% occur in Brazil, mainly affecting the pediatric group, with the most affected group being children under 10 years of age (58%) and males  $(61\%)^{1,2}$ .

On average, about 3,500 cases are registered annually, with an incidence rate of 2 cases/100,000 inhabitants in 2018. In addition, the disease has shown important changes in the transmission pattern, initially predominating in wild and rural environments and, more recently, in urban centers<sup>1,2</sup>.

VL has a broad clinical spectrum of severity. In most cases, it is characterized by irregular, prolonged fever, pallor, hepatosplenomegaly, and progressive weight loss, associated with impaired general health<sup>3</sup>.

Diagnosis can be made using immunological and parasitological techniques. Among them, the rapid immunochromatographic test and cerebrospinal fluid analysis. The classes of drugs used for the treatment of visceral leishmaniasis in Brazil are restricted. However, in the 1980s, amphotericin B deoxycholate was introduced, followed by lipid formulations such as liposomal amphotericin B. The latter has high efficacy and low toxicity<sup>3,4</sup>.

The objective of this study was to report a case of visceral leishmaniasis in a child from an endemic area in the Northeast, in Quixeramobim, Ceará, Brazil.

#### **METHODS**

This is a descriptive case report study of a patient admitted to the general pediatric ward of a secondary hospital in the city of Fortaleza-CE.

The study was carried out in accordance with Resolution No. 466/12 of the National Health Council (CNS), and data collection was carried out through the review of medical records, including clinical and epidemiological characteristics and the analysis of diagnostic tests in the period from October to December 2023.

After data collection, the report was described and the case studied, focusing on the clinical presentation of the disease and the diagnostic methods used during the investigation of the patient's VL.

As an inclusion criterion, it was considered to be a case with the result of a diagnostic investigation for infrequent VL in a pediatric patient. After writing the manuscript, the report was forwarded to the Research Ethics Committee of the Health Institution and approved with opinion number 6,625,773.

#### RESULTS

A 7-year-old male patient, brown, from Quixeramobim-CE, was admitted to the pediatric ward of a secondary hospital in the State of Ceará, presenting a history of intermittent fever for one month, associated with hypoactivity, drowsiness, increased abdominal volume, abdominal pain in the topography of the right hypochondrium, dry cough, weight loss, hyporexia and occasional nausea.

Cadernos ESP. 2024, v.18: e1896

During the anamnesis, the companion reported the presence of stray dogs in the neighborhood and that there had been no previous contact with family members or with people with active tuberculosis or those undergoing treatment.

On physical examination, the child was emaciated, pale, hydrated, acyanotic, anicteric, afebrile, with generalized lymph node enlargement and no other alterations observed during the evaluation of the pulmonary and cardiovascular systems.

Examination of the abdomen revealed a flaccid abdomen, semiglobose abdomen, bowel sounds, percussion tympanism, hepatomegaly with palpable hepatic border 4 cm from the right costal margin, and splenomegaly with a palpable spleen 3 cm from the left costal margin.

The patient had laboratory tests performed in the city of origin, which showed a complete blood count with bicytopenia (hemoglobin - 10.1; platelets - 127,000; and leukocytes - 6,900) and urine summary without abnormalities.

At the time of admission, albendazole and ceftriaxone were prescribed, and complementary tests were requested, which showed chest x-rays with reticulonodular interstitial pattern, hepatic function, hepatic, canalicular and pancreatic enzymes, renal function, LDH, bilirubin, electrolytes, uric acid and lactate, and ultrasensitive CRP <sup>3,11</sup>.

A new blood count showed hemoglobin - 9.4, leukocytes - 5,700 and platelets - 173,000. In addition to serology for CMV and EBV with reactive IgG and non-reactive IgM; Toxoplasmosis and anti-HIV with non-reactive IgG and IgM; non-reactive anti-HBS; non-reactive anti-HCV; anti-hva IgG and non-reactive IgM; herpes simplex 1 and 2 IgG and IgM reagents and non-reactive rK39.

Because the presence of vesicular lesions in any region of the patient's body was not observed or reported during physical examination, a false-positive result was considered and acyclovir was not initiated. During hospitalization, the patient presented daily fever peaks even after 72 hours on antibiotics, maintained hyporexia, hypoactivity, report of dry cough and pain in HCD.

Thus, normal ECG and ECOTT were requested, abdominal US with splenomegaly with diffusely heterogeneous echotexture, AFB in gastric lavage were tested, with all three samples being negative, iron profile (ferritin 935 ng/ml, STI 28%, TIBC 191 mcg/dl, serum iron 54 mcg/dl), lipidogram (CT 137 mg/dl, HDL 181 mg/dl, LDL 84 mg/dl, TGL 175 mg/dl) and fibrinogen 438 mg/dl, normal electrolytes and myelogram, which showed the presence of leishmanias in the smear, confirming the diagnosis of kala-azar.

Thus, the notification was filled out, and Liposomal Amphotericin B was prescribed, considering that the patient was at risk for malnutrition (Z-score weight 2.7), then with comorbidity that compromises the immune system.

In addition, laboratory tests were requested for initial control of the therapy and ceftriaxone was discontinued. After the beginning of the treatment, the child progressed with an improvement in the general condition, remaining afebrile and presenting a reduction in the spleen.

In view of the need to continue the diagnostic investigation of visceral leishmaniasis by means of myelogram, some difficulty in performing this test was perceived, since it was not performed at the secondary hospital where the child was

hospitalized. Therefore, as a strategy to solve this situation, a partnership with the reference children's hospital in the state of Ceará was used so that the myelogram could be performed.

## **DISCUSSION**

Visceral leishmaniasis is a neglected tropical disease that is a global public health problem, considered by the World Health Organization as one of the five most relevant endemic infectious and parasitic diseases 5.6. Brazil has 95% of the visceral leishmanias is recorded in Latin America, and it is growing rapidly and expanding<sup>7</sup>.

VL is a parasitic disease that has a high lethality, exceeding the rate of 90%, when drug therapy is not instituted. This pathology is caused by intracellular protozoan species of the genus Leishmania and has varied clinical manifestations<sup>8-11</sup>.

The disease can present itself through asymptomatic forms or classic conditions such as fever, hepatosplenomegaly, anemia, lymph node enlargement, hemorrhages, weight loss, and dry cough, the latter being a less frequent and confounding symptom, as it increases the possibilities of differential diagnoses, such as tuberculosis, being one of the hypotheses put forward in the diagnostic elucidation of the patient in this study, after the negative K39 result<sup>8-11</sup>.

Ceará is considered endemic for this disease and in a survey between 2007 and 2022, 6,926 confirmed human cases were observed, with an average of 433 cases per year, most of which were autochthonous  $(86.7\%)^{12}$ .

The years 2007 and 2009 had the highest values, 7.6 and 7.5 cases per 100,000 inhabitants, respectively. The incidence coefficients showed a more significant decline in the incidence of cases in 2012 (4.4 cases per 100,000 inhabitants) and in the last three years, from 3.4 (2019) to 1.8 cases per 100,000 inhabitants in 2022<sup>12</sup>.

The involvement of pediatric patients by kala-azar is an important fact to be highlighted in this pathology, since the age group from 0 to 9 years represents 31.39% of VL cases in Ceará between 2011 and 2018<sup>13</sup>. And the younger the child, the greater the risks, considering that immunity develops with age, making them more susceptible to infection and its complications due to immunity that is not yet fully developed 14.

The laboratory diagnosis of VL includes the finding of Leishmania by direct microscopy or culture in clinical samples, detection of specific antigen or antibodies, and detection of parasite DNA<sup>15</sup>.

The definitive diagnosis of VL requires the detection of the parasite from a medullary aspirate in organs such as the spleen, bone marrow or lymph node. However, as this is an invasive procedure with potential complications, it is not widely used, except in specialized hospitals, which are references for neglected tropical diseases. Therefore, the diagnosis of kala-azar is mainly based on serological tests rk39-ICT<sup>15</sup>.

The rK39-ICT rapid test does not depend on highly qualified personnel and laboratories and the results can be read within minutes to a few hours, becoming a tool of great importance for the elucidation of cases and showing high sensitivity and specificity for the investigation of VL<sup>16,17</sup>. However, sometimes, in the face of a suspected case, the rK39 may be negative, as observed in the patient in this report.

Cadernos ESP. 2024, v.18: e1896

When considering the epidemiology and clinical picture strongly suggestive of kala-azar, there is a need for more than one different methodology to confirm the result<sup>18</sup>. Investigation for VL should be maintained, opting for the performance of the myelogram, since microscopy is the gold standard due to its high specificity, and amastigote forms are observed in smears of the analyzed sample<sup>19</sup>.

## **CONCLUSION**

During the diagnostic investigation of VL, the patient's clinical picture should be strongly considered, even in the face of negative results of the initial methods chosen, and thus other tests should be sought to help us confirm the initial diagnostic hypothesis or to rule out differential diagnoses.

Even with the limitation of some methodologies for diagnosing VL in public hospitals, it is valid to persist in the so-called gold standard tests, seeking solutions that involve partnerships with the public or private network. Such partnerships proved to be potential for the present study, considering that they contributed to the early diagnosis and, therefore, to the initiation of appropriate therapy.

Thus, it is emphasized that in case of suspicion of VL, the patient should be referred to the public hospital of the State of Ceará, São José Hospital for Infectious Diseases.

## **REFERENCES**

- 1. Ministério da Saúde. Situação Epidemiológica da Leishmaniose Visceral. Disponível em: https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/l/leishmaniose-visceral/situacao-epidemiologica-da-leishmaniose-visceral.
- 2. Ministério da Saúde. Manual Vigilância e Controle da Leishmaniose Visceral. 1. ed, 5ª reimpressão. Ministério da Saúde: Brasília-DF; 2014. Disponível em:

https://bvsms.saude.gov.br/bvs/publicacoes/manual\_vigilancia\_controle\_leishmaniose\_visceral\_1edicao.p df.

- 3. Ministério da Saúde. Leishmaniose Visceral. Disponível em: https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/l/leishmaniose-visceral.
- 4. Lemos EM, Carvalho SFG, Dietze RC R. Avaliação do teste rápido utilizando o antígeno recombinante K39 no diagnóstico da leishmaniose visceral no Brasil. Rev Soc Bras Med Trop [Internet]. 2003 [citado 2022-11-11];36:36–8. Disponível em:

https://www.scielo.br/j/rsbmt/a/qhjVDm8mp9qXGQ4zp9CkSds/?lang=pt.

5. Ministério da Saúde, Secretaria de Vigilância em Saúde, Departamento de Vigilância Epidemiológica;. Guia de Vigilância em Saúde. 2. ed; 2017. Disponível em:

https://bvsms.saude.gov.br/bvs/publicacoes/guia\_vigilancia\_saude\_volume\_2.pdf.

- 6. Vasconcelos JM, Gomes CG, Sousa A, Teixeira AB, Lima JM. American integumentary leishmaniasis: epidemiological profile, diagnosis and treatment. Braz J Clin Analyses. 2018;50(3):221-7.
- 7. Ministério da Saúde, Secretaria de Vigilância em Saúde, Coordenação Geral de Desenvolvimento da Epidemiologia em Serviços. Guia Manual de Vigilância em Saúde. 1. ed.; 2016. 25 p. Disponível em: http://bvsms.saude.gov.br/bvs/publicacoes/guia\_vigilancia\_saude\_1ed\_atual.pdf.

8. World Health Organization (WHO) [Internet]. Control of the leishmaniases WHO TRS n° 949. [citado 2023-12-26]. Disponível em: https://www.who.int/publications/i/item/WHO-TRS-949.

- 9. Guerin PJ, Olliaro P, Sundar S, Boelaert M, Croft SL, Desjeux P, Wasunna MK, Bryceson ADM. Visceral leishmaniasis: current status of control, diagnosis, and treatment, and a proposed research and development agenda. The Lancet Infectious Diseases. 2002;2(8):494–501. Disponível em: https://doi.org/10.1016/s1473-3099(02)00347-x.
- 10. Fu Q, Li SZ, Wu WP, Hou YY, Zhang S, Feng Y, Zhang LP, Tang LH. Endemic characteristics of infantile visceral leishmaniasis in the People's Republic of China. Parasites & Vectors. 2013;6(1). https://doi.org/10.1186/1756-3305-6-143.
- 11. Barbosa IR, Costa Í do CC. Aspectos clínicos e epidemiológicos da leishmaniose visceral em menores de 15 anos no estado do Rio Grande do Norte, Brasil. Scientia Med. 2013;23(1):5. https://doi.org/10.15448/1980-6108.2013.1.12970.
- 12. Leishmaniose Visceral. Disponível em: https://www.saude.ce.gov.br/wp-content/uploads/sites/9/2018/06/Boletim-Epidemiologico-Leishmaniose-Visceral-23-11-2022.pdf.
  13. da Silva Paz J, Pinheiro AQC, Ribeiro RL, Ferreira JLM, da Silva LP. Epidemiologia da leishmaniose
- visceral no Ceará entre 2011 e 2018. Cadernos ESP. 2021;15(1):23–32. Disponível em:

https://cadernos.esp.ce.gov.br/index.php/cadernos/article/view/450.

- 14. Rey LC, Martins CV, Ribeiro HB, Lima AAM. American visceral leishmaniasis (kala-azar) in hospitalized children from an endemic area. J Pediatria. 2005;81(1):73–8. https://doi.org/10.2223/jped.1286.
- 15. Elmahallawy EK, Sampedro Martinez A, Rodriguez-Granger J, Hoyos-Mallecot Y, Agil A, Navarro Mari JM, Gutierrez Fernandez J. Diagnosis of leishmaniasis. J Infec Develop Count. 2014;8(8):961–72. Disponível em: https://doi.org/10.3855/jidc.4310.
- 16. Cunningham J, Hasker E, Das P, El Safi S, Goto H, Mondal D, Mbuchi M, Mukhtar M, Rabello A, Rijal S, Sundar S, Wasunn M, Adams E, Menten J, Peeling R, Boelaert M. WHO/TDR Visceral Leishmaniasis Laboratory Network. A global comparative evaluation of commercial immunochromatographic rapid diagnostic tests for visceral leishmaniasis. Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America. 2012;55(10):1312–9. Disponível em: https://doi.org/10.1093/cid/cis716.
- 17. World Health Organization (WHO). Control of the leishmaniasis: report of a meeting of the WHO Expert Committee on the Control of Leishmaniases. WHO technical report series. 2010:22–6.
- 18. Farias RC de, Santos JP dos, Nascimento EF do, Mendes JR, Sousa RFV de, Cardoso DRF, et al. Estudo comparativo entre metodologias para o diagnóstico da leishmaniose visceral humana: uma revisão integrativa/comparative study methodologies for the diagnosis of human visceral leishmaniasis: an integrative review. Braz J Develop. 2020;6(9):71398–409. https://doi.org/10.34117/bjdv6n9-547.
- 19. Fonseca AM. Diagnóstico da Leishmaniose Visceral utilizando proteínas de Leishmania infantum com função desconhecida; 2013.