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Atypical Cutaneous Leishmaniasis by *Leishmania mexicana*: A Case Report with Dermoscopic, Histopathological and Molecular Study

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Abstract

Cutaneous leishmaniasis is a neglected tropical skin endemic disease, with worldwide distribution. By 2020 in the Americas, Mexico was in 12th place with 11 states reporting new cases. Molecular biology with different targets for diagnosis and species identification has been used for decades, also dermoscopy, a non-invasive diagnostic tool has shown its usefulness. We present the first case of cutaneous leishmaniasis in non-endemic place (Guerrero, Mexico) identifying *Leishmania mexicana* with molecular biology, and treated with itraconazole.

Keywords

Atypical Cutaneous Leishmaniasis, Neglected Tropical Skin Diseases, *Lutzomyia*, *Leishmania mexicana*, Itraconazole

1. Introduction

Cutaneous leishmaniasis is one of the ten neglected tropical skin diseases included in the list of the World Health Organization (WHO) worldwide except Oceania.

The clinical forms are tegumentary cutaneous, mucocutaneous, and visceral. It is endemic in 18 countries (2020), and in the Americas, Mexico is in 12th place [1] [2] [3].

Caused by intracellular protozoa of the genus *Leishmania* spp., it is transmi-

tted to humans through the bite of infected female insects of the genus *Lutzomyia* in the New World. The diagnosis is based on the identification of the parasite in the skin and bone marrow test, biopsy, as well as immunological and molecular biology tests [4].

The State of Guerrero, Mexico is not endemic for cutaneous leishmaniasis [5]. The purpose of this article is to present the first case due to *Leishmania mexicana* diagnosed by clinical correlation, dermoscopy, histopathology and molecular biology.

2. Clinical Case

A 30-year-old male, farmer, resident of municipality of Tecpan de Galeana, Guerrero, Mexico with no history of traveling to endemic areas of leishmaniasis in the country or abroad.

Refers a 3-month evolution with an infiltrated plaque in the dorsal aspect of the nose. Initially treated with isotretinoin, serratiopeptidase and clindamycin gel without improvement. Skin examination showed a 2 cm erythematous crusted plaque, with desquamation (**Figure 1(A)**).

Digital dermoscopy (Dermlite DL200 Hybrid) with polarized light showed, diffuse erythema, punctate vessels and yellow tears (**Figures 2(A)-C)**).

Histopathological examination showed numerous Langhans cells, and vacuolated histiocytes with amastigotes more evident with PAS staining (**Figures 3(A)-(C)**). Cutaneous leishmaniasis was confirmed.

Treatment was established with oral itraconazole 200 mg/daily, after a month follow-up, there was no clinical improvement and increased the size of the plaque, with peripheral papules (**Figure 1(B)**). Itraconazole dosage was increased to 400 mg/daily for 3 months with clinical cure (**Figure 1(C)**)

Molecular Identification. DNA extraction. The DNA from the paraffin-embedded tissue was extracted and quantitated. Twenty ng were used for the PCR reaction performed with primers HSP70-F25 and HSP70-R617 (Van der Auwera

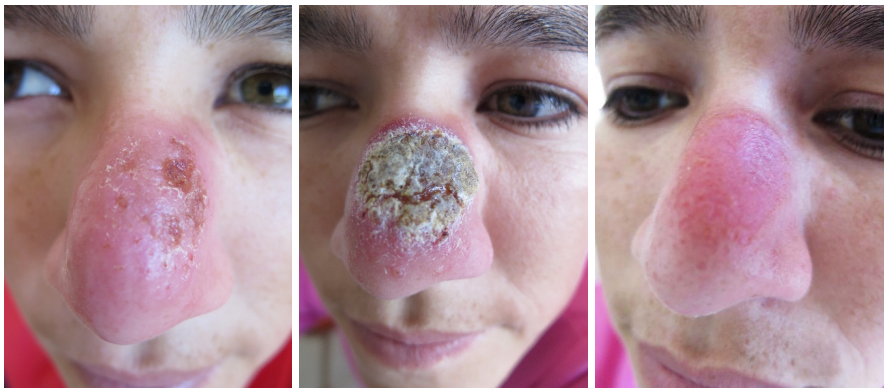
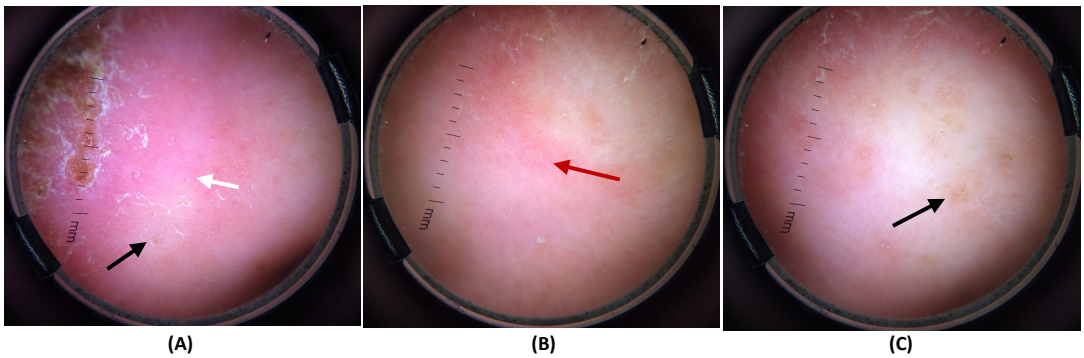
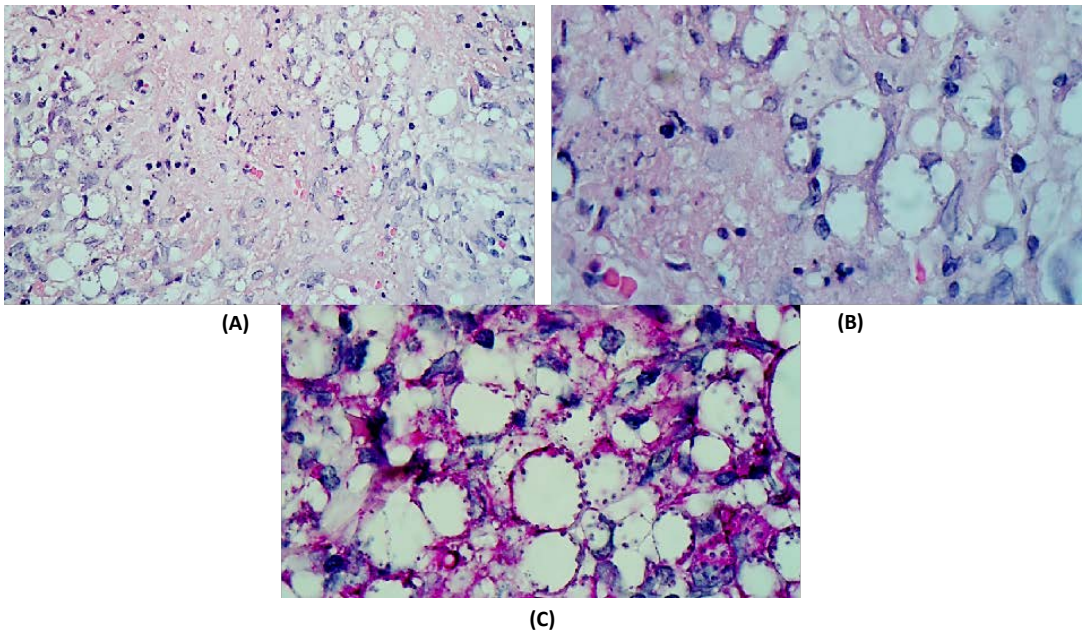


Figure 1. (A) Erythematous infiltrated crusted plaque of 2 × 2 cm, with areas of erosion and desquamation; (B) Enlarged plaque and crusts and peripheral papules; (C) After 3 months of Itraconazole.



(A) (B) (C)

Figure 2. (A) Diffuse erythema (white arrow), yellow globules or yellow tears (black arrow); (B) Punctate vessels (red arrow); (C) Yellow blood cells or yellow tears (black arrow).



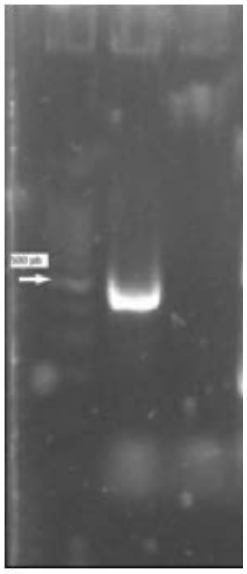
(A) (B) (C)

Figure 3. (A) Dense inflammatory infiltrate of lymphocytes and vacuolated histiocytes, amastigotes inside them, (HE 40×); (B) Magnification (A), (HE 60×); (C) Abundant histiocytes with numerous parasitic structures (amastigotes) (PAS 60×).

G, Maes I, De Doncker S, *et al.*) [6]. PCR reaction used 200 µM of each dNTP, 0.8 µM of each PCR primer, and 1U of HotStarTaq Plus DNA polymerase (Qiagen). Up to 2.5 µl of template were used. Cycling conditions were as follows: 5 min at 95˚C denaturation; 35 cycles of 40 sec at 94˚C, 1 min at 61˚C, 2 min at 72˚C; and finally, 10 min at 72˚C. PCR products were analysed on a 2% agarose gel to check for sufficient and specific amplification, based on the expected product sizes [6]. Amplicons were purified and the nucleotide sequence was obtained by capillary electrophoresis method using the primers described above, identifying *Leishmania mexicana* (**Figure 4**).

3. Discussion

Cutaneous leishmaniasis is the most frequent clinical variety worldwide. Endemic



(A) (B) (C)

Figure 4. PCR analysis of the sample. Primers F25/R167 that amplify a 593-bp fragment of the gene that codes for the HSP70 protein were used; (A) 100-bp molecular weight markers (Thermo Fischer Scientific); (B) sample; (C) Bidistilled water blank. 1.5% agarose gel stained with Biotium.

#	State	cases
1	Tabasco	195
2	Quintana Roo	140
3	Campeche	38
4	Veracruz	23
5	Chiapas	22
6	Nayarit	09
7	Jalisco	06
8	Yucatan	02
9	Oaxaca	02
10	Estado de Mexico	01
11	Ciudad de Mexico	01
	Total	439

Secretaria de Salud. Anuarios de Morbilidad. Casos nuevos de leishmaniasis cutánea (B55.1) por grupos de edad. Estados Unidos Mexicanos 2020.

Figure 5. New cases of cutaneous leishmaniasis in Mexico, 2020.

in 85 countries by 2020, 51 of them (60%) reported 207,717 new cases in 5 of the WHO regions [7]. Endemic in the Americas in 21 countries, 18 (86%) reported 39,728 cases [3].

In Mexico during 2020, the states with more cases of cutaneous leishmaniasis were Tabasco, Quintana Roo, Campeche, Veracruz, Chiapas, Nayarit, Jalisco, Oaxaca, Yucatan, State of Mexico, and Mexico City [4] (**Figure 5**).

In 2009, a case was reported in Durango, a non-endemic state, confirmed by PCR identifying *Leishmania mexicana* [8]. The state of Guerrero (residence of

our patient) is not endemic either, that's why our case is the second report from the Mexican Republic, with no history of traveling to endemic areas of the country or abroad.

Molecular biology for the diagnosis and identification of species has been used for decades, different methodologies have been evaluated without a consensus regarding protocols and molecular targets. In 2016 the Pan American Health Organization (PAHO) promoted the standardization and validation of three molecular targets: SSUrDNA, KDNA and HSP70 in 7 Latin American countries, the HSP70 target presented a higher specificity for species identification, it was the one used in our study [6] [9].

Dermoscopy has been used as an auxiliary tool since 2009 [10]. The most frequent findings were generalized erythema, yellows tears, white starburst-like patterns (localized parakeratotic hyperkeratosis around the lesions), irregular linear vessels, hairpin, coma [11]. The findings in our patient were punctate vessels and yellow tears [12].

In 2017 Galvão *et al.* [13], conducted a systematic review of evidence, efficacy, and safety of itraconazole, ketoconazole, and fluconazole therapy, the cure rates were 65%, 64%, and 61% respectively. In our case, it was treated with itraconazole with a clinical cure due to complete re-epithelialization.

4. Conclusions

We present the first case of atypical cutaneous leishmaniasis caused by *L. mexicana* complex in Guerrero, Mexico, using HSP70-R617 as a target, standardized by WHO in the Americas. The case was treated with itraconazole 400 mg a day for three months with a good response. There is insufficient evidence to support the exclusive use of azole therapy. More studies are needed to evaluate the efficacy and safety of itraconazole in *L. mexicana*.

Cutaneous leishmaniasis is a neglected tropical skin disease, under diagnosed by physicians. It should preferably have parasitological and molecular confirmation to regulate the criteria of treatment.

Ethics Declaration

Written informed consent was obtained from the patient for the publication of the cases and clinical images.

Declaration of the Information Availability

The data that support the findings of this report are available in Pub Med.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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