Case report

Cutaneous leishmaniasis mimicking cutaneous lymphoma

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\section*{Introduction}

Cutaneous leishmaniasis (CL) is a non-contagious vector-borne disease caused by protozoa of the \textit{Leishmania} (L.) genus that are transmitted to humans through the bite of sand flies (\textit{Lutzomyia} and \textit{Phlebotomus}) \cite{1}. The infection affects skin and/or mucous membranes and has a great capacity to cause deformities \cite{2}. CL is endemic in more than 90 countries and approximately 0.7–1.2 million of cases occur each year worldwide \cite{3}. In American continent, Brazil accounts for almost 35% of the CL occurrences \cite{4}.

CL is known to have a large clinical polymorphism, which are generally associated with the infecting \textit{Leishmania} specie and the immunological relationship between host and parasite \cite{5}. The classic presentation is the appearance of a papule or erythematous nodule, usually in exposed areas of the skin, that after weeks or months evolve into a painless ulcer with regular contours, raised infiltrated borders and grained background covered by a seropurulent exudate \cite{2}. If untreated, the lymphatic or hematogenous dissemination of the \textit{Leishmania} can also lead to additional destructive mucosal lesions \cite{1}. More rarely, CL may present as uncommon clinical forms, such as eczematous, zosteriform, verrucous, lupoid, sporotrichoid, hyperkeratotic, among others.

Some of these variants are able to mimic other cutaneous disorders, contributing to misdiagnosis and unnecessary treatments \cite{6}.

In this paper, we described a case of CL mimicking cutaneous lymphoma in a previously healthy patient.

\section*{Case}

A 27-year-old man, resident in the municipality of Barcarena (01°30’ S and 48°37’ W), northern Brazil, presented at the Dermatology Outpatient Clinic of Pará State University (Belém, Pará, Brazil) with the complaint of solid pruritic lesions on the trunk for the past 3 months. The case was empirically diagnosed as herpes zoster by another medical service and the patient was referred to our department for a skin biopsy procedure. At admission, he denied comorbidities/allergies and assumed to using oral and topical acyclovir irregularly without clinical improvement. Cutaneous examination revealed an infiltrated erythematopapular plaque with well-defined borders and irregular contours measuring about 15 cm in its largest diameter. The eruption presented a band-like appearance and was located on the left anterior region of the trunk (Fig. 1A). Moreover, an erythematous nodule located on the right cheek was also observed (Fig. 1B).

Based on clinical presentation, the initial hypotheses were CL, cutaneous lymphoma or herpes zoster. Diagnostic investigation was started by performing a skin biopsy and serum serologies for HIV-1/2, HTLV-1 and hepatitis B/C. Two months later, the patient

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returned without clinical change and negative serologies. Histopathological evaluation of the specimen demonstrated dermis with fibrous thickening and lymphoid cell proliferation characterized by diffuse and focal clusters of atypical cells infiltrating from the surface into the hypodermis. An intense vascular alteration in the epidermis was also noticed. In addition, microscopic direct detection of Leishmania had a negative result. The case was then assumed as an inconclusive segmental lymphoid proliferation, with relevant similarities to cutaneous lymphoma. Thus, further medical exams were carried out for better elucidation. A subsequent immunohistochemistry of the sample revealed chronic dermatitis with intense superficial and deep inflammatory lymphoplasmocytic infiltrate (CD20+, CD3+, CD138+), as well as foci of epithelioid reaction, but without signs of malignancy. Giemsa staining highlighted sparse clusters of small structures suggestive of Leishmania sp. (Fig. 2) and the polymerase chain reaction (PCR) was positive for Leishmania (Viannia) sp. Consequently, the diagnosis of CL was made and a 20-day cycle of 15 mg/kg/day of meglumine antimoniate (Glucantime®) was started. The medication was well-tolerated by the patient and clinical regression of the lesions was observed after 2 therapeutical cycles.

**Discussion**

In Brazil, CL is mainly caused by 3 species: L. (Viannia) braziliensis, L. (Viannia) guyanensis and L. (Leishmania) amazonensis [2]. The majority of cases occur in the northern areas of the country, primarily due to the favorable conditions of temperature, rainfall and humidity that strongly affect the distribution of Lutzomyia phlebotomines [2]. In the present case, the patient inhabited a municipality located in Brazilian Amazon and also had the habit of entering forest areas, which supports his exposure to the zoonotic transmission cycle of CL [7].

The clinical scenario of CL is extensively variable and may present with single to multiple skin ulcers developing at the site of parasite inoculation (localized-CL), non-ulcerative nodulations covering large cutaneous extensions (diffuse-CL) or papular and aceniform lesions that affect several body segments (disseminated-CL) [1,2]. Such polymorphism is probably determined by the host immunological mechanisms against Leishmania, including the expansion of distinct CD4+ Th subpopulations. The activation of a Th1-response is associated with parasite control, while cytokines stimulated by a Th2-response are inefficient in attenuating the infection, leading to aggravation [8].

More rarely, CL can manifest with atypical dermatological lesions that are able to simulate other cutaneous disorders [6]. In the present study, we reported a patient with an unusual presentation of CL mimicking a clinical picture of cutaneous lymphoma. The reason of this was unknown, but was probably influenced by the host’s immune response pattern [6,8]. At first sight, both the uncommon appearance of the eruption and the biopsy made it difficult to confirm CL. Cutaneous lymphomas, as well as CL, have a broad spectrum of lesions, which in many cases impedes the immediate diagnosis [9]. In addition, some skin lymphocytic infiltrates can exhibit histopathological overlap between the features of lymphomas and inflammatory dermatoses [9,10]. Therefore, in these cases, the investigation of CL has to focus on the clinicopathological correlation, prioritizing the patient’s history, personal background and epidemiological data, especially in endemic areas [2,6,8,10].

Laboratory tests can also be performed in order to confirm CL. Direct detection is usually the first choice due to the satisfactory cost-benefi [2]. The microscopic examination aims to find the
amastigote forms of the parasite, but they are not always visualized [11], as was the case of our patient. The typical histopathological finding is an ulcerated granulomatous dermatitis, generally with a lymphoplasmocitary infiltrate [2,11]. On immunohistochemistry, lymphoma-like CL lesions can also reveal a mixture of B and T lymphocytes [12,13] or a natural killer/T-cell lymphoma pattern when associated with the use of anti-TNFα medication [14]. In the present case, we confirmed the diagnosis using PCR, which has a high sensitivity and specificity, even when there is low parasitic load [5].

The treatment was performed with meglumine antimoniate (Glucantime®), which is the first-line treatment drug for CL [2]. The therapeutic regimen involves 10–20 mg/kg/day during 20 consecutive days, for both localized and disseminated forms [5]. If there is no complete healing in 12 weeks, the therapeutic regimen may be repeated. If done properly, the patient’s clinical cure can be obtained.

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**Consent**

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

**CRediT authorship contribution statement**

Carla Andréa Avelar Pires: Conceptualization, Data curation, Formal analysis, Project administration, Supervision, Validation, Visualization, Writing - review & editing. Nathalia Gabay Pereira: Investigation, Methodology, Writing - original draft, Writing - review & editing. Amanda Gabay Moreira: Investigation, Methodology, Writing - original draft, Writing - review & editing. Julie Marie Costa Sena: Investigation, Methodology, Writing - original draft, Writing - review & editing. Caio César Chaves Costa: Investigation, Methodology, Writing - original draft, Writing - review & editing. Thalita dos Santos Bastos: Investigation, Methodology, Writing - original draft, Writing - review & editing. Fernanda do Nascimento Rodrigues: Investigation, Methodology, Writing - original draft, Writing - review & editing. Evelyn de Paiva Faustino: Investigation, Methodology, Writing - review & editing. Jéssica Rayanne Corrêa da Silva: Investigation, Methodology, Writing - original draft, Writing - review & editing. Maria Amélia Lopes dos Santos: Conceptualization, Data curation, Formal analysis, Project administration, Supervision, Validation, Visualization, Writing - review & editing.

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