

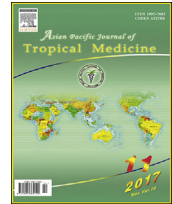
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journal homepage: <http://ees.elsevier.com/apjtm>Case report <https://doi.org/10.1016/j.apjtm.2017.10.001>An atypical case of disseminated cutaneous leishmaniasis due to *Leishmania peruviana* in the valleys of Ancash-PeruDiego Espinoza-Morales¹, Aldo Lucchetti Rodríguez^{1,2}, Wilmer Silva-Caso^{1,3}, Luis Suarez-Ognio¹, María J. Pons³, Juana del Valle Mendoza^{1,3✉}¹School of Medicine, Health Sciences Faculty, Universidad Peruana de Ciencias Aplicadas, Av. San Marcos cdra 2 Cedros de Villa, Lima, Peru²Infectology Service, Hospital Arzobispo Loayza, Av. Alfonso Ugarte 848, Cercado de Lima, Lima, Peru³Research Center and Innovation of the Health Sciences Faculty, Universidad Peruana de Ciencias Aplicadas, Av. San Marcos cdra 2 Chorrillos, Lima, Peru

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ABSTRACT

We present an atypical case of disseminated cutaneous leishmaniasis in the Sihuas district, located in the Andean valleys of Ancash-Peru. A 62-year-old man with no particular medical history presented multiple lesions located on the inferior abdomen, lumbar region and the right anterior thigh. Histological analysis found leishmanial amastigotes in the lesion sample, the Montenegro reaction was positive for *Leishmania* spp, and the polymerase chain reaction was positive for *Leishmania peruviana*. In conclusion, the atypical presentation of this disease may be related to the presence of an uncommon parasite strain or host immune deficiencies. The molecular identification of the etiology for disseminated leishmaniasis, will allow a better understanding of the presentation and proper treatment, as well as associated risk factors.

1. Introduction

Leishmaniasis is a disease with a worldwide distribution, about 15 million people in the world are infected, and 350 million are at risk of acquiring the disease. An estimated 1.5 to 2 million new cases occur each year worldwide, and it causes 70000 deaths per year [1]. The cutaneous form represents more than 75% of the cases of *Leishmaniasis* with a higher incidence when subclinical infections are included [2]. In Latin America, this disease is transmitted by phlebotomine sand flies mainly from the genera *Phlebotomus* and *Lutzomyia*. In South America, it is estimated

that around 60000 new cases (including all types) occur each year [3]. In Peru, *Leishmaniasis* is considered the second most common endemic tropical infection and the third cause of morbidity which follows malaria and tuberculosis. Therefore it is considered a public health problem that has not yet been resolved [4]. In 2016, 7140 cases of *Leishmaniasis* were reported; most of the cases were cutaneous leishmaniasis accounting for 6724 of cases (92.5%) followed by mucocutaneous leishmaniasis in 541 of cases (7.5%) [5]. Other more serious dermatological presentations of leishmaniasis have been described, such as “diffused cutaneous leishmaniasis” and “disseminated leishmaniasis”; however, these presentations are not usually reported in Peru [6].

Peru is one of the most endemic countries for cutaneous leishmaniasis, and eight *Leishmania* species are recorded as causative agents; *Leishmania* (*V.*) *braziliensis* (*L.* (*V.*) *braziliensis*), *Leishmania* (*V.*) *peruviana*, *Leishmania* (*V.*) *guyanensis*, *Leishmania* (*V.*) *lainsoni*, *Leishmania* (*V.*) *shawii*, *Leishmania* (*L.*) *mexicana*, *Leishmania* (*L.*) *amazonensis*, and a hybrid of *L.* (*V.*) *braziliensis*/*Leishmania* (*V.*) *peruviana*. Of these, the first three species have been identified as predominant causative agents: *L.* (*V.*) *braziliensis* is mostly found in the tropical rainforest, *Leishmania* (*V.*) *peruviana* in Andean highland areas, and *Leishmania* (*V.*) *guyanensis* in northern and central rainforest

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regions [7]. During the infection, the host's cellular immunity is inhibited, allowing for the proliferation of parasites as they invade new cells and development of nodulations is similar to those observed in lepromatous lepra. The abnormal cellular immune response is responsible for the lack of ulcerations and the presentation of the nodular lesions [6,8].

We present an atypical case of a patient with cutaneous leishmaniasis, characterized by multiple nodular lesions from the valleys of Sihuas in Ancash Peru, who was hospitalized in the Hospital Nacional Arzobispo Loayza in Lima, Peru.

2. Case report

A 62 years-old male from the village Uhugaga Sihuas district of Ancash, who presented skin lesions in the lower abdomen and bilateral lumbar region, was admitted to the Hospital Nacional Arzobispo Loayza for diagnosis and treatment. The patient recalled that 18 months before hospitalization, a pustular lesion with erythematous borders appeared on the right lumbar area. After 17 months, the initial injury progressively enlarged and evolved to an ulcerated lesion with a crusty plate, a new lesion appeared around the periumbilical abdominal area and on the anterior region of the right thigh (Figure 1). No signs or symptoms of systemic involvement were presented at admission. *Leishmania* amastigotes were observed in the primary lesion edge; and the histopathology examination showed granulomatous dermatitis without microorganisms. Similar lesions appeared at periumbilical abdominal area and on the anterior region of the right thigh. The lesions were erythematous, round shaped with sharp edges and an adhered dry crust in the middle of the lesion which bled upon removal. The patient stated that the lesions were not pruriginous or painful. Another ulcerated lesion appeared 6 months before the admission on the anterior portion of the right thigh.

Indirect immunofluorescence was positive for IgG anti-*Leishmania* and for the Montenegro reaction (Vircell Microbiologists). The polymerase chain reaction amplified a sequence of 1 300 bp

corresponding to the *Hsp70* gene, specific to the genus *Leishmania* using the primers *Hsp70*sen 5' GACGGTGCCTGCCTACTTCAA 3 and *Hsp70*ant 5' CCGCCCATGCTCTGGTACATC 3' as described by Garcia L *et al* [9]. The obtained amplicon was sent to genetic sequencing for confirmation, resulting in *Leishmania peruviana* (Macrogen-Korea).

In addition, basic laboratory tests were performed to verify the baseline condition of the patient and the presence of infectious comorbidities. The results were within normal values. A serological test for HIV was performed and the result was negative. The patient was treated with sodium stibogluconate (20 mg/kg) IV for 30 d with a favorable evolution and then was discharged with no complications or related adverse effects.

3. Discussion

Leishmaniasis is endemic in Peru, in regions such as the Andes and the Amazon. They are caused by a diverse group of protozoa of the genus *Leishmania*, which produces various clinical manifestations, characterized by cutaneous and mucocutaneous lesions and in some cases visceral compromise. This disease is transmitted by the bite of insects of the Phlebotomidae family [6,8,10].

Cutaneous leishmaniasis has been described to have different dermatological presentations including injuries such as a single painless lesion, typically ulcerated, with clear borders. Any member of the neotropical subgenera *Viannia* and *Leishmania* can cause cutaneous leishmaniasis. However, *L. (V) braziliensis* has been described as the most common cause for this presentation. The more serious presentation of *Leishmaniasis* known as diffuse or disseminated cutaneous leishmaniasis is most commonly associated to a *Leishmaniasis mexicana* complex infection followed by *Leishmaniasis amazonensis* and *Leishmaniasis pifanoi* [10,11].

In this context the clinical manifestations of *Leishmania* infection are determined by a series of factors including the genetic make-up and the immune status of the host, the varying virulence between species, and factors associated with vectors [12].

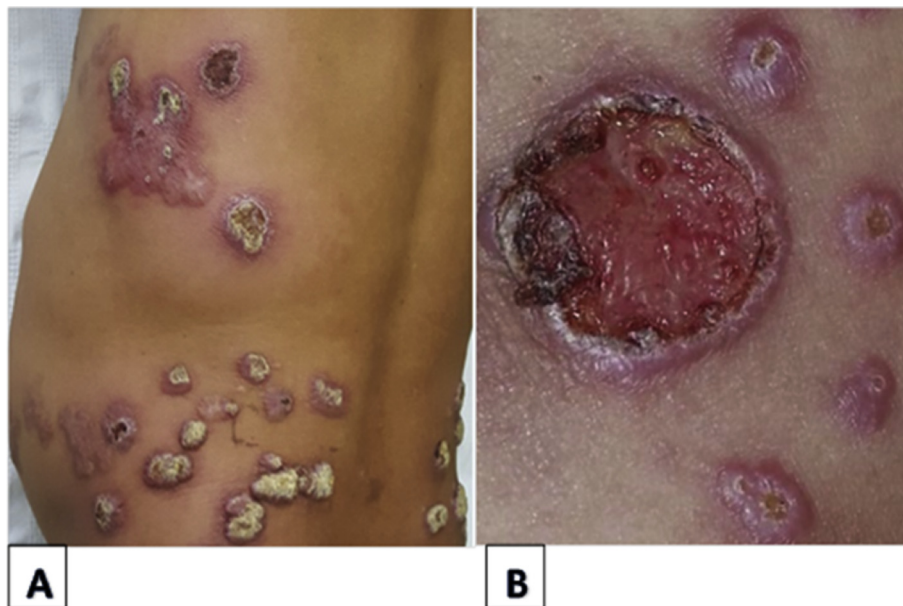


Figure 1. A) Patient supine with keratitis diffuse nodular lesions in abdomen. B) Ulcerated lesion with crusty border and non-bleeding erythematous center placed in thoracic part at the level of the axillary midline with satellite lesion.

Disseminated cutaneous leishmaniasis and diffuse cutaneous leishmaniasis are rare manifestations usually related to an inadequate immune response to the *Leishmania* parasite, in which the innate immunity fails to prevent the infection. When the parasite manages to overcome innate immunity, it adheres to the macrophages surface and it is internalized by receptor mediated phagocytosis. The parasite is transported inside the infected macrophages to the regional lymph system where they transform into amastigotes, facilitating their migration and survival. Th1 cells are responsible for the antigenic response, and produce IFN- γ and IL-12 associated with protection against intracellular pathogens. The adaptive immunity in DCL is characterized by a diminished Th1 response and a normal Th2 response with the release of IL4, IL5 and IL10. The balance between Th1 and Th2 responses is essential to control the disease as well as for diagnostic tests. The poor Th1 and Th2 responses allow amastigotes to proliferate in infected macrophages within their phagolysosomes eventually triggering its lytic function and leading to hematological dissemination [10,13,14].

It is widely described that in cases of diffuse cutaneous leishmaniasis there is a lack of cellular immune response to parasite antigens. This allows the hematological dissemination of the parasite leading to the development of diffuse skin lesions in most of the body, except in the scalp, and sometimes with mucocutaneous involvement [3]. In this case, the Montenegro reaction was positive. However, diffuse cutaneous leishmaniasis usually shows a negative reaction to the Montenegro intradermal test. Other diagnostic criteria for diffuse cutaneous leishmaniasis is the histological presence of scarce lymphocytes and abundant parasites. The histological analysis in this case described abundant lymphocytes and few parasites. This atypical presentations of the disease may be due to an uncommon strain or to a cross-reactivity of the patient's immune system. It is necessary to emphasize that this clinical form is very difficult to treat, there is no spontaneous resolution, and a long evolution of up to 20 years has been described [3].

In conclusion, it is clear that the clinical presentation and diagnosis of infectious diseases remain a challenge today and the clinical spectrum of diseases caused by the genus *Leishmania* is not the exception. Atypical forms of this disease are reported, which usually have little agreement with what an experienced physician might expect with the help of non-molecular diagnostic tests. The varying presentations of this disease rely on a large number of variables such as the host's genetic make-up and immune status, the virulence of the species, and factors associated with vectors [3].

Conflict of interest statement

The authors have no conflict of interests.

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