A case of periocular plaque-type cutaneous leishmaniasis successfully treated with intralesional amphotericin B

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Summary
Leishmaniasis is still an endemic infectious disease in many areas of the world. The two most typical clinical forms of localized cutaneous leishmaniasis are the papulo-nodular plaque type and the ulcerative type. Periocular involvement is present in only 2-5% of localized cutaneous leishmaniasis, mainly in papular and nodulo-ulcerative forms. A case of periocular plaque-type localized cutaneous leishmaniasis in a 38-year-old Tunisian man successfully treated with intralesional deoxycholate amphotericin B is reported. This treatment, sporadically reported in other infectious skin diseases (chromoblastomycosis, chromomycosis, alternariosis, Candida granuloma, lymphocutaneous sporotrichosis), have never been suggested for localized cutaneous leishmaniasis.

KEY WORDS: leishmaniasis; amphotericin B; intralesional therapy.

Case report
A 38-year-old Tunisian atopic man, who had been living in Italy since 20 years, referred to us with a 5-year history of asymptomatic papulo-nodular lesions grouped in a nummular red-brownish plaque localized on the external side of the right periocular region (Figure 1a). The lesion was treated many times with topical antibacterials, included paromomycin ointment, without benefit. Physical examination showed bilateral multiple laterocervical and submandibular lymph nodes. The ultrasonography showed enlarged lymph nodes, with normal structure and echogenic hilus. Laboratory tests, including routine blood analysis and immunological parameters (white blood cells, proteins electrophoresis, IgA, IgG, IgM, HIV) were within the limits, except for total serum IgE (1.848 KU/l). Histopathology revealed lymphocytes and histiocytes infiltration in deep dermis (Figure 2a). Giemsa staining showed intrahistiocytic bodies of L (Figure 2b). Smear examination and serologic detection of Abs anti-L by indirect immunofluorescence were negative.

Based on the clinical and histological findings, a diagnosis of periocular plaque-type localized cutaneous leishmaniasis (LCL) was made. After informed consent, deoxycholate amphotericin B was used intralesionally by diluting the drug (5 mg) in lidocain (1 ml) in order to reduce pain in the injection site. Treatment (4 times every fortnight) induced progressive improvement of the lesion with residual atrophic and pigmented area (Figure 1b). There were no systemic side effects. The patient denied a post treatment biopsy. No relapse was observed after one year follow-up.
Discussion

The two most typical clinical features of LCL are the nodular type (from *L. major* and *L. tropica*) and the ulcerous type (from *L. mexicana* and *L. braziliensis*). The other reported aspects (erysipeloid, lupoid, zosteriform, sporotrichoid, micetoma-like, chancriform, discoid lupus erythematosus-like, squamous cell carcinoma-like, eczematous, verrucous) are rare or anecdotal (3). Although LCL occurs mostly on the face, the periocular involvement is present in only 2-5% of the cases. Moreover, in this site the plaque-type is less frequent than papular and nodulo-ulcerative forms (4).

Systemic amphotericin B and trivalent and pentavalent antimony are the first-line treatments in visceral and diffuse cutaneous leishmaniasis. However, the first is often responsible for life-threatening side effects, such as hypokalemia and renal, hepatic and cardiac toxicities. Nowadays, antimonial compounds are the treatment of choice, but they are available only for veterinary use in Italy. LCL single lesions in immunocompetent subjects can be treated with topical (paromomycin, liposomal amphotericin B, imidazole compounds, imiquimod), physical (cryotherapy, thermotherapy, excimer or CO2 laser, photodynamic therapy, nitric oxide, surgical excision), and intralesional therapies (pentavalent antimony compounds as meglumine and sodium stibogluconate, interferon γ, zinc sulphate, chloroquine, ciprofloxacin) (5). It is also possible the sequential application of cryotherapy and intralesional injections of antimony. This treatment ensures positive outcomes in most cases, without risks of systemic adverse events (6). Recent guidelines recommend using local therapy whenever possible, and systemic therapy if local therapy fails or cannot be
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performed (7). For these reasons and because our patient showed a single lesion, we chose a topical treatment with intralesional deoxycholate amphotericin B. We hypothesize that previous treatment failure with paromomycin ointment was due to the deep dermal involvement. For this reason we did not use topical liposomal amphotericin B, recently reported with the same efficacy as intralesional glucantime in the treatment of cutaneous leishmaniasis (8). Intralesional use of amphotericin B was sporadically reported in other infectious skin diseases, such as chromoblastomycosis (9), chromomycosis (10), and alternariosis (11). In the past we successfully used intralesionally deoxycholate amphotericin B in 2 patients with infectious diseases caused by Candida albicans and Sporothrix schenckii, respectively. The first one was a 41-year-old immunocompetent man affected by candidal granuloma of the left auricular pavilion (12). The second one was a 64-year-old woman who presented to us with nodular lesions in the right leg. The lesions had appeared 6 months after starting immunosuppressive therapy with cyclosporine, azathioprine and methylprednisolone for renal transplantation; histological, microscopic, and cultural findings of fresh tissue specimens concurred to formulate the diagnosis of lymphocutaneous sporotrichosis (13).

To our knowledge, intralesional use of amphotericin B was never suggested for LCL. In our patient the therapy was well tolerated, except for moderate and transient erythema and pain in the injection site. These side effects were already recorded (9-13). Finally, our therapeutic approach is not expensive. In fact, the deoxycholate form of amphotericin B is less expensive than other forms (liposomal, lipidic and colloidal cholesterol dispersion) which have been recently marketed to reduce systemic amphotericin B toxicities (14).

References