CANINE VISCERAL LEISHMANIASIS: CASE REPORT DIAGNOSED IN SÃO PAULO CITY

Leishmaniose visceral canina: relato de caso diagnosticado na cidade de São Paulo

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Abstract

Visceral leishmaniasis (VL), popularly known as Kala-azar, is a zoonotic parasitic disease that can affect wild and domestic animals. Its transmission in the Americas occurs mainly through the bite of sandflies of the genus *Lutzomyia* spp., especially by the species *L. longipalpis* spp. known in Brazil as the ''straw mosquito''. The main clinical manifestations presented by dogs affected by VL include progressive weight loss, hyporexia and skin lesions, the latter being present in 81% to 89% of dogs with leishmaniasis. The present work aims to report an allochthonous case of canine visceral leishmaniasis treated at a veterinary hospital located in the capital of São Paulo refractory to the use of Miltefosine (Milteforan®).

Keywords: Leishmaniasis; zoonosis; dog; dermatopathy.

Resumo

A leishmaniose visceral (LV), conhecida popularmente como Calazar, é uma doença parasitária de caráter zoonótico que pode acometer os animais silvestres e domésticos. Sua transmissão nas Américas ocorre principalmente pela picada de flebotomíneos do gênero *Lutzomyia* spp., sobretudo, pela espécie *L. longipalpis* spp. conhecida no Brasil como ''mosquito palha''. As principais manifestações clínicas apresentadas pelos cães acometidos pela LV incluem perda progressiva de peso, hiporexia e

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lesões cutâneas, sendo esta última presente entre 81% e 89% dos cães com leishmaniose. O presente trabalho objetiva relatar um caso alóctone de leishmaniose visceral canina atendido em hospital veterinário localizado na capital paulista refratário ao uso de Miltefosina (Milteforan®).

Palavras-chaves: Leishmaniose; zoonose; cão; dermatopatia.

Introduction

Visceral leishmaniasis (VL) is the most severe form of leishmaniasis caused by *Leishmania infantum*—synonymous with *L. chagasi*—and is transmitted through the bite of sandflies, particularly *L. longipalpis*, infected with the promastigote forms of this protozoan (Jericó; Andrade Neto; Kogika, 2023; Ivănescu *et al*., 2023).

With the adaptation of sandflies to domestic environments, dogs have become the primary source of infection for humans in urban areas (Ayres *et al*., 2022). Infected dogs may remain asymptomatic, develop protective immunity, or present severe clinical manifestations, including ulcerative, scaling, and alopecic skin lesions associated with lymphadenomegaly, anorexia, muscle atrophy, lethargy, splenomegaly, onychogryphosis, vomiting, and diarrhea (Ayres *et al*., 2022). Even in the absence of clinical signs, dogs may harbor the parasite in the skin, maintaining the potential to infect sandflies and perpetuate the transmission cycle to other dogs and humans (Ivănescu *et al*., 2023; Ayres *et al*., 2022; Saout *et al*., 2024).

In advanced stages, canine visceral leishmaniasis may lead to glomerulonephritis and interstitial nephritis, frequently resulting in renal failure, a poorer prognosis, and, often, death (Jericó; Andrade Neto; Kogika, 2023).

Laboratory tests are essential for the diagnosis of leishmaniasis, as it may mimic other hemoparasitic diseases—such as babesiosis and ehrlichiosis—and may also predispose to secondary infections due to immunosuppression, further complicating diagnosis (Larsson; Lucas, 2022).

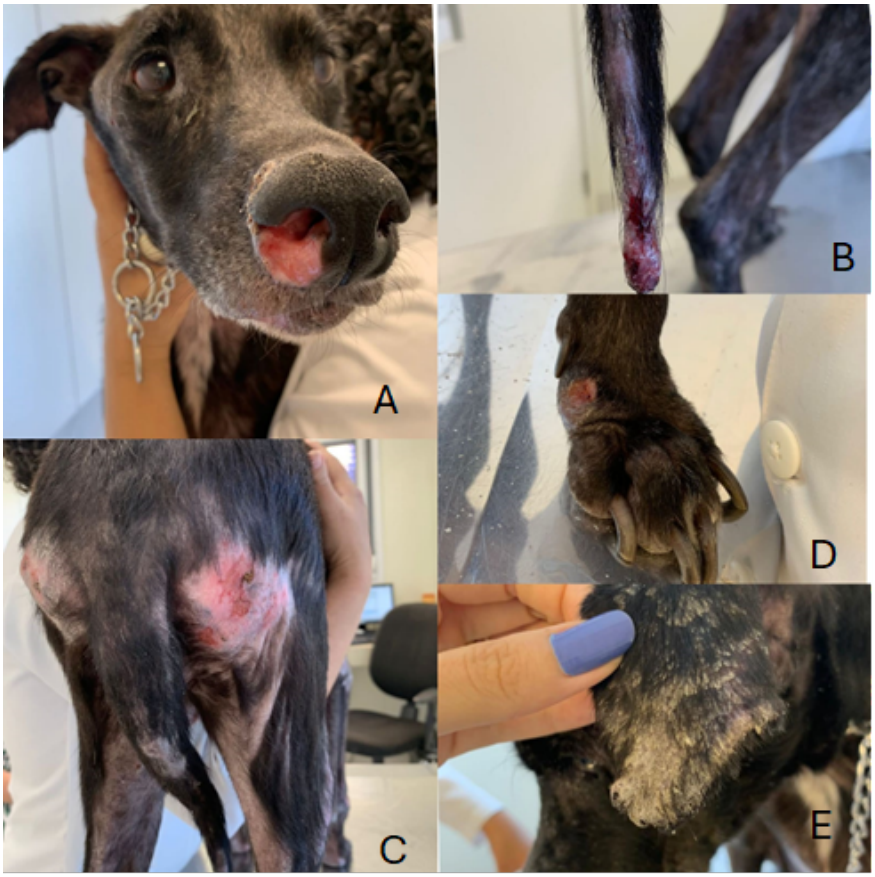
The present study aims to report an allochthonous case of canine visceral leishmaniasis treated at a veterinary hospital in the city of São Paulo.

Case Report

A female canine patient of mixed breed, seven years old, was attended at a veterinary hospital in São Paulo. The animal presented with a history of pruritus, apathy, and hyporexia, which began two years after traveling to the state of Goiás, in the Central-West region of Brazil.

On physical examination, muscle atrophy in the temporal region was observed, along with vasculopathic cutaneous lesions characterized by alopecic, ulcerative, and exudative lesions on the nasal planum (Figure 1A), tail tip (Figure 1B), and bony prominence regions—ischial and carpal areas (Figures 1C and 1D). Additionally, a dyskeratotic condition was noted, characterized by whitish, micaceous scales distributed over the entire dorsal region and on the external surface of the auricular pinnae (Figure 1E).

Figure 1 – Cutaneous clinical manifestations of canine visceral leishmaniasis[1]



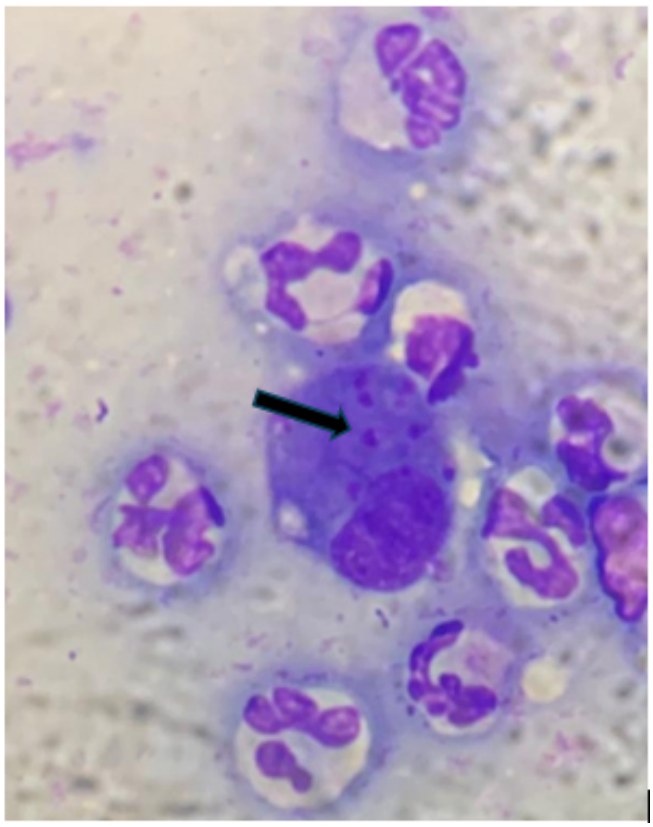
Source: Odaguiri (2024).

Based on the association between the cutaneous lesions and the anamnesis findings, a diagnosis of canine visceral leishmaniasis was suspected. For diagnostic confirmation, the following tests were requested: cutaneous cytopathology, serology (ELISA and indirect immunofluorescence assay—IFA, total dilution), complete blood count, blood glucose, ALT, alkaline phosphatase, total protein and fractions, as well as abdominal ultrasound and urinalysis.

Cytological examination was performed using an imprint smear of the serosanguineous exudate from the ulcerative lesion on the nasal planum, revealing the presence of amastigote forms within macrophages (Figure 2), which is a confirmatory finding for the diagnosis of canine visceral leishmaniasis.

1 Note: (A) Terebrant ulcer on the nasal planum; (B) alopecic, erosive-ulcerative, and exudative lesion on the tail tip (''lipstick tail''); (C) alopecia, erythema, and erosive-ulcerative lesion in the ischial region; (D) onychogryphosis and ulcerative lesion in the carpal region; (E) alopecic lesion covered by whitish scales on the left auricular pinna.

Figure 2 – Amastigote forms of *Leishmania* spp. observed within macrophages from serosanguineous exudate collected from an ulcerative lesion on the nasal planum



Source: Odaguiri (2024).

Serological testing was positive using both methods: ELISA, with an optical density of 2.852 (cut-off value: 0.791), and indirect immunofluorescence assay (IFA), with a total dilution titer of 1:80. Hyperglobulinemia was also observed (9.3 g/dL; reference value: 2.5–4.5 g/dL), while the remaining evaluated parameters—complete blood count, renal and hepatic function, and blood glucose—were within normal limits. Although abdominal ultrasonography and urinalysis were requested, they were not performed by the person in charge during the follow-up.

Following the diagnosis of canine visceral leishmaniasis, treatment was initiated with miltefosine (Milteforan®) at 2 mg/kg/SID orally, allopurinol at 10 mg/kg/BID orally, domperidone at 1 mg/kg/SID orally, and a deltamethrin collar (Scalibor®). After 21 days, there was a worsening of ulcerative cutaneous lesions located on the tail, nasal planum, ischial region, and carpal region, in addition to persistent pruritus. Prednisolone (Prediderm®) at 0.5 mg/kg/SID orally—administered for 14 days and then on alternate days for the same period—was added to control the vasculopathic cutaneous condition.

At the end of this period, a reduction in pruritus was observed, along with resolution of ulcerative lesions on the tail, nasal planum, and ischial region. Only the lesion in the carpal region persisted, albeit with reduced extent and depth, as well as a decrease in auricular dyskeratosis. However, the patient continued to exhibit temporal muscle atrophy and developed lameness in the left pelvic limb, suggesting the onset of possible osteoarticular involvement.

Given the suspected progression of the systemic clinical condition, marbofloxacin (Marbopet®) at 2 mg/kg/SID orally for 28 days was added to the existing protocol with prednisolone, allopurinol, and domperidone. Additional tests were requested—including serology for *Ehrlichia canis and Babesia* spp.,

urea, creatinine, urinalysis, and urinary protein-to-creatinine ratio—to assess possible comorbidities that could explain the lack of response to the instituted therapy, as well as potential systemic disease progression despite treatment. The patient did not return for clinical reassessment or for evaluation of the requested test results. Approximately 45 days after the last evaluation, the patient died, likely due to systemic complications of canine visceral leishmaniasis (CVL).

Discussion

The diagnosis of canine visceral leishmaniasis (CVL) was initially suspected based on clinical, cutaneous, and systemic manifestations, combined with a history of travel to an endemic region—Goiás, in the Central-West of Brazil—and was confirmed through complementary diagnostic tests. The visualization of amastigote forms within macrophages in the cutaneous cytopathological examination, along with an ELISA titer three times higher than the cut-off value, was sufficient for definitive diagnosis, as cytology has 100% specificity and ELISA titers at least three times above the cut-off are considered diagnostic (Hernandez-Bures *et al*., 2021; Larsson; Lucas, 2022). Clinical signs such as pruritus, ulcerative lesions, onychogryphosis, whitish scales, temporal muscle atrophy, and lameness are described in CVL, although they are nonspecific (Larsson; Lucas, 2022). Although the IFA result was reactive, it was interpreted in conjunction with other complementary test results to ensure proper diagnostic correlation, since positive CVL results may also occur in infections caused by *T. cruzi*, *E. canis*, *T. gondii*, *N. caninum*, and *B. canis* (Zanette *et al*., 2014).

Additional complementary tests—including complete blood count, renal and hepatic biochemical profiles, serum proteins, and urinalysis—were essential for disease staging, treatment planning, and prognosis (Brasileish, 2018). According to Brasileish (2018), the patient described in this report fits stage IV of CVL, with a guarded to poor prognosis, based on parasitological findings, hypergammaglobulinemia, and clinical signs indicative of immune complex deposition, such as vasculopathic lesions and suspected arthritis.

The treatment aimed to reduce the parasitic load, as parasitological cure cannot be achieved in cases of CVL (Ayres *et al*., 2022). Miltefosine (Milteforan®) was used in combination with allopurinol due to their leishmanicidal and leishmaniostatic effects, respectively, along with domperidone for its immunomodulatory action favoring a Th1 response (Larsson; Lucas, 2022).

The response to treatment is correlated with the type of immune response developed by the patient in response to infection, which may be classified as Th1 or Th2. Macrophages infected with amastigote forms act as antigen-presenting cells for CD4+ T lymphocytes, leading to the production of interleukins that promote the differentiation of Th1 and Th2 lymphocytes. Infected dogs with a predominance of the Th1 response produce pro-inflammatory cytokines, playing a key role in controlling the infection. Conversely, those with a predominance of the Th2 response are more prone to antibody production, particularly of the IgG class, which is responsible for the formation of immune complexes. These complexes may deposit in various tissues, leading to different clinical manifestations such as arthritis, glomerulonephritis, uveitis, and vasculopathic cutaneous lesions, thereby contributing to disease progression—even in the presence of appropriate treatment (Larsson; Lucas, 2022; Brasileish, 2018). Given the clinical manifestations suggestive of immune complex deposition—namely vasculopathic skin lesions and suspected arthritis—a possible explanation for the refractoriness to the instituted therapy, and consequently the disease progression observed in the dog described in this report, would be the presumed predominance of a Th2 response and/or the possibility of *Leishmania* spp. resistance to miltefosine, as previously reported by some authors (Carvalho *et al*., 2022).

Another cause of refractoriness in the treatment of CVL is coinfection—such as babesiosis and ehrlichiosis—which contributes to immunosuppression, favoring disease progression and worsening prognosis (Beasley *et al*., 2021). The inability to perform complementary diagnostic tests during

the course of treatment prevented the assessment of potential comorbidities that might have been associated with treatment failure, as well as the systemic progression of leishmaniasis that ultimately led to the patient's death.

Final considerations

The CVL is a zoonosis of significant public health importance. Its treatment is challenging due to high costs, the need for frequent laboratory monitoring, and dependence on the animal's immunological profile, which directly influences therapeutic success and infection control. &

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- **Conflicts of interest:** The authors declare no conflicts of interest.
- **Ethical approval:** This study adhered to ethical standards throughout its development. It was not submitted to an ethics committee, as it consists solely of a case description conducted the routine activities of a veterinary dermatology service in a private institution.
- **Data and materials availability:** The data and materials used in this study are available at www.pubmed.com and www.scielo.com.
- **Author contributions:** The first author, PAIXÃO, E., contributed to the literature review, organization of information related to the reported case, and manuscript writing. The second author, ODAGUIRI, J., contributed by providing the clinical case, as well as supervising and revising the manuscript.

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