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Case Report

Sporotrichoid cutaneous leishmaniasis: atypical form

Walter Belda*, Pablo A. Vale, Caroline H. C. Carvalho

Department of Dermatology, Faculty of Medicine, University of São Paulo, São Paulo, Brazil

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***Correspondence:**
Walter Belda,
E-mail: walterbelda26@gmail.com

ABSTRACT

Leishmaniasis comprises a heterogeneous and extensive group of infectious and non-contagious diseases caused by protozoa of the genus *Leishmania* spp. It is a disease considered endemic in 92 countries, with at least 1 million new cases of integumentary forms annually. Cutaneous leishmaniasis is endemic in the tropics and neotropics. It is often referred to as a group of diseases because of the varied spectrum of clinical manifestations, which range from small cutaneous nodules to gross mucosal tissue destruction. Cutaneous leishmaniasis can be caused by several *Leishmania* spp. and is transmitted to human beings and animals by sandflies. Despite its increasing worldwide incidence, because it is rarely fatal, cutaneous leishmaniasis has become one of the so-called neglected diseases, In endemic countries, diagnosis is often made clinically and, if possible, by microscopic examination of lesion biopsy smears to visually confirm leishmania parasites as the cause. Cutaneous leishmaniasis often presents as an ulcerated lesion, with raised, infiltrated edges, classically described as frame-like edges at the site of the mosquito bite. We report an uncommon case of a patient who presented with a lesion on the face, sporotrichoid in appearance, and thigh, which appeared simultaneously, of clinical lesions of cutaneous leishmaniasis, laboratory-confirmed and which showed excellent clinical evolution with the use of liposomal amphotericin B.

Keywords: Cutaneous leishmaniasis, Sporotrichoid leishmaniasis, Treatment, Liposomal amphotericin B

INTRODUCTION

Leishmaniasis is a tropical and subtropical disease caused by an intracellular parasite transmitted to humans by the bite of a sandfly, mainly *Phlebotomus* and *Lutzomyia*.[1,2] According to the WHO, leishmaniasis is one of the seven most important tropical diseases and it represents a serious world health problem that presents a broad spectrum of clinical manifestations with a potentially fatal outcome.[3] The clinical features include a broad range of manifestations with different degrees of severity that depend on the species of *Leishmania* involved and the immune response of the host.[3]

It is endemic in Asia, Africa, the Americas, and the Mediterranean region. In the American continent, it is mainly a jungle zoonosis, transmitted by sand flies mainly of the genera *Phlebotomus* and *Lutzomyia*. It is found in many countries, from the southern United States to the northern provinces of Argentina with the exceptions of Chile, Uruguay, and El Salvador.[4-6] In Latin America, it is estimated that around 60,000 new cases occur each year. The disease is typical of environments with an altitude of 0 to 1500 m above sea level, temperatures higher than 20 °C, and an annual rainfall of 1,500 to 3,000 mm.[2,7]

The clinical features vary depending on the parasite's characteristics and on the genetic aspects of the host that determine the effectiveness of the immune response. According to the clinical manifestations, it can be divided into cutaneous (localized and disseminated); muco-cutaneous; and visceral or kala-azar.[2] LTA is characterized by a rich and heterogeneous expression, which begins after an incubation period of between 2 weeks and up to 2 years, most commonly around 1

month. Its different clinical manifestations depend on several factors: the environment in the endemic area, genetic variations between *Leishmania* species and strains, and the host's immune response. The main clinical forms of LTA are divided into: cutaneous leishmaniasis (CL); mucous leishmaniasis (LM); disseminated leishmaniasis (LD) and diffuse cutaneous leishmaniasis (LCD). CL is the most common clinical form of LTA in different endemic areas with a predominance of *L. braziliensis* or *L. guyanensis*.[8,9]

The lesions are rounded, oval or occasionally irregular, with raised and infiltrated edges and a grainy base. They are mainly located in exposed areas with a predilection for the lower limbs.[10] Bulky regional adenopathy is very common (approximately 85% of cases), especially in the initial phase of the disease, and often precedes ulceration. Lymphangitis can also occur, with or without adenopathy and, eventually, ulcers can appear along the path. This appearance is called sporotrichoid.[11-13]

Diagnosis is based on the clinical and epidemiological context. The protozoan is found in the scraping of cutaneous or mucosal ulcerations (especially scraping the borders) as well as in non-ulcerated lesions.

Histopathological examination, may reveal atrophy or hyperplasia of the epidermis and an inflammatory process rich in macrophages, lymphocytes, and plasma cells. In the initial phase of infection, parasites can be recognized in cytoplasmic vacuoles within histiocytes, and in the late stages, infected macrophages are less numerous with few amastigote forms and lymphohistiocytic infiltrate forming tuberculoid granuloma.[2]

Culture can be performed in NNN medium or in a variant of the Evans biphasic medium.[14,15] The Montenegro skin test is sensitive and specific. It is positive for the localized forms and negative for the anergic forms; a positive test supports the diagnosis (especially when the patient does not live in endemic areas), but a negative test does not exclude it. This allergic index is useful to determine whether previous contact with the parasite has occurred, even in the absence of lesions. A positive skin test is when the reaction is greater than 5 mm after 72 hours.[16,17] The parasites are observed in the smear or in the imprint stained with Giemsa or Wright; this is the most common and useful diagnostic method.[4,16]

The complement fixation test is used to detect antibodies; titers equal to or above 1:8 are consistent with infection, as are titers equal to or above 1:16 in immunofluorescence tests. However, lower titers do not exclude the infection.[18]

PCR has a reported specificity in LCL of 100% with an improved sensitivity of 20 to 30% when compared with conventional parasitology diagnosis; it can also be used in cases of mucosal leishmaniasis.[4]

Skin lesions of leishmaniasis must be differentiated from cases of *Pyoderma gangrenosum*, traumatic ulcers, ecthyma, furunculoid myiasis, sarcoidosis, cutaneous neoplasms, atypical mycobacteriosis, cutaneous tuberculosis and systemic mycoses such as paracoccidiodomycosis and sporotrichosis.[19]

We reported below a rare case of an immunocompetent patient who simultaneously presented with sporotrichoid cutaneous leishmaniasis on the face and classic lesions of cutaneous leishmaniasis on the right thigh.

CASE REPORT

A 66-year-old patient, from the rural area of Januária (Minas Gerais), where he worked on a small farm, presents with a lesion on the right hemiface that began in April 2023 as a discrete papular, infiltrated lesion, which quickly evolved into ulceration, with mild local pain and right submandibular lymph node infarction. After approximately 2 weeks, new lesions appeared, erythematous and infiltrated, following a trajectory towards the right ear pinna, with the appearance of new ulcerated lesions and infiltration with erythema of the right auricular lobe, with papular and ulcerated lesions, with well-defined edges, covered by crust. serous, on an erythematous and infiltrated base, accompanied by mild local pain (Figure 1). Simultaneously, two initially erythematous papular infiltrated lesions appear, which quickly evolve into ulceration, with well-defined edges, covered by serous crusts, approximately 0.5 cm in diameter each, on the external surface of the right thigh, without symptoms (Figure 2). The patient denied using oral medications, reporting only the use of neomycin ointment twice a day since the onset of the condition, without improvement. A histopathological examination of the right preauricular lesion and a lesion on the right thigh was performed, which revealed an epidermis with hyperparakeratosis, hypogranulosis, and irregular acanthosis. In the dermis, there was a lymphohistiocytic infiltrate with numerous superficial and deep plasma cells with outlines of granuloma, presenting rounded bodies compatible with leishmania (Figure 3 A and B). The specific histochemical examination of this material was positive for leishmania, as well as the PCR exam. Simultaneously with the biopsy, material was collected from the edge of the ulcer on the face and an imprint of the material was made with Giemsa stain, material was also collected from the edge of the thigh ulcer by fine needle aspiration, both material collections revealed the presence of amastigote forms in the collected material. The IDR Montenegro reaction test showed a positive result of 9 mm.

Biochemical tests and serology for syphilis, HIV, and viral hepatitis were normal or negative. Due to the patient's age, it was decided to start treatment with liposomal amphotericin B, at a dose of 3 mg/kg/day intravenously, having received a total dose of 2250 mg. The patient progressed without clinical or laboratory

complications, having adequately tolerated the infusion, progressing with significant improvement in the lesions, with a significant reduction in erythema and infiltration, with no further complaints of local pain and disappearance of the submandibular lymph node infarction. She returned after 60 days for outpatient follow-up, presenting fully healed thigh lesions, as well as ulcerated facial lesions, also presenting mild diffuse erythema on the face and a completely de-infiltrated ear lobe. Remains under monthly outpatient follow-up.

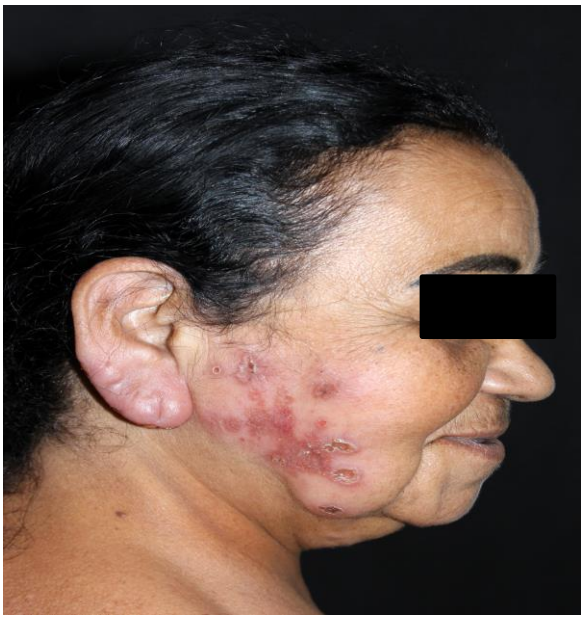

Figure 1: Papular and ulcerated lesions, with well-defined edges, covered by a serous crust, on an erythematous and infiltrated base.

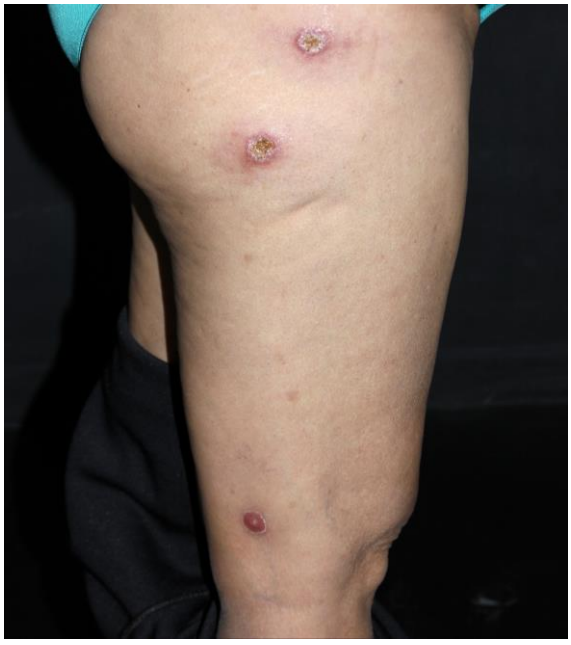

Figure 2: Ulcerated lesions, with well-defined edges, covered by serous crusts, approximately 0.5 cm in diameter each.

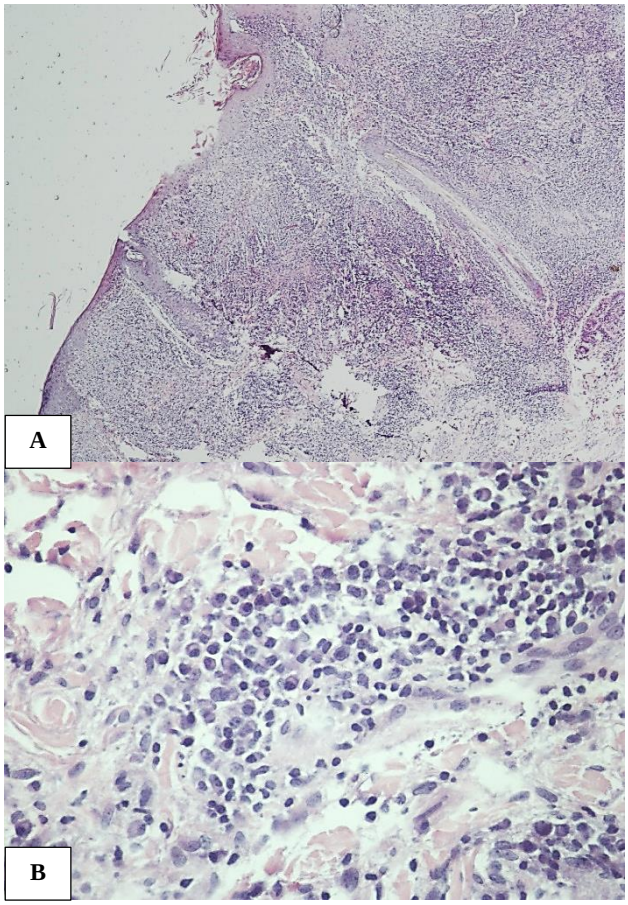

Figure 3: (A) Epidermis with hyperparakeratosis, hypogranulosis, and irregular acanthosis; in the dermis, there was a lymphohistiocytic infiltrate with numerous superficial and deep plasma cells with outlines of granuloma; (B) epidermis with hyperparakeratosis, hypogranulosis, and irregular acanthosis; in the dermis, there is a lymphohistiocytic infiltrate with numerous superficial and deep plasma cells with outlines of granuloma.

DISCUSSION

The leishmaniases afflict the world's poorest populations. Among the two million new cases each year in the 88 countries where the disease is endemic. Human infections with *Leishmania protozoan* parasites, transmitted via the bite of a sandfly, cause visceral, cutaneous, or mucocutaneous leishmaniasis

Leishmaniases are a clinically heterogeneous group of diseases caused by protozoa of the genus *Leishmania*. There is growing evidence that the true incidence of the disease is underestimated, especially in hyperendemic regions. Moreover, climate changes together with the increasing movement of humans and animals raise concerns about the possible introduction of *Leishmania* infection in previously spared areas.[20]

It is caused by numerous *L. protozoa* species, which are responsible for its clinical diversity.

The wide variety of *Leishmania* species responsible for human American cutaneous leishmaniasis combined with the immune mechanisms of the host results in a large spectrum of clinical, histopathological, and immunopathological manifestations. At the middle of this spectrum are the most frequent cases of localized cutaneous leishmaniasis (LCL) caused by members of the subgenera *Leishmania* and *Viannia*, which respond well to conventional therapy. At the middle of the clinical spectrum, LCL with one or multiple ulcerated skin lesions represents the most frequent form of the disease, having as the etiologic agent any member of the neotropical subgenera *Viannia* and *L. braziliensis*.[21] Depending on the infecting species, an infection with Leishmania parasites can give rise to three clinical manifestations. The first is localized CL with single to multiple skin ulcers, satellite lesions, or nodular lymphangitis. The second is CL with MCL and the third is systemic visceral leishmaniasis (VL) with involvement of internal organs, such as the liver, spleen, and bone marrow, which is lethal if not appropriately treated.[22] The diagnosis of CL is based on clinical features (supported by epidemiologic data) and laboratory testing. Numerous diagnostic methods have been described with a huge variation in diagnostic accuracy, including direct parasitologic examination (microscopy, histopathology, and parasite culture) and/or indirect testing with serology and molecular diagnostics. The selection of the diagnostic test employed often depends on the available infrastructure and resources of the diagnostic facility and not on diagnostic accuracy.[23] Parasitologic diagnosis is still considered the gold standard in leishmaniasis diagnosis because of its high specificity. This is typically undertaken by histopathologic examination of fixed tissue or parasite in vitro culture from material from suspected lesions. Microscopical diagnosis of CL is performed by the direct identification of amastigotes in Giemsa-stained lesion smears of biopsies, scrapings, or impression smears. Amastigotes appear as round or oval bodies, about 2-4 mm in diameter, with characteristic nuclei and kinetoplasts. The material from the ulcer margin usually has the highest yield. A comparative study between widely used scraping smears and fine needle aspiration cytology found a significant difference between the two methods in favor of fine needle aspiration in the detection of amastigotes and microgranuloma, slide background, and patient comfort.[24]

Parasite culture in tubes containing Novy-MacNeal-Nicolle medium from suspected lesions is difficult, requires significant technical expertise, is prone to contamination, and is time consuming.[25]

Many molecular diagnostic tests have been developed for the diagnosis of CL, as these are assumed to have better sensitivity and specificity than traditional diagnostic methods and allow the use of less invasive sampling for diagnosis. In particular PCR, either as a single test or in a nested format, or as a quantitative assay, has been widely exploited.[26,27]

Atypical clinical forms of cutaneous leishmaniasis are uncommon, particularly that classified as sporotrichoid form, characterized by the presence of lymphangitis, generally accompanied by adenopathy and the presence of ulcers along the path, being described in leishmaniasis caused by *L. guyanensis* and *L. braziliensis*.[28]

In the present work, we reported the occurrence of an unusual clinical form of sporotrichoid leishmaniasis on the face, simultaneously with the appearance of classic skin lesions on the thigh of this patient. The infrequent clinical aspect often complicates the initial diagnosis, making it imperative to diagnose it differentially with other diseases, such as sporotrichosis, paracoccidioidomycosis, and cutaneous carcinomas, particularly in patients with a history of frequent exposure to the sun due to their type of work.

In the present case, the diagnosis was established by the clinical appearance of the lesions, the patient's work activity, and available laboratory tests such as direct search for the parasite by imprint and aspirate from the edge of the lesion, histopathological examination and intradermal Montenegro reaction. The patient was treated with liposomal amphotericin B and progressed very satisfactorily, remaining under monthly outpatient follow-up.

CONCLUSION

Cutaneous leishmaniasis is classified as one of the most important neglected diseases. Delay in diagnosis can lead to complications and sequelae in these patients when mucous involvement eventually occurs. Atypical forms of cutaneous leishmaniasis, such as verrucosa and sporotrichoid, must be remembered, at the risk of not making an early diagnosis.

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