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Case Report

Successful treatment of cutaneous leishmaniasis with intralesional meglumine antimoniate: A case series

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Abstract

Cutaneous leishmaniasis (CL) is a high-morbidity, vector-borne disease endemic to Colombia. Unlike conventional systemic antileishmanial therapy, intralesional meglumine antimoniate administration has fewer adverse effects and can be as effective and safe. We describe 12 patients treated with intralesional meglumine antimoniate: seven with primary and five with recurrent lesions. The majority (11/12) met all cure criteria after 1–7 sessions of meglumine antimoniate administration (1–5 mL). Adverse effects comprised mainly of local pain and edema. Intralesional meglumine antimoniate administration could be an excellent alternative treatment for uncomplicated CL; however, controlled clinical trials are needed to test the efficacy and safety thereof.

Keywords: Cutaneous leishmaniasis. Intralesional meglumine antimoniate infusion. Treatment.

INTRODUCTION

Cutaneous leishmaniasis (CL) is an infectious disease caused by numerous species of *Leishmania* protozoa, characterized by ulcers, nodules, or plaques on exposed regions of the body, mainly the face, arms, and legs. There may be one or multiple injuries that leave permanent scars and may cause disfigurement, disability, and subsequent social rejection and psychological suffering[1]. The epidemiology of CL in the Americas is very complex, with intra- and inter-specific transmission cycles, multiple circulating *Leishmania* species, reservoir hosts, sand-fly vectors, and clinical manifestations in the same geographical area; the response to therapy also varies widely[1]. CL represents a serious public health problem, with approximately 50,000 annual cases in the 17 countries that comprise the Americas, 70% of which are from Brazil, Colombia, and Perú. In 2016, >10,000 cases were reported in Colombia, with an incidence of >33 cases/100,000 inhabitants[2]. The most prevalent *Leishmania* species causing CL are *L. braziliensis* and *L. panamensis*, followed by *L. guyanensis*, *L. amazonensis*, and *L. mexicana*[2].

The characteristic lesion is a clean ulcer with a granular base and raised, indurated, and erythematous edges. The lesion is usually painless and may be accompanied by enlarged regional lymphadenopathy. Although the classic lesion is very suggestive of CL, diagnosis must be confirmed through visualization of the amastigote forms of *Leishmania* spp. in Giemsa-stained smear samples, taken from the border or base of the ulcer. Additionally, biopsy, culture or molecular testing can be performed in cases in which direct examination is inconclusive.

Traditionally, first-line treatment for CL has been based on the intramuscular (IM) administration of meglumine antimoniate at a dose of 20 mg/kg × 20 days, regardless of the number of lesions. However, in 2010 the WHO expert committee began to promote the use of local therapies to treat cases of uncomplicated CL, thereby reducing the cost of care caused by the toxicity of systemic treatment. The most recent Pan American Health Organization (PAHO) guidelines recommend intramuscular or intravenous (IV) infusion of pentavalent antimoniate

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salts (meglumine antimoniate [Glucantime®] and sodium stibogluconate), with a maximum dose of 15 mL (1215 mg) per day as first-line treatment. Mild side effects include fever, chills, myalgia, arthralgia, and headache, while serious adverse events include nephrotoxicity, hepatotoxicity, acute pancreatitis, cardiac alterations and reports of varicella zoster reactivation[3,4]. The PAHO guidelines also recommend the use of intralesional antimonial therapy when systemic treatment is not indicated or if local treatment for CL is required, per established criteria[5]. However, there are no controlled or randomized studies that demonstrate the efficacy and safety of intralesional treatment[5]; some studies have shown good results in terms of efficacy, adverse effects, and incidence of recurrence compared with other local and systemic treatments[6].

The cure of the lesion was determined by the following criteria: healing with complete re-epithelization and flattening of the edge of the injuries; disappearance of the induration of the base; disappearance of lymphangitis or adenitis in case it has happened; and absence of new injuries.

This case series describes 12 patients with parasitological diagnoses of CL that were treated with intralesional meglumine antimoniate at the Colombian Institute of Tropical Medicine (ICMT) in Apartadó, Colombia from 2014–2017. Data are presented as mean ± standard deviation.

CASE REPORT

Parasitological diagnosis of CL was made through direct microscopy visualization of the parasite in Giemsa-stained tissue scrapes or cultured sample aspirates. *L. panamensis*, identified by PCR-RFLP[7], was the causative organism in two patients. All patients fulfilled the criteria for intralesional meglumine antimoniate administration, including difficult geographic access, presence of less than 3 lesions respecting face and joint surfaces, or recurrence of single lesions that failed to respond to systemic treatment. Meglumine antimoniate was administered intralesionally, covering the entire surface of the lesion. In each session, 1–5 mL (depending on the size of the lesion) of meglumine antimoniate was infused, not exceeding one ampoule (5 mL) per lesion.

The male:female ratio was 4:8, with an average age of 27.8 ± 13.8 years (Mean ± standard deviation). Only one patient received a single dose; the remaining 11 patients received 4.36 ± 1.55 doses. The average time for all dosage sessions was 6.5 ± 2.3 days. The illness time was between 2 months and 3 years with an average of 7.5 months, and the healing time was between 14 and 60 days, with an average of 34.7 days. **Table 1** shows the sociodemographic characteristics of the patients, the number of intralesional meglumine antimoniate sessions, and the number of days between each session.

Only one patient had three lesions, while the rest had only one lesion each. The average lesion size was 18.6 x 13.5 mm. Lesions were located in arms (50%), legs (14.3%), neck (14.3%), shoulder (7.1%), forearm (7.1%), and thigh (7.1%).

The lesions were mostly clean ulcers (10/14) 1–7 cm in diameter, with raised erythematous borders; the rest (4/14) were erythematous plaques 1–2 cm in diameter. Some presented with perilesional lymphadenopathies. **Table 2** shows the clinical characteristics of the lesions and the adverse effects reported by patients. **Figure 1** summarizes the evolution of the lesions for each patient in response to treatment.

The five patients who had recurrent CL had reactivation of the lesion 2 to 24 months (8 months average) after completing

TABLE 1: Sociodemographic characteristics and type of lesions in patients with cutaneous leishmaniasis treated with intralesional meglumine antimoniate.

Case number	Age (years)	Gender	CL´s recidivans	Number of session	Interval between sessions (days)
01	39	Female	No	2	6
02	25	Male	No	6	7
03	35	Male	No	4	7
04	30	Male	No	6	7
05	36	Female	No	3	7
06	22	Male	No	3	7
07	0.63	Female	Yes	4	7
08	5	Male	Yes	3	9
09	27	Male	Yes	4	4
10	25	Male	Yes	7	4
11	23	Male	Yes	6	7
12	39	Female	No	1	-

TABLE 2: Clinical characteristics in patients with CL. Apartadó, 2014-2017.

Case number	Lesions number	Size of lesion (mm)	Location	Adverse effects
01	1	22x20	Right arm	Burning, erythema and edema, Local pain
02	3	#1 70x30	Right shoulder	Local pain
02	-	#2 8x8	Right forearm	None
02	-	#3 17x15	Right arm	None
03	1	12x9	Left arm	Local edema
04	1	25x25	Right thigh	Local pain
05	1	15x6	Left arm	Local edema
06	1	17x8	Neck	Local pain and edema
07	1	9x9	Right arm	Local pain
08	1	8x10	Left arm	Local pain
09	1	18x18	Left arm	Local pain, edema and fever
10	1	10x10	Neck	Pruritus
11	1	22x17	Right leg	Local pain
12	1	9x11	Left leg	Local pain and fever

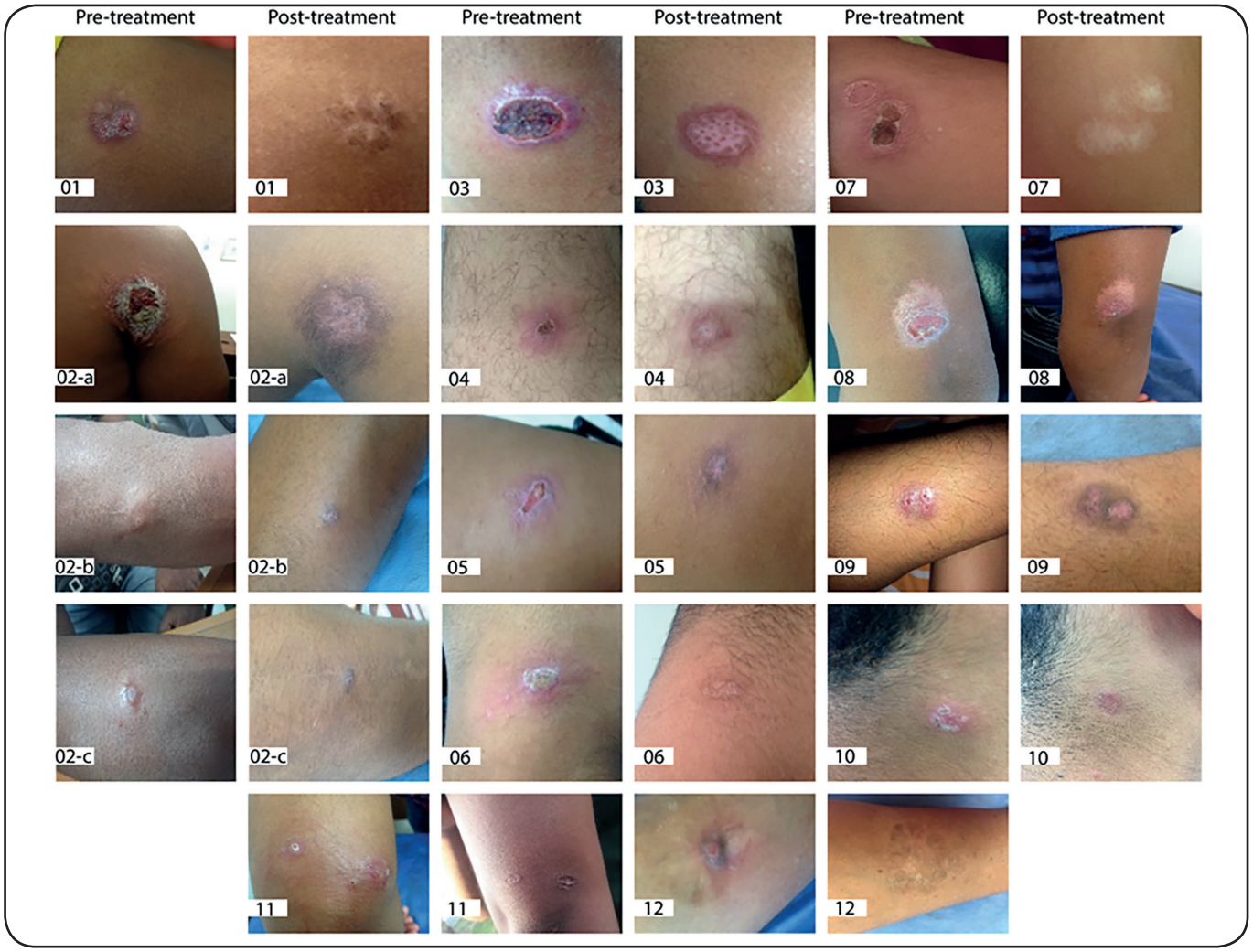

FIGURE 1: Clinical response after treatment with intralesional meglumine antimoniate.

therapy with IM meglumine antimoniate, at a dose of 20 mg/kg/day per 20 days; all of them achieved healing criteria with the systemic therapy.

Only one patient (#10) had therapeutic failure to the intralesional therapy. This patient was in the group of recurrences; he completed 20 days of meglumine antimoniate IM 20 mg/kg/day and achieved the healing criteria. However, 2 months after healing he had reactivation of the lesion. He completed 7 sessions of intralesional meglumine antimoniate and never achieved healing criteria. He was eventually cured using cryotherapy.

DISCUSSION

Intralesional meglumine antimoniate administration has been used as a therapeutic alternative in patients who have contraindications for systemic treatment; however, its true efficacy has not been established. For approximately 30 years, intralesional meglumine antimoniate administration has been compared in literature to other local methods, such as intralesional sodium stibogluconate[8], zinc sulfate, topical paromomycin[9], trichloroacetic acid, and cryotherapy[10], or its efficacy and safety was retrospectively described[11].

Since 2013, PAHO guidelines have indicated intralesional meglumine antimoniate administration, every 3–7 days, as a therapeutic alternative in patients with single lesions <3 cm and not located on joint or face surfaces and patients contraindicated to systemic therapy or those who are not immunosuppressed[5].

The present study shows a series of 12 cases of CL treated with intralesional meglumine antimoniate: seven had primary lesions, and five had recurrent lesions. Eleven cases (91.6%) achieved complete cure, and only one patient showed therapeutic failure. Despite the small sample size, these findings are similar to that of Soto et al., who obtained cure rates of 70% with intralesional meglumine antimoniate administration. While another Brazilian study showed cure rates >70%[10], others showed lower cure rates, probably due to different species of *Leishmania* as the causative organism[7]. One of the patients presented with three lesions that were >3 cm and met all the criteria for cure after six treatment sessions with intralesional meglumine antimoniate.

Interestingly, in four of the five patients with recurrent CL, intralesional meglumine antimoniate was a successful alternative in the patients who received systemic meglumine antimoniate for 20 days and in one patient who received oral miltefosine for 28 days in addition to the systemic meglumine antimoniate. Literature is scarce in reference to cases of relapsing CL treated with intralesional meglumine antimoniate; the contribution of the present case report is invaluable in this regard.

Another valuable finding from this study is the fact that the intervals between sessions were long (up to 9 days) but didn´t affect the healing of the lesions. The patients achieved healing criteria in a similar time to those who had shorter intervals between sessions. On the other hand, the number of sessions needed to achieve healing criteria were similar to those used by Duque et. al[11] (3-4 sessions), except for 4 patients who needed more sessions (up to 7). This observation is important because it shows that if the patient does not achieve healing criteria in 3 sessions, more infiltrations can be used to complete it, in a way that does not mean that the patient's treatment has failed.

After a follow-up period ranging between 4 months and 3 years, none of the 12 cases experienced recurrent lesions. A retrospective study conducted in Brazil in the time period 2000–2006 showed that when 24 patients were treated with this intralesional therapy followed by a 60-month follow-up, none of the patients presented with recurrence or muco-cutaneous forms of the disease, supporting the hypothesis that this treatment lowered the risk of recurrence[10,11,12].

The patients reported here had an excellent clinical response, even when the sessions were held every 4–9 days, allowing for a longer healing time and fewer treatment sessions. This also facilitated adherence in patients with difficult access to the treatment centers. These results suggest that intralesional meglumine antimoniate administration is an excellent option for older patients or those with comorbidities that contraindicate systemic treatment.

With systemic therapy, there is a risk of cardiac, hepatic, pancreatic, and renal toxicity. Therefore, a follow-up with laboratory tests is indicated, ideally between 7–13 days. Intralesional treatment has fewer adverse effects, since absorption of the medication is minimal. The most common adverse effects in the patients, including pain, edema, pruritus, and local erythema, were always benign and self-limiting. These effects are similar to those described in literature. However, Esfandiarpour et al. identified the following adverse effects with intralesional therapy: pain, erythema, pruritus, secondary infection, nausea, vomiting, and urticaria; and with less incidence: local necrosis, sporotrichoid lesions, dizziness, dyspnea, and anaphylactic shock[6].

This study shows promising results using intralesional meglumine antimoniate as a first line therapy for patients with recurrent CL and for first-time CL patients, and those for whom systemic therapy is contraindicated or who have experienced therapeutic failure with conventional treatment. There are fewer adverse effects (in type and intensity) as well as lower costs for the health system. A greater adherence to treatment by patients is also observed. This study shows that the intervals between sessions could be longer without affecting treatment efficacy.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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