Case report: disseminated cutaneous leishmaniasis (LCD)

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Abstract

The World Health Organization (WHO) has classified leishmaniasis as an uncontrolled and emerging disease. In Ecuador, the only anecdotal cases of diffuse cutaneous leishmaniasis were recorded in 1994 and have not been formally published. This form can be differentiated from classical localized cutaneous leishmaniasis by the number of injuries, the clinical type of the main elementary lesions (papular and acneform), and a weak response to standard treatments. The case we report is a 34-year-old woman who presented with disseminated nodular lesions and ulcers of various sizes with erythematous edges and scars. We report the case and review diffuse cutaneous leishmaniasis and the differences that can be found with the other cutaneous variants. The diagnosis requires to be considered by primary care physicians in endemic areas and specialists, taking into account that this presentation can also occur in immunocompetent hosts.

KEY WORDS: *Leishmaniasis. Disseminated cutaneous. Immunocompetent host. Case report.*

Introduction

Leishmaniasis constitutes a public health problem in Ecuador, owing to its wide distribution, mainly in rural areas[5]. It is transmitted by vectors, and there are more than 20 species that affect human beings[6]. American cutaneous leishmaniasis (ACL) variants include localized cutaneous leishmaniasis (LCL), mucocutaneous leishmaniasis (MCL), which can accompany any variant, and diffuse cutaneous leishmaniasis (DCL), which should be differentiated from the diffuse allergic form (ADCL)[7] and from a new intermediate or borderline category (ICL)[4,7]. The disseminated form is characterized by the presence of multiple lesions (more than 10) that vary between acneiform papules, nodules and ulcers in at least two different parts of the body[7,8]. The number of DCL cases has shown a significant increase in last 20 years' statistics[2,3].

Clinical case

This is the case of a 34-year-old woman, originating from Quito, who attended the dermatology outpatient clinic presenting with disseminated dermatosis affecting the head, the trunk and upper and lower limbs; distribution was bilateral, asymmetric, with predominance on the left malar zone and left scapular zone, arms and thighs; characterized by erythematous nodules, multiple ulcers of varying sizes (0.3-1 cm), with rolled, erythematous borders and plaques with cicatricial appearance (Fig. 1).

As previous history, she referred having travelled to a warm climate zone in the Ecuadorian northeast. Lesions' smear microscopic analysis confirmed the leishmaniasis diagnosis. The patient referred having received treatment with meglumine antimoniate (5 ml, by intramuscular route, 25 days). Fifteen days after treatment completion new lesions appeared, with wider dissemination with regard to initial presentation, and the patient attended the hospital's dermatology department. Prior to treatment initiation, baseline clinical tests were performed, the results of which were normal; in addition, human immunodeficiency virus was ruled out.

A biopsy revealed an ulcer covered by fibrinoid material and polymorphonuclear infiltrate. In the dermis,

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Date of reception: 26-11-2015
Date of acceptance: 12-01-2016

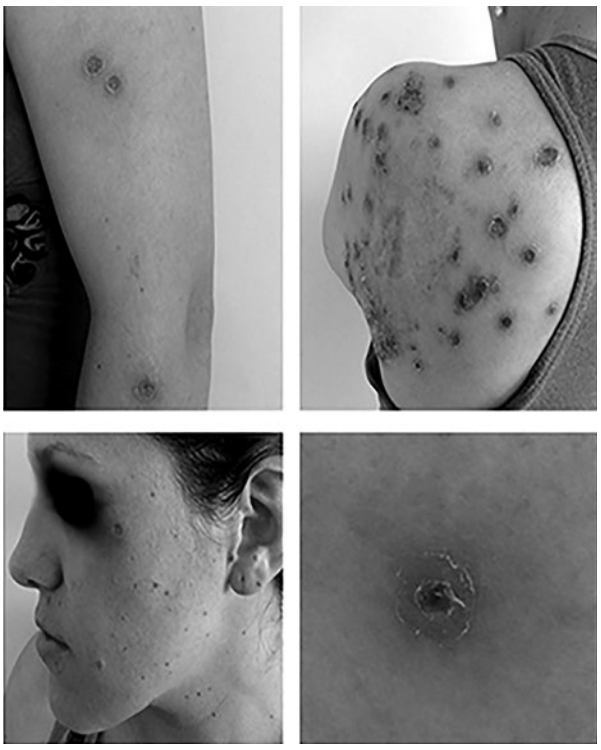

Figure 1. *DCL affecting the head, the trunk and upper and lower limbs, characterized by multiple erythematous nodules, multiple ulcers and plaques with cicatricial aspect* (source: Archivo fotográfico, Mancheno A. Hospital Gonzalo González, Quito, Ecuador, 2015).

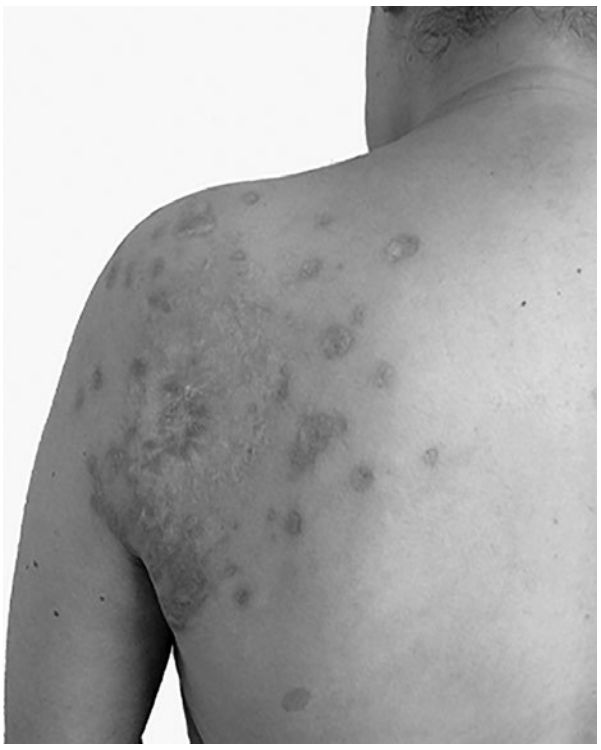

Figure 2. *DCL 2 months post-treatment with meglumine antimoniate, 20 mg/kg/day for 21 days* (source: Archivo fotográfico, Mancheno A. Hospital Gonzalo González, Quito, Ecuador, 2015).

presence of abundant histiocytes was reported, with cellular residues where organisms suggestive of *Leishmania* amastigotes were found.

Treatment with meglumine antimoniate was started at 20 mg/kg/day for 21 days, whereby clinical improvement was obtained, and the patient was discharged 2 months after treatment completion (Fig. 2).

The case is reported, and a review is made on DCL main characteristics, differences that can be found with regard to other ACLs and on recommended treatment.

Discussion

The WHO classifies leishmaniasis as an emerging and uncontrolled disease, since it is endemic in 88 countries from 4 continents, and around 2 million new cases are reported every year[1]. In Ecuador, cases have been recorded in 23 of the 24 provinces of the country and, according to the Public Health Ministry, 1,537 annual cases were reported during the 2002-2012 period, with an incidence rate that ranged from 6.14 to 19.15 per 100,000 population[5]. A study conducted in Pedro Vicente Maldonado concluded that prevalence has doubled during the past 2 years[9].

The number of DCL cases has shown a statistically significant increase in the past 20 years[2,3,7]. However, in Ecuador there are no reported cases about it, and the only reports, although on diffuse leishmaniasis, are from the Esmeraldas province and as anecdotal cases[2].

To decipher leishmaniasis variants' enigmas, we must understand that its dissemination is determined by patient immunogenetic characteristics, rather than by parasite-specific virulence[7]. This is argued because there is an absence of DCL cases' cohorts and, in addition, there is variability in the causative species in reported cases (*L. guayanensis*, *L. braziliensis* and *L. amazonensis*, among others)[3,7,10,11].

In DCL, individual nodules appear that then develop in multiple sites of the skin. Failed immune response has been suggested to be the mediator of this type of presentation. CD8+ T cell clones cause the lysis of *Leishmania*-infected cells but, as a result of their specificity, they are not able to recognize the released antigens; i.e., the immune response itself may contribute to the spread of the parasite by the hematogenous route[12].

DCL is differentiated from LCL by a larger number of lesions and by main primary lesions' clinical type (papular and acneiform)[3,4]. It can be accompanied by mucosal involvement in 38% of cases[13] and, according to the literature, it is different from ADCL, since the latter has a negative response to the Montenegro skin test (MST)[14], which is generally found in immunocompromised patients[15,16]. Both are of a chronic, progressive and treatment-refractory nature. In our patient, the test was not performed due to unavailability.

In 2,206 patients with cutaneous leishmanisis in northeastern Brazil, a DCL prevalence of 19% was found, without relevant risk factors being described, in comparison with patients with LCL[7]. Parasitological diagnostic methods are specific, but poorly sensitive (79%); however, they are accessible and should be applied in all clinical forms of the disease. They include microscopic examination of smear, scrape or aspirate taken from lesion borders[17]. Histopathological examination has a sensitivity of 70%[18].

Polymerase chain reaction demonstrated the highest sensitivity in typical (100%) and atypical (94%) presentations, and specificity of 100%, followed by immunohistochemistry, with 97% sensitivity and 100% specificity. MST assesses cell hypersensitivity late response[14]; in ICL, it is positive in at least 50% of cases, and this variant is therefore between DCL and ADCL, and its evolution is equally chronic and progressive[4].

Currently, first-choice treatment for cutaneous leishmaniasis in our region is pentavalent antimony compounds: N-methylglucamine antimoniate or sodium stibogluconate[19,20]. Other medications that have been used as second-line drugs are miltefosine[13] and amphotericin B[21], and even ketoconazole[22] as alternative therapy. In general, pentavalent antimonial dose for all forms of leishmaniasis is 20 mg/kg/day[20]. It should be noted that DCL treatment is associated with worse prognosis owing to a high probability of recurrence[4,23].

Amphotericin B has moderate effectiveness, but it is a good option in cases that also have mucosal involvement, at doses of 0.5-1 mg/kg/day by the intravenous route for up to 8 weeks[21]. Miltefosine, a drug accepted by the US Food and Drug Administration in 2014 for oral treatment of ACL at doses of 2.5 mg/kg/day[24], has effective results for DCL[25] at a dose of 100 mg (50 mg twice daily, by oral route) administered for 3 months[13], or in combined regimens with other treatments, such as photodynamic therapy[26]. However, this is an expensive medication, and disease recurrence is not eliminated[4,27]. Other useful regimen in cases of poor response to antimonials is pentoxifylline in association with N-methylglucamine, which has demonstrated to be an effective tratment[23]. Pentoxifylline inhibits tumor necrosis factor gene transcription and potentiates nitric oxide synthase expression that leads to nitric oxide formation[23].

Based on the knowledge of an altered immune response in DCL, some studies mention the relevance of creating a vaccine[28] and, on the other hand, they suggest conducting investigations with immunotherapy[4,29]. The fact that implementing efficacious and early treatment will make a lot of difference for the patient is important, since epithelization and total flattening of lesions will anyway leave notorious scars.

Conclusion

Although rare, DCL appears to be increasingly occurring because the causative agent and its vector go hand in hand with social and geographic factors that are characteristic of our country. We consider the disseminated variant to be under-reported and, since we are in an endemic zone, it should be taken into account both by first-contact physicians and specialists, bearing in mind that it can also occur in immunocompetent patients. Lesions rapid evolution compromises patients' wellbeing, and we don't know if late or underdosed treatment has an influence on DCL in addition to patients' immunogenetic factors.

Conflicts of interest and contribution

The authors declare no conflicts of interest. All authors contributed with the design and data acquisition and have approved the published final version.

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