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Old World Cutaneous Leishmaniasis

Successful response to topical imiquimod

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Leishmaniasis includes a complex diseases transmitted by sand fly vectors and caused by a heterogeneous group of protozoa belonging to the genus *Leishmania spp*. Leishmaniasis comprise two clinical forms of presentation: cutaneous and visceral. Traditionally, the cutaneous forms (CL) have been classified into Old World Cutaneous Leishmaniasis (OWCL) and New World Cutaneous Leishmaniasis (NWCL) depending on the geographical distribution.

A 43-year-old female patient with no relevant medical history was referred to our outpatient dermatologic clinic on account of two lesions on the right hand for 3 months. The patient referred lack of clinical improvement despite treatment with mometasone furoate 0.1% cream for one month. On clinical examination, two erythematous, squamous 1.2cm and 1.5cm of larger diameter plaques were observed on the back of the right hand (fig. 1A,1B). Dermoscopy showed an inflammatory pattern, composed by a central keratotic crust on an erythematous background and tear structures (fig. 1C). Histopathological examination back up clinical suspicion of OWCL revealing non-necrotizing epithelioid in the middle and deep dermis, with multiple leishmania amastigotes detected by Giemsa stain (fig. 2). Complementary tests ruled out the presence of systemic involvement. Because of the patient did not accept intralesional treatment with meglumine antimoniate due to needle phobia, it was decided to start topical

treatment with imiquimod 5% cream five consecutive nights a week for four weeks, followed by applying a repair cream. The inflammatory reaction during treatment was moderate to severe, with ulceration of the treated area (fig. 3A). A complete skin recovery was appreciated at two months check-up (fig. 3B, 3C, 3D) and histopathological study besides of PCR of the control sample did not show persistence of the disease. Currently the patient is being followed up every 3 months, with no recurrence of Leishmania infection. Written consent was obtained for publication.

Imiquimod was approved by the *Food and Drug Administration* (FDA) for the treatment of anogenital warts, actinic keratosis and superficial basal cell carcinoma. In addition, it has been used off-label in the treatment of several infectious and neoplastic diseases.

Imiquimod activates macrophages by inducing the production of nitrous oxide (NO), which leads to the intracellular destruction of Leishmania amastigotes in vitro.[1] The first observational study on the application of imiquimod in leishmaniasis dates from 1999, being effective on an experimental model of leishmaniasis.[2] Nevertheless, the effectiveness of Imiquimod in CL has not been entirely clear in later research studies. Seeberger J *et al* in a placebo-controlled prospective study concluded that topical application of imiquimod on monotherapy was not effective in OWCL, after treating with imiquimod cream 5% three times a week during two months.[3] Although the majority of cutaneous lesions improved within the first 2 weeks, the benefit did not last for more than 4 weeks and was followed by in both size and scaling. In a study by Firooz A *et al*, patients were randomly assigned to receive a combined 4-week course of imiquimod or placebo with meglumine antimoniate treatment in an endemic area of L. *tropica*.[4] This study did not find clinical differences between both combinations. A concentration of imiquimod 7.5% combined with meglumine antimoniate should be more effective than the meglumine antimonate alone.[5] Successful response with imiquimod on monotherapy after debulking punch biopsies have also been communicated.[6] Further studies would be necessary to determine the more propitious role of imiquimod as a non-systemic useful alternative therapeutic option in OWCL.

Authors' Contribution

All authors contributed equally to data collection, drafting and revision of the manuscript. All authors approved the final version of the manuscript.

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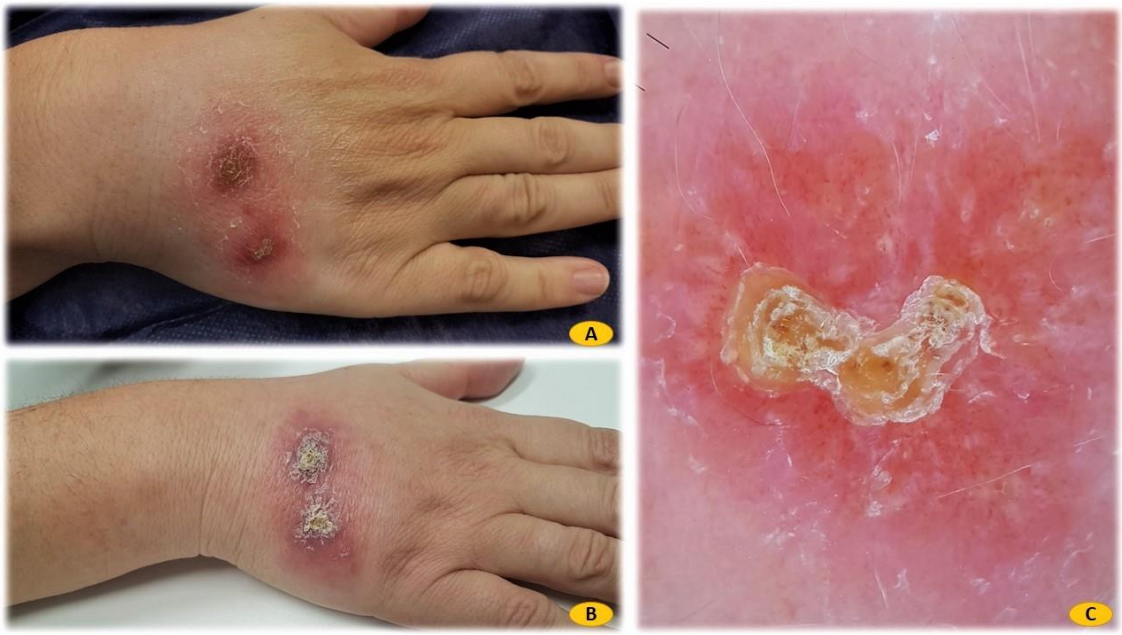

Figure 1. (A) Two erythematous, squamous, 1.2cm of larger diameter plaques on the back of the right hand at first visit. (B) Both lesions after 21 days. (C) Dermoscopy (*Dermlite 4*©) x10: Erythematous fundus with central hyperkeratosis, whitish burst at periphery, white-cottony structures and a polymorphic vascular pattern of irregular linear vessels, hairpin vessels and dotted vessels.

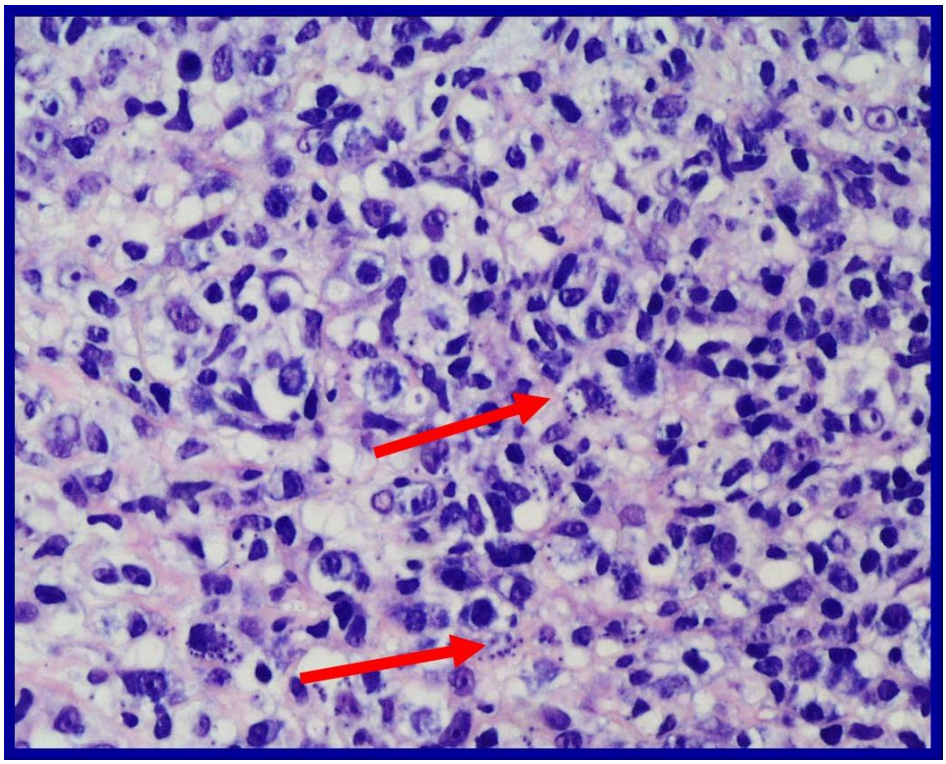

Figure 2. Histopathological examination. Non-necrotizing epithelioid in the middle and deep dermis, with multiple leishmania amastigotes detected by Giemsa stain.

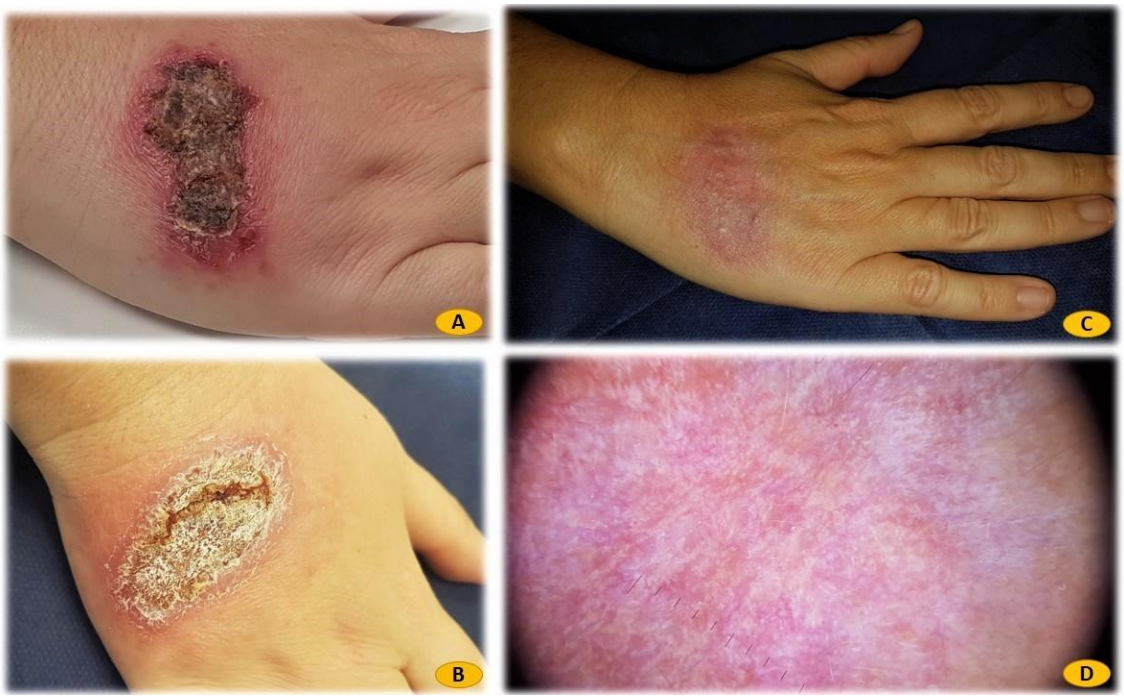

Figure 3. (A) Ulceration and crust surrounded by inflammatory erythematous halo after finishing treatment with Imiquimod 5% cream. (B, C) 14 days after finishing imiquimod and 30 days after finishing imiquimod cream and using daily repair cream (D). Dermoscopy (*Dermlite 4*©) x10: stairs vascular pattern and shiny white streaks compatible with regeneration of collagen fibres.