

LEISHMANIASIS: A CASE REPORT IN THE INTERIOR OF SÃO PAULO

Flaviana Rossato

Gabriela Rosânia Dantas Moysés

Jorge Luis dos Santos Pereira

Luiza Teodoro Campos Faleiros

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Abstract: Leishmaniasis is a neglected tropical disease of great importance in global public health, more than 1 billion people live in endemic areas at risk of infection around the world. Such a disease is caused by intracellular protozoa from the family Trypanosomatidae and genus *Leishmania*; where the literature describes about 20 species of *Leishmania*, the variety of species is related the many different manifestations clinics. To the Leishmaniasis are divided into two large groups: visceral leishmaniasis (VL) and cutaneous leishmaniasis (LT). The integumentary form of the disease is the most common clinical spectrum of leishmaniasis and can present in three different forms: cutaneous leishmaniasis, mucocutaneous leishmaniasis and diffuse cutaneous leishmaniasis. The present study aims to carry out a case report of a female patient, 22 years old, without comorbidities, resident in the city of Franca-SP, referred to the outpatient clinic school of Infectious Diseases due to a cat scratch, causing a painful and itchy ulcerated lesion on the left lower limb, measuring approximately 2.5 cm, in a circular shape. Due to the appearance of the lesion and the anamnesis collected, the initial clinical suspicion was Cat Scratch Disease, Sporotrichosis and Leishmaniasis, therefore, requests were made. serologies for diagnostic investigation and compulsory notification. After requesting the tests, they were subsequently evaluated, with results of reactive IgM and non-reactive IgG for Leishmaniasis. Therefore, treatment for Leishmaniasis was started and a biopsy of the lesion was requested. The work presents the evolution of the lesions, the diagnostic criteria that included clinical and epidemiological data, in addition to monitoring the patient after treatment and resolution of the condition. A brief review of the relevant literature was carried out to better understand the subject. The importance of the report is due to the

fact that it is an unusual case of cutaneous leishmaniasis in the region, that despite the increase in the number of cases and expansion of their geographic occurrence in the country, there is a lack of knowledge on the part of the population and health services regarding the diagnosis. Furthermore, it is essential to control the vectors and the natural history of the disease, so that it is possible to promote health and prevent leishmaniasis, points which are essential in primary care.

Keywords: *Leishmania*; Leishmaniasis; Leishmaniasis integumentary.

INTRODUCTION

Leishmaniasis are infectious-parasitic diseases that affect humans, caused by several species of protozoa of the genus *Leishmania*. The disease can present different clinical forms, depending on the species of *Leishmania* involved and the relationship between the parasite and its host. It is an intracellular infection caused most frequently by *L. (Viannia) braziliensis*, or more rarely, by

L. panamensis or *L. guianensis*. Transmission is carried out by a vector classified as a sandfly, of the genus *Lutzomyia*. According to the WHO, leishmaniasis occurs in 88 countries. According to already recorded cases, 90% occur in just 6 countries: Iran, Saudi Arabia, Syria, Afghanistan, Brazil and Peru. (GOMES, et al., 2004)

Regarding the historicity of American cutaneous leishmaniasis (ATL), historians explain that it is a disease that has affected men since ancient times, as there are narratives and descriptions about the disease found in literature indicating its existence since the 1st century, AD After this period, on the American continent researchers found mummies with skin lesions, characteristic of the disease. In Brazil, the first mention of ATL was made in 1827 by the religious Dom Hipólito Sanches, shortly after his trip

from the State of Amazonas to the country of Peru, in which he traveled through regions of the Amazon Valley, where he noticed signs of the disease in people who lived in this region. Brazilian region and then prepared documents in this regard for the Religious Pastoral. When it comes to the beginning of cases of American cutaneous leishmaniasis in Brazil, the Ministry of Health (2022) points out that the first cases occurred in 1909, when: forms of leishmania were described in cutaneous and nasobuccopharyngeal ulcers in individuals who worked in the construction of highways in the interior of São Paulo. Since then, the disease has been described in several municipalities in all Federated Units. (NOGUEIRA, et al., 2008)

In the country, on average, around 21,000 cases/year are registered, with an incidence rate of 8.6 cases/100,000 inhabitants in the last 5 years. The North region has the highest coefficient (46.4 cases/100,000 inhabitants), followed by the Central-West (17.2 cases/10,000 inhabitants) and Northeast regions (8 cases/100,000 inhabitants). (GOMES, et al., 2004)

American cutaneous leishmaniasis (ATL) constitutes a serious public health problem in Brazil and worldwide, being considered the second most important disease among those caused by protozoa with medical relevance, surpassed only by malaria. (DINIZ, et al., 2011)

The infection cycle involves two stages: the amastigote phase occurs in the form of parasites present in hosts, such as humans, dogs and rodents. The parasites invade macrophages and other reticuloendothelial cells, multiply and cause rupture in the cell membrane, releasing into the bloodstream. When the female insect (phlebotome) feeds on the blood of infected animals, the parasites in her body develop and pass into the promastigote phase. The cycle is completed when the insect inoculates another host, developing the disease. With rare exceptions,

leishmaniasis constitutes zoonoses of wild and, more rarely, domestic animals, including marsupials, toothless animals, carnivores and even primates. Man represents an accidental host and does not seem to have an important role in maintaining parasites in nature. (STOLF, et al., 1993)

Leishmania inoculation causes skin lesions at the entry point, in papulovesicular or impetigoid aspect, which often progresses to spontaneous regression. The infection can continue its natural evolution, emerging cutaneous injuries disseminated and subsequent invasion of the nasopharyngeal mucosa. Therefore, ATL is an infectious, non-contagious disease, caused by different species of protozoa of the genus *Leishmania*, which affects the skin and mucous membranes. (FOLLADOR, et al, 2002) According to the observation of cases of infection in closed populations and identification of the moment of inoculation, an incubation period of ten to 60 days is observed. The predominant clinical form in 95% of reported cases is cutaneous, followed by mucosal in 3%-5% of cases. This disease can affect the skin, viscera or mucocutaneous areas, varying according to geographic areas, different *Leishmania* species and host response. There are 3 clinical entities caused by cutaneous leishmaniasis, such as the cutaneous, diffuse cutaneous and mucocutaneous variants. Cutaneous leishmaniasis is defined by lesions exclusively on the skin, at the point of inoculation of promastigote parasites. (FOLLADOR, et al, 2002)

In most cases, mucosal disease occurs after skin lesions, and the diagnosis of mucosal involvement is established only months to years after clinical healing of the site of initial skin infection. Some patients may present with nasal involvement in the absence of skin disease. Briefly, the diagnosis is clinical and supported by other tests, such as the intradermal skin test.

Montenegro and the biopsy of the lesion in which a direct smear is taken, and culture can be done in hamster or histopathological exam itself, with visualization of the protozoan intracellular. (FOLLADOR, et al, 2002)

The objective of this work was to report a clinical case of mucocutaneous leishmaniasis. The patient was informed about the objectives, methodology, possible risks and benefits of the study, and a written Informed Consent Form was obtained.

CASE REPORT

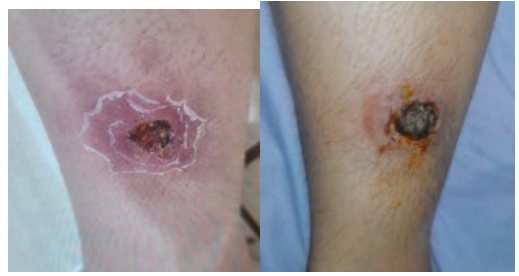
Patient, female, 28 years old, pregnant (33rd week of gestation), sales technician, white. She sought care on 06/07/2023 reporting that two days ago she had suffered a cat scratch and that she was experiencing pain in the area of the wound located on her left lower limb. She denied systemic symptoms. On physical examination, the presence of an ulcer measuring approximately 1 cm in diameter, a hyperemic region with no edema or secretion, preserved peripheral pulses, free calves, without signs of swelling.



Image 1: injury 4 days after it occurred.

At the time, Cephalexin was prescribed 500 mg, every six hours, for seven days and symptomatic.

After one month, in a prenatal consultation with a gestational age of 36S+6D, the use of Kollagenase and Itraconazole was prescribed for one month due to the persistence and evolution of the lesion. Furthermore, he reported that the cat had passed away.



Images 2 and 3: injury during the first month after the injury.

After two months, the lesion evolved into a circular shape with a progressive increase in diameter (approx. 2.5 cm in diameter), ulceration, a clean bottom, raised edges associated with severe pain and secretion leakage. Azithromycin 500 mg was prescribed for 7 days, evolving over the next few days with maculopapular rash.



Image 4: injury 2 months after it occurred.

The next consultation occurred a few days later, and the patient complained of burning epigastric pain, sporadic pain in the suprapubic region and nausea. She denied a fever. In this session, the hypotheses were questioned diagnostics in sporotrichosis, cat scratch disease and cutaneous-mucosal leishmaniasis, and prescribed Neomycin and symptoms.

The case was notified to Epidemiological Surveillance, which advised referral to the Infectious Diseases outpatient clinic.

Three months after the incident, the patient attended the Infectious Diseases outpatient clinic and reported that the wound had

increased in size and was associated with a foul odor, with improvement after starting Kollagenase. On physical examination, there was the presence of an ulcer rounded 5 cm in the left lower limb with the release of a small amount of secretion without a foul odor, presence of granulation tissue and absence of active bleeding. Glucantini was prescribed for thirty days with reassessment after the end of treatment. The search for IgG and IgM antibodies to *Leishmania* was carried out, resulting in reactive IgM and non-reactive IgG.

Approximately four months after the appearance of the lesion, a biopsy was performed, with nonspecific histological results: focus of ulceration with deposition fibrinoleukocyte, epidermis with hyperplasia, without atypia and spongiosis; presence of exudative inflammation and granulation tissue in the dermis; lymphocytic infiltrate in the deep dermis and subcutaneous tissue.



Image 5: injury 3 months after it occurred.

Due to the suspicion of Leishmaniasis, the sample was sent to a support laboratory for additional research, at this time no report is yet available.

After five months, the patient returns to the consultation reporting improvement in pain in the region. The wound looked good, healed without secretions leaking out and without the presence of phlogistic signs and/or alarm signs.



Image 6: injury 5 months after it occurred.

The patient continues to be monitored at the Infectious Diseases Outpatient Clinic in the Municipality of Franca/SP with return visits every 30 days to monitor the clinical condition. In the last consultation, he showed a significant improvement in his condition, which responded to the proposed treatment with Glucantini. It will remain under service monitoring for one year.

CONSENT FOR PUBLICATION

Informed consent written form was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent was given to the patient and is also available for review if necessary.

DISCUSSION

Cutaneous leishmaniasis (CL) is defined by the presence of lesions exclusively on the skin, which begin at the point of inoculation of infective promastigotes, through the vector bite, for any of the *Leishmania* species that cause the disease. (GOMES, et al., 2004)

The primary lesion is generally single, although occasionally multiple sandfly bites or local spread can generate a high number of lesions. It appears after an incubation period varying from 10 days to three months, as an erythematous papule that slowly progresses to a nodule. (GOMES, et al., 2004)

However, the investigation of cutaneous leishmaniasis can be difficult, especially if it occurs chronically or the patient does not come from endemic regions and also due to the vast possibility of differential diagnoses of skin ulcers, such as: traumatic ulcers, stasis ulcers, tropical ulcers of the lower limbs due to sickle cell anemia, pyoderma, paracoccidioidomycosis, neoplasms, syphilis and cutaneous tuberculosis. The differential diagnosis of mucosal manifestations may reveal paracoccidioidomycosis, lepromatous leprosy, rhinoscleroma, yaws, tertiary syphilis, midfacial granuloma and neoplasms. (GOMES, et al., 2004)

Mucous leishmaniasis (LM), also called spundia, is a condition that is difficult to treat and has a poor prognosis regarding the possibility of cure. It is associated with *L. braziliensis*, in most cases occurring within a variable time interval after the onset of the initial skin lesion. (NETTO, et al., 1995)

The factors that contribute to an initially cutaneous disease progressing to this late form are not completely known, but it is known that delay in healing of the primary lesion and inadequate initial treatment may be associated. (NETTO, et al., 1995)

Mucosal involvement may appear while the skin lesion is still active, or years after its occurrence.

healing. Among the mucous lesions, the following varieties can be distinguished: ulcerative-infiltrating, polyposis and terebranous forms. Early diagnosis of mucosal leishmaniasis is the main challenge of the American Tegumentary Leishmaniasis Surveillance Program of the Ministry of Health, which aims to reduce deformities caused by the disease. The investigation covers epidemiological aspects, clinicians It is laboratory (parasitological research and immunological diagnosis). (NETTO, et al., 1995)

Often the association of some of these elements is necessary to reach the final diagnosis. Parasitological diagnosis is the diagnosis of certainty and is only obtained by demonstrating the parasite, which can be achieved through different parasitological techniques of direct and indirect research. The simplest examination, and for this reason generally the first to be carried out, is the direct search for amastigote forms in material obtained from the lesion by scarification, aspiration or edge biopsy, stained with Giemsa or Leishman. (ALMEIDA and SANTOS, 2011)

The chance of finding the parasite is inversely proportional to the duration of the lesion and the sensitivity of the method in cases produced by *L. braziliensis* is around 100% in the first two months of evolution, 75% at six months and 20% above of 12 months. Furthermore, the polymerase chain reaction (PCR) is a test that allows DNA sequences to be amplified on an exponential scale. Endowed with high sensitivity, it is capable of detecting quantities as small as 1 femtogram (1 femtogram = 10⁻¹⁵g) of *Leishmania* DNA, equivalent to 1/10 of the parasite. However, technical requirements and relatively high costs still limit their routine use. (ALMEIDA and SANTOS, 2011)

Among immunological diagnoses, we have: Montenegro intradermal reaction (IDRM) which detects the presence of delayed hypersensitivity since, immunologically, ATL is characterized by the appearance of a cellular response during the disease and after the infection has been cured, whether spontaneously or after treatment. Furthermore, among the serological methods, the immunofluorescence reaction indirect (RIFI) is the most used. It is a sensitive technique, but with the possibility of cross-reactions, especially with Chagas disease and kala-azar. (ALMEIDA and SANTOS, 2011)

RIFI presents variable results in ATL, either due to the reduced antigenicity of the parasite or the low levels of circulating antibodies. Usually negative in the diffuse cutaneous form, its sensitivity was estimated at 71% in the cutaneous form and 100% in the mucosal form. In patients with recent lesions (one to six months of evolution), serological negativity is common. In positive cases, average titers are significantly higher in those with multiple lesions, reflecting the greater antigenicity induced by the greater number of parasites. (ALMEIDA and SANTOS, 2011)

Furthermore, the number of negative serological reactions is higher among those who have a positive parasitological test when compared to those in whom direct parasite testing is negative. After treatment and healing, the titers may fall or disappear in some months. (ALMEIDA and SANTOS, 2011)

The drug of first choice is pentavalent antimony, available in two forms: N-methylglucamine antimoniate and sodium stibogluconate, the latter of which is not sold in Brazil. In order to standardize the therapeutic regimen, the World Health Organization (WHO) recommends that the antimony dose be calculated in mg/SbV/Kg/day. (SbV = pentavalent antimony). This antimonial is indicated for the treatment of all forms of cutaneous leishmaniasis, although mucous forms require greater care and may present slower responses and a greater possibility of relapses. Ulcerated lesions may suffer secondary contamination, which is why local care must be prescribed. Amphotericin B, a polyene antibiotic with

recognized leishmanicidal action, is the drug of second choice, used when there is no response to treatment with an antimonial or when its use is impossible. Considered more effective than antimonials in the treatment of mucosal lesions, it is presented in 50 mg vials (Fungizonâ) for IV use. (STOLF, et al., 1993)

The cure criterion is clinical, monthly follow-up is recommended for three consecutive months and, after clinical cure, follow-up for up to 12 months after the end of treatment. In the cutaneous form, the cure criterion is defined by the clinical appearance of the lesions: re-epithelialization of ulcerated or non-ulcerated lesions, total regression of infiltration and erythema, up to three months after completion of the therapeutic regimen. And in the mucous form, it is defined by the regression of all signs and confirmed by otorhinolaryngological examination, up to six months after completion of the therapeutic regimen. (BRACHO, et al., 2007)

Knowing the population affected by ATL in our country is of fundamental importance for establishing effective measures to control the disease. The differences in morbidity, response to treatment and prognosis, related in part to the species of *Leishmania*, highlight the importance of characterizing the parasite prevalent in a given region. Therefore, we trust that this study can also contribute to researchers in the development of new studies on high. The main purpose is to alleviate suffering of people, mainly those most socially vulnerable, as demonstrated, they are the most likely to be infected by American cutaneous leishmaniasis. (BRACHO, et al., 2007)

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