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Case Report

Intralesional treatment with meglumine antimoniate in three patients with New World cutaneous leishmaniasis and large periarticular lesions with comorbidities

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Abstract

Although New World cutaneous leishmaniasis is not itself a life-threatening disease, its treatment with systemic antimonials can cause toxicity that can be dangerous to some patients. Intralesional meglumine antimoniate provides a viable, less toxic alternative. Herein, we describe an alternative treatment with subcutaneous intralesional injections of meglumine antimoniate into large periarticular lesions of three patients with cutaneous leishmaniasis and comorbidities. This treatment was safe, successful, and well tolerated. This case series suggests that intralesional meglumine antimoniate is an effective therapy for cutaneous leishmaniasis, even with periarticular lesions. This hypothesis should be tested in controlled clinical trials.

Key words: Cutaneous leishmaniasis. Meglumine antimoniate. Intralesional injections.

INTRODUCTION

The first-choice treatment for American tegumentary leishmaniasis (ATL) is systemic pentavalent antimonials. However, these drugs are widely known for their toxic side effects. Recently, the World Health Organization recommended that decisions regarding treatment must be based mainly on the risk–benefit ratio of the intervention for each patient, and that local and less toxic treatments should be explored since mucocutaneous leishmaniasis occurs in less than 5% of cases, and systemic treatment does not prevent its occurrence[1].

The National Institute of Infectious Diseases (INI), Oswaldo Cruz Foundation (Fiocruz), is a referral center for the treatment of ATL in Rio de Janeiro, Brazil. At this institution, intralesional (IL) treatment with meglumine antimoniate (MA) has been performed for over 30 years in selected patients with cutaneous leishmaniasis without mucosal lesions[2], especially in those with contraindications to the systemic use of MA[3]. Recently, a standardized protocol of the IL therapy performed in the INI was published[4].

The Pan-American Health Organization (PAHO) recommends that IL therapy should be administered via the intradermal route in referral centers for single lesions up to 900 mm^2 in any location except the head and periarticular sites when immunosuppression is absent and patient follow-up is possible[5]. We, however, describe three cases of parasitological confirmed cutaneous leishmaniasis and comorbidities, with larger periarticular lesions, successfully treated with IL MA via the subcutaneous route, and followed-up for at least 12 months after therapy.

CASE REPORTS

Three patients with cutaneous leishmaniasis were treated with IL MA (Aventis Pharma, São Paulo, Brazil), supplied by the Brazilian Ministry of Health, via the subcutaneous route according to standard techniques that have been previously reported[4]. All patients signed informed consent forms for diagnostic procedures and treatment. There was no need for local anesthesia in any patient, and the procedure had good acceptability. No patient relapsed in the subsequent 12-month follow-up. The characteristics of the patients before and after IL treatment with MA are shown in **Table 1.** The aspects of cutaneous lesions before and after treatment (at the time of complete healing) are shown in **Figure 1**.

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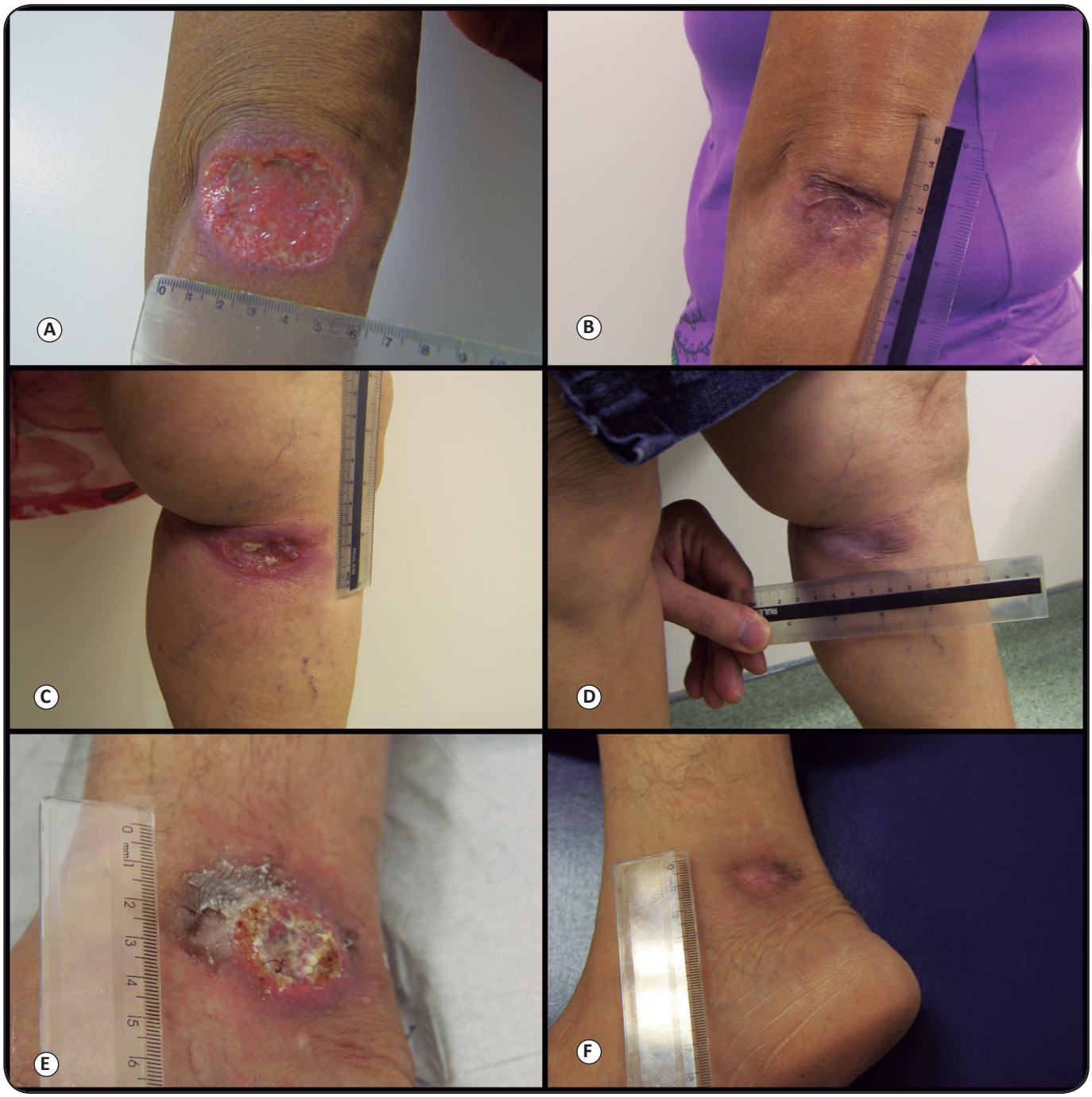

FIGURE 1 - Cutaneous leishmaniasis with large periarticular lesions in three patients treated with intralesional meglumine antimoniate, before and after therapy. Figure 1A, C, and E: Patients 1, 2, and 3, respectively, pre-treatment. Figure 1B, D, and F: Patients 1, 2, and 3, respectively, post-treatment (complete healing).

DISCUSSION

Herein, we describe three cases of parasitological confirmed cutaneous leishmaniasis with large periarticular lesions that were successfully treated with IL MA despite the presence of comorbidities and the paucity of treatment options. All patients were followed-up for at least one year after treatment without relapse or development of mucosal lesions. In the INI/Fiocruz, ear, nose, and throat specialists routinely perform a fiber optic examination of the upper aero-digestive pathways once a year for at least five years after clinical cure. In our institution, the evolution of treated cutaneous leishmaniasis to mucosal leishmaniasis is a very rare event.

Because of the virtual absence of mucosal leishmaniasis in the Old World, cutaneous leishmaniasis can frequently be managed with local wound care or topical specific treatment[1]. In the New World, the rate of occurrence of mucosal leishmaniasis

TABLE 1

Characteristics of three patients with New World cutaneous leishmaniasis with large periarticular lesions treated with intralesional meglumine antimoniate.

Characteristics	Patient 1	Patient 2	Patient 3
Age (years)	63	69	71
Gender	female	female	male
Comorbidities	Angina pectoris, dilated cardiomyopathy, hypertriglyceridemia, 2 previous acute myocardial infarctions	Diabetes mellitus, hypertension, dyslipidemia, asymptomatic hyperamylasemia	Community-acquired pneumonia by the time of the diagnosis of cutaneous leishmaniasis
Number of lesions	1	1	1
Length of the major axis	70mm	60mm	40mm
Area of the lesion*	3,023.8mm^2	1,178.1mm^2	942.5mm^2
Location of the lesion	Extensor surface of the left elbow	Upper third, medial face, left leg, near the knee	Right medial malleolus
Method of parasitological confirmation	Culture for *Leishmania* genus positive in NNN	Culture for *Leishmania* genus positive in NNN	Presence of amastigotes on histopathology
Disease duration before treatment (months)	4	3.5	3
Number of IL infiltrations	2	2	2
Total amount of infiltrated MA (mL)	19mL	23mL	14mL
Adverse effects of IL MA	Tinnitus, light local edema, transient hyperlipasemia 1.5 times the reference value	No	No
Time interval between infiltrations (days)	21	21	21
Time to epithelialization (months after treatment)	3	1	2.5
Time to complete healing (months after treatment)	8	3	3.5
Follow-up (months after treatment)	12**	66	12

IL: intralesional; **MA:** meglumine antimoniate; **NNN:** Novy, McNeal, and Nicolle medium. *Area of the ellipse – formula: major axis/2 X minor axis/2 X π. ** Patient 1 died because of previous comorbidities after 12 months of follow-up.

limits the option of not providing specific treatment to a patient with cutaneous leishmaniasis.

Cutaneous leishmaniasis in Rio de Janeiro is almost exclusively due to *Leishmania braziliensis*[6]. A recent systematic review of American cutaneous leishmaniasis revealed a very low (6%) spontaneous cure rate for *L. braziliensis* infection[7]. Specific treatment is thus almost mandatory. Patients with contraindications to systemic treatment, however, can benefit from IL MA treatment[3,8]. Recently, Soto et al.[9] found that treatment with IL MA has comparable efficacy to treatment with IL pentamidine in Bolivian patients with cutaneous leishmaniasis caused by *L. braziliensis*.

The PAHO recommendations[5] were based on the scarce literature available up to 2013 on IL treatment of ATL. However, PAHO also invited researchers to report local experiences in order to establish local and regional profiles. Our experience differs from the PAHO recommendations for IL MA therapy on the following issues: 1) contraindication for periarticular lesions; 2) contraindication for lesions >900mm^2; and 3) the use of the intradermal route. Notably, the periarticular location of the lesions did not prevent epithelialization or complete healing in our patients. The large area of the lesions in patients 2 and 3 did not hinder healing process either, although the lesion in patient 1, which was larger than the lesions in the other two patients, took longer to heal. Finally, intradermal infiltration of a considerable amount of medication (>1.0mL) would not be advisable, if at all feasible. We hypothesize that passive diffusion from the hypodermis could explain the success of IL therapy via the subcutaneous route, which is much easier to perform than intradermal injection is. In addition, although IL therapy can be painful, the discomfort caused by the subcutaneous injection was well tolerated, and local anesthesia was not needed in any patient.

We therefore recommend IL MA when comorbidities hamper or contraindicate systemic treatment, even in larger periarticular lesions. The results obtained with the treatment of these three patients suggest that IL treatment with MA in periarticular lesions, when systemic treatment is not feasible, may be successful, safe, and well tolerated. Good monitoring of the skin lesions and inquiry into complaints of the mucous membranes in the upper aero-digestive tract is desirable for at least one year after treatment. In addition, patients should be instructed to seek medical advice whenever they experience nose- and throat-related symptoms. IL use of MA in ATL should be better studied through controlled clinical trials, including in patients with periarticular lesions.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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