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CASE REPORT

DISSEMINATED CUTANEOUS LEISHMANIASIS: LESIONAL POLYMORPHISM AND LATE DIAGNOSIS IN AN IMMUNOCOMPETENT PATIENT

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ABSTRACT

Tegumentary leishmaniasis (TL) is considered a neglected tropical disease and it is endemic in Brazil. Among the wide morphological spectrum that composes TL, the disseminated cutaneous leishmaniasis (DL) stands out, which is characterized by multiple lesions in two or more non-contiguous body regions. This clinical form may be rarely associated with immunosuppression. The wide range of cutaneous manifestations is a remarkable DL feature, and its diagnosis may represent a challenge even for the specialists and experienced professionals. We report a case of an immunocompetent 55-year-old man, who has presented with polymorphic and disseminated skin lesions and he was treated incorrectly due to the absence of clinical suspicion of leishmaniasis.

KEY WORDS: *Leishmania; Leishmania braziliensis*; leishmaniasis.

INTRODUCTION

Considered as a neglected tropical disease, leishmaniasis is an infection caused by protozoa of the genus *Leishmania* and it is transmitted by the vectors female sand flies *Phlebotomus* and *Lutzomyia* (de Vries et al., 2022). It is separated into two main clinical forms: visceral leishmaniasis (VL or kala-azar) and tegumentary leishmaniasis (TL), with a wide morphological spectrum and multiple variants (Kaye et al., 2020). The infection is endemic in almost 100 countries, and two million new cases are registered every year (Sasidharan et al., 2021; de Vries et al., 2022). Brazil is one of the top 10 countries with higher rates of TL, this group accounts for 75% of cases of the disease (Lopes et al., 2023). Autochthonous occurrence of tegumentary leishmaniasis have been reported in all Brazilian States (Anversa et al., 2018).

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Despite being endemic in Brazil, TL may represent a diagnostic challenge even for specialists and experienced professionals. The diverse clinical manifestations, some rare and nonspecific, are responsible for the incorrect diagnosis which culminates in inadequate treatment, local and systemic complications (Gurel et al., 2020). We report a case of a 55-year-old man with polymorphic and disseminated skin lesions, who was treated incorrectly in other services due to the absence of clinical suspicion of leishmaniasis.

CASE REPORT

A 55-year-old man, who was born in the city of Afonso Cláudio, Espírito Santo State, a rural worker, former smoker and former alcoholic, reported in the emergency room with skin lesions with itching and burning sensation on his face and scalp for about three months. After a few days, pustules erupted on his back, trunk, and lower limbs, which evolved to rupture and formation of crusts. The patient denied he had had any fever, adynamia, arthralgia and myalgia, however he reported unexplained weight loss (10 kg) during the period. Previously, he had been medicated with benzathine penicillin and promethazine, under the suspicion of pyodermitis. At another appointment, he was submitted to therapy with topical corticosteroids, due to the hypothesis of pharmacodermia, which also his body did not respond to. Two weeks after, he had a secondary myiasis in the left lateral malleolar lesion and he was admitted in another hospital. During this examination, erythematous papules with a center covered by blood crust and an erythematous halo on his face were noted (Figure 1a), as well as infiltrated erythematous crusted papules and some pustules on his trunk, back and upper limbs (Figures 1b, 1c, 2a and 2b). On his lower limbs, the exulcerations covered by crusts predominated, associated with infiltrated erythematous papules (Figure 2c). There was tachycardia (102 bpm) and palpable hepatomegaly 4.5 cm from the right costal margin, without lymphadenopathy or mucosal lesions.

The diagnostic hypotheses of malignant syphilis, disseminated cutaneous leishmaniasis, and paracoccidioidomycosis were suggested. Rapid syphilis, HIV and hepatitis B and C tests were negative. Materials were obtained from skin scarification of the lesion edge for smears. Direct microscopy revealed the presence of *Leishmania* amastigotes, although rare in this situation, in addition to a mononuclear infiltrate without granulomas or plasma cells (Figure 3). Renal function and other laboratory tests did not show alterations, as well as the electrocardiogram. A diagnosis of the disseminated cutaneous form of tegumentary leishmaniasis was established, and treatment with intravenous meglumine antimoniate was prescribed. Shortly after the beginning of this therapy, the patient evolved with improvement of previous skin lesions, however he had the appearance of lesions on his penis and on his right nasal septum. Throughout the treatment, there was a complete resolution of the cutaneous-mucosal condition. After one year of follow-up, there were no clinical signs of recurrence.

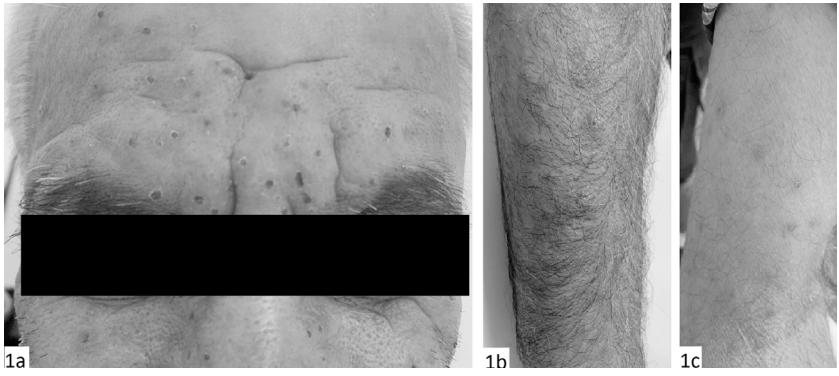

Figure 1. (1a) During the examination, the patient had erythematous papules with the center covered by hematic crust and an erythematous halo on the patient´s face; (1b) Infiltrated erythematous crustal papules on the right forearm; (1c) Infiltrated erythematous papules on the left arm.

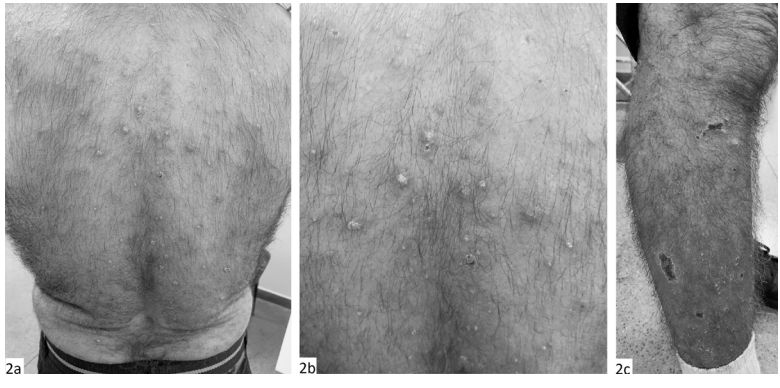

Figure 2. (2a) On the back, the physical examination revealed multiple infiltrated erythematocrust papules, interspersed with some pustules; (2b) Detailed lesions on the back; (2c) Exulcerations covered by crusts and infiltrated erythematous papules on the right leg.

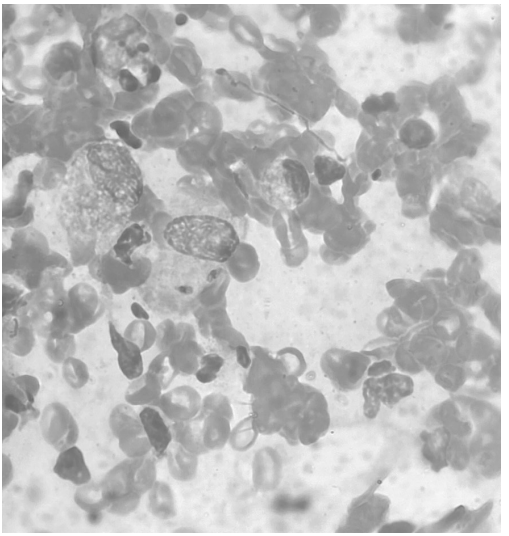

Figure 3. Rare amastigotes of *Leishmania* sp. observed on the direct examination.

DISCUSSION

The TL is the most common form of leishmaniasis, accounting for 600,000 to 1 million new cases per year (de Vries et al., 2022). In Brazil, the infection is endemic, and between the years of 2009 and 2017, more than 176,000 cases of TL were diagnosed. In this period, the detection rate in the country was 9.7 per 100,000 inhabitants (Lopes et al., 2023). TL may be associated with a decrease in quality of life, formation of unsightly scars, stigmatization, and the appearance of psychological disorders, which are often serious (Gurel et al., 2020). Therefore, an early diagnosis and treatment are considered extremely important (Gurel et al., 2020; Kaye et al., 2020; Sasidharan et al., 2021; de Vries et al., 2022).

According to the characteristics of the parasite, the immune response of the host, the location of the vector bite and the clinical evolution, TL may be classified into localized cutaneous leishmaniasis (LCL), disseminated cutaneous leishmaniasis (DL), diffuse or anergic cutaneous leishmaniasis (DCL) and mucosal leishmaniasis (ML) (Anversa et al., 2018; Burza et al., 2018). LCL is the most frequent clinical manifestation of leishmaniasis, which is characterized by the appearance of erythematous papules adjacent to the sand fly bite site, which evolve into nodules and, later, circumscribed ulcers (Burza et al., 2018; Gurel et al., 2020; Volpedo et al., 2021). Spontaneous cure occurs in 0% to more than 70% of patients (Morizot et al., 2013). In LM, destructive lesions are observed in the nasal septum, lips and palate,

often accompanied by rhinorrhea or epistaxis (Burza et al., 2018; Gurel et al., 2020). More than 90% of the cases are preceded or concomitant with LCL, the vast majority determined by hematological spread of the parasite (Burza et al., 2018; Sasidharan et al., 2021; Volpedo et al., 2021). DCL is less common, affects immunocompromised patients and establishes itself slowly and persistently, with papules and tubercles on the extremities or face, which spread without ulceration (Burza et al., 2018; Gurel et al., 2020; Volpedo et al., 2021). The disease, in addition to being chronic, tends to be refractory to treatment. Characteristically, the dermis is teeming with protozoa (Burza et al., 2018; Gurel et al., 2020; Volpedo et al., 2021).

Patients with disseminated cutaneous leishmaniasis (DL), as described, exhibit multiple lesions affecting two or more non-contiguous body regions (Burza et al., 2018; Sasidharan et al., 2021). This clinical form is considered rare, although emerging in northeastern Brazil, regarding only for 1.9% of all TL cases (Volpedo et al., 2021). Immunosuppression is considered a risk factor for DL, although it is also observed in young and immunocompetent individuals (Gurel et al., 2020; Sasidharan et al., 2021; Volpedo et al., 2021). There may be a combination of papular, nodular, acneiform and ulcerative manifestations, with nasal mucosa involvement being common (up to 44% of cases). The dissemination of the parasite is fast, and new lesions appear in days to weeks (Burza et al., 2018; Sasidharan et al., 2021; Volpedo et al., 2021). Unlike DCL, in DL there are few parasites in the lesions, and these often ulcerate (Gurel et al., 2020; Volpedo et al., 2021). This demonstrates the importance of the immune response in the determination of clinical manifestations (Burza et al., 2018; Gurel et al., 2020).

In DL, such as the case described in this report, there is a temporary initial impairment of the adaptive response, allowing the hematological dissemination of the parasite (Burza et al., 2018; Kaye et al., 2020). CXCL9, a T-cell chemoattractant, is increased, and attracts T lymphocytes to the lesion site, with a reduction in systemic Th1 activity and low levels of peripheral IFN-γ and TNF-α. In the lesioned territory, on the other hand, IL-10, TNF-α and IFN-γ were found at levels similar to those in the LCL (Kaye et al., 2020; Volpedo et al., 2021; de Menezes et al., 2022).

The diagnosis of TL is based on epidemiology, clinical presentation and laboratory tests (Gurel et al., 2020; de Vries et al., 2022). As in the reported case, the characteristic lesioned pleomorphism of the disease may make diagnosis difficult based only on the physical examination (Kaye et al., 2020; de Vries et al., 2022). The wide variety of skin and mucosal lesions in TL results in extensive differential diagnosis, including impetigo, ecthyma, furunculosis, leprosy, tuberculosis, atypical mycobacterial infections, syphilis, deep fungal infections (such as sporotrichosis, blastomycosis, mycetoma, histoplasmosis), sarcoidosis, pyogenic granuloma, lupus and neoplasms (Burza et al., 2018; Gurel et al., 2020).

Multiple propaedeutic methods have been described, with variable diagnostic accuracy (Gurel et al., 2020; Kaye et al., 2020; Kumari et al., 2021). In general, however, the observation of amastigotes in a single sample, obtained by aspirate, biopsy or culture material, establishes the diagnosis, as reported in this paper (Burza et al., 2018; Kumari et al., 2021). Specially in disseminated cutaneous leishmaniasis, the high titers of anti-*Leishmania* antibodies stand out in comparison to the other clinical forms of TL, being related to increased mucosal involvement (Volpedo et al., 2021).

Traditionally, pentavalent antimony is considered the first-line treatment in TL (Brasil, 2017; Carvalho et al., 2019; Gurel et al., 2020; Kumari et al., 2021; Sasidharan et al., 2021; de Vries et al., 2022). The treatment for DL should be performed in a reference center with parenteral meglumine antimoniate, as noted in this report. In severe cases or with a large number of lesions (over 20) and in patients older than 50 years of age, pregnant women, kidney transplant recipients or patients with renal, cardiac and hepatic failure, liposomal amphotericin B is indicated as the first choice (Ministério da Saúde, 2017). In this reported case, the patient evolved with a satisfactory clinical response, and remained without lesions after 12 months of follow-up.

TL may manifest itself in atypical or unusual ways, and a high index of clinical suspicion is required to consider it as a diagnosis, even in endemic areas. In the reported case, the patient was evaluated by multiple health professionals before the hypothesis of DL was suggested. Although the cutaneous forms of leishmaniasis are associated with a better prognosis, the sequelae potentially resulting from the late diagnosis involve cutaneous and invisible scars, such as low self-esteem, rejection and depression.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest to disclose.

REFERENCES

1. Anversa L, Tiburcio MGS, Richini-Pereira VB, Ramirez LE. Human leishmaniasis in Brazil: A general review. *Rev Assoc Med Bras 64*: 281-289, 2018.
2. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância das Doenças Transmissíveis. *Manual de Vigilância da Leishmaniose Tegumentar*. 2017. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/manual_vigilancia_leishmaniose_tegumentar.pdf Accessed in: 04.jan.2023.
3. Burza S, Croft SL, Boelaert M. Leishmaniasis. *Lancet 392:* 951-970, 2018.
4. Carvalho SH, Frézard F, Pereira NP, Moura AS, Ramos LMQC, Carvalho GB, Rocha MOC. American tegumentary leishmaniasis in Brazil: a critical review of the current therapeutic approach with systemic meglumine antimoniate and short-term possibilities for an alternative treatment. *Trop Med Int Health 24*: 380-391, 2019.

5. de Menezes JPB, Brodskyn C, Gonçalves R, Bacellar O. Editorial: Immunology and immunopathogenesis of human leishmaniasis. *Front Cell Infect Microbiol 12*: 1055221, 2022.
6. de Vries HJC, Schallig HD. Cutaneous Leishmaniasis: A 2022 Updated Narrative Review into Diagnosis and Management Developments. *Am J Clin Dermatol 23*: 823-840, 2022.
7. Gurel MS, Tekin B, Uzun S. Cutaneous leishmaniasis: A great imitator. *Clin Dermatol 38*: 140-151, 2020.
8. Kaye PM, Cruz I, Picado A, Van Bocxlaer K, Croft SL. Leishmaniasis immunopathology-impact on design and use of vaccines, diagnostics and drugs. *Semin Immunopathol 42*: 247-264, 2020.
9. Kumari D, Perveen S, Sharma R, Singh K. Advancement in leishmaniasis diagnosis and therapeutics: An update. *Eur J Pharmacol 910*: 174436, 2021.
10. Lopes LC, Trindade GVM, Bezerra JMT, Belo VS, Magalhães FC, Carneiro M, Barbosa DS. Epidemiological profile, spatial patterns and priority areas for surveillance and control of leishmaniasis in Brazilian border strip, 2009-2017. *Acta Trop 237*: 106704, 2023.
11. Morizot G, Kendjo E, Mouri O, Thellier M, Pérignon A, Foulet F, Cordoliani F, Bourrat E, Laffitte E, Alcaraz I, Bodak N, Ravel C, Vray M, Grogl M, Mazier D, Caumes E, L Lachaud, Buffet PA, French Study Group. Travelers with cutaneous leishmaniasis cured without systemic therapy. *Clin Infect Dis 57*: 370-380, 2013.
12. Sasidharan S, Saudagar P. Leishmaniasis: where are we and where are we heading? *Parasitol Res 120:* 1541-1554, 2021.
13. Volpedo G, Pacheco-Fernandez T, Holcomb EA, Cipriano N, Cox B, Satoskar AR. Mechanisms of immunopathogenesis in cutaneous leishmaniasis and post Kala-azar dermal leishmaniasis (PKDL). *Front Cell Infect Microbiol 11:* 685296, 2021.