BRIEF REPORT

MANIPULATION OF CUTANEOUS LEISHMANIASIS LESIONS: CASE SERIES IN A PERUVIAN HOSPITAL

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ABSTRACT

In cutaneous leishmaniasis endemic areas it is a common practice for patients to manipulate their lesions with traditional treatments as a first therapeutic option. A case series study was conducted in order to describe the frequency and the variations of the patient manipulation of cutaneous leishmaniasis lesions at the Cayetano Heredia Hospital. The study included 124 patients with cutaneous leishmaniasis. From the patient population it was found that 54% (67/124) manipulated their lesions. Of this, 92.5% (62/67) did so with chemicals, and 43.3% (29/67) with plants. The most frequent local changes reported by patients were increased lesion size in 35.8% (24/67) and increased inflammation in 28.4% (19/67). Manipulation by patients decreased the positivity of the parasitological diagnosis in those patients with ulcerative lesions.

Keywords: Leishmaniasis, Cutaneous; Medicine, Traditional; Diagnosis (source: MeSH NLM).

INTRODUCTION

Leishmaniasis is a neglected disease caused by protozoa of the genus *Leishmania*, which are transmitted by insects of the genus *Lutzomyia* [(1)]. Cutaneous leishmaniasis (CL) is the most common clinical form and approximately 7,000 cases are reported each year in Peru [(1-4)].

In endemic areas, particularly in rural areas, the use of traditional medicine is usually a first option, due to the lack of access to health services, mistrust of Western medicine, unavailability of standardized treatment, fear of side effects, among others [(3, 5)]. Traditional treatments include topical application of plants, chemical or thermal substances, antibiotics, etc. [(3,5-7)]. The use of these products could alter the lesion morphology and decrease its parasitic load; but also alter the histopathology and, consequently, the diagnosis of the disease. Therefore, the use of such products is relevant in Peru, where observation of the parasite is a requirement for the initiation of free standardized treatment [(8)]. It should be noted that currently there are other methods for the diagnosis of CL, such as culture, histopathology and molecular methods, which are less accessible in our context.

To date, the prevalence of lesion manipulation in referral hospitals, how it would affect light microscopy diagnosis and the appearance of the lesion are unknown. This study describes the frequency and types of manipulation, as well as the results from light microscopy (smear) and the clinical characteristics of CL lesions.

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THE STUDY

A descriptive, case series type, observational study was conducted by using information obtained from clinical records of the Leishmaniasis Program of the Alexander von Humboldt Institute of Tropical Medicine from the Universidad Peruana Cayetano Heredia, a referral hospital in Lima. Leishmaniasis was diagnosed and treated in patients who attended the aforementioned hospital, from June to December 2017.

Physicians of the Leishmaniasis Program considered as study cases the medical records from patients of all ages, with established diagnosis of uncomplicated CL (without mucosal involvement and in immunocompetent host). Epidemiological, clinical, parasitological and/or immunological criteria were evaluated. The clinical diagnosis was based on the presence of ulcers with regular, well-defined, indurated, purplish, raised edges, with granulomatous and thick background [9]. We included medical records that had smear test and leishmanin skin test (LST) results when at least one of these was positive, and excluded records with incomplete data.

Lesion manipulation was defined as the topical application of plants on at least two occasions (direct placement, plasters, infusion), chemicals (battery acid, blue stone or pharmaceutical chemicals, such as antibiotic, antifungal or corticoid creams) or heat. It was the patients themselves, with the exception of underage patients, who handled the lesions. The changes made by lesion manipulation were described in this research as what was reported in the clinical records by the patients themselves. Changes were classified as increase/decrease in size of the lesion (diameter), increase/decrease in inflammation (erythema, pain, edema, secretions) or none.

The information was entered into an Excel® database, and the data was analyzed in Stata 15 (StataCorp, College Station, Texas, USA) and StatCalc at EpiInfo™. Frequencies, proportions, central tendency measures, and dispersion were calculated. The qualitative variables of microscopy, gender, time of illness, age group, and lesion type were crossed with the presence of manipulation and the smear result. Their statistical significance was determined with chi square and Fisher's exact tests.

The project was approved by the ethics committees of the Universidad Peruana Cayetano Heredia and the Cayetano Heredia Hospital (Certificate No. 0670519).

KEY MESSAGES

Motivation for the study: Currently, the frequency of manipulation of cutaneous leishmaniasis (CL) lesions in hospitals and its impact on microscopy diagnosis are unknown.

Main findings: More than half of patients with CL manipulated their wounds, most of them with chemicals. There was an increase in the size of lesions after manipulation. In patients with ulcers, manipulation was found to be negative on light microscopy.

Implications: The diagnosis of leishmaniasis by microscopy is widely used in the first level of healthcare, so patients must be educated to avoid the manipulation of lesions; this will help achieving early diagnosis and getting timely treatment.

FINDINGS

From June to December 2017, 150 patients with CL were identified and 26 were excluded due to incomplete information; thus, the total number of patients enrolled was 124. The male/female ratio was 2.64. The median age was 38 years old (interquartile range 22-50) and the predominant age group was constituted by adults in 71.8% (89/124) of the study population (Table 1). 68.6% (85/124) of patients were from the department of Lima. The city of Lima, Madre de Dios and Cusco were the main places of contagion.

The majority of patients, 59.7% (74/124), had only one lesion, and 16.9%, three or more. A total of 205 lesions were registered. Ulcers were the most common lesion in 72.7% (149/205) of the total registered lesions (Table 1), followed by nodular and infiltrative lesions. The most frequent lesion locations were upper limb, 32.7% (67/205), head and lower limb, both 27.8% (57/205).

The smear test was positive in 73.4% (91/124) of the patients and the LST in 91.9% (114/124) (Table 1). Analyzing all types of lesions, no statistical difference (p = 0.198) was observed in the smear positivity between manipulated (50.5%) and non-manipulated (49.5%) lesions. However, considering only ulcerative lesions, manipulation significantly reduced smear positivity (p = 0.029). From the total of patients, 67 (54.0%) manipulated their lesions, both adults and children, 65.7% (44/67) and 16.4% (11/67), respectively. The patients who manipulated their lesions were mainly from Lima (Table 1).

In lesions with a longer time of illness (more than three months), parasitological demonstration was significantly lower regardless of the occurrence of manipulation (Table 2). The most used products were chemicals in 92.5% (62/67) of cases, and plants in 43.3% (29/67). 49.3% (33/67) of the patients used only chemicals and 6.0% (4/67) used only plants, while 34.3% (23/67) reported using both products.

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Table 1. Clinical and laboratory characteristics of 124 patients with cutaneous leishmaniasis and manipulation of lesions who were treated at the Institute of Tropical Medicine of Universidad Peruana Cayetano Heredia.

Characteristic	Manipulated n (%)	Non-manipulated n (%)	p-value[b]
Gender			0.800
Male	48 (53.7)	42 (46.7)	
Female	19 (55.9)	15 (44.1)	
Place of origin			0.678
Lima	47 (55.3)	38 (44.7)	
Province	20 (51.3)	19 (48.7)	
Smear test			0.198
Positive	46 (50.5)	45 (49.5)	
Negative	21 (63.6)	12 (36.4)	
Smear test from ulcer patients (n=100)			0.029
Positive	35 (46.7)	40 (53.3)	
Negative	18 (72.0)	7 (28.0)	
Time of illness [a]			0.111
≤3 months	28 (46.7)	32 (53.3)	
>3 months	39 (60.9)	25 (39.1)	
Age group [a]			
Infant	8 (53.3)	7 (46.7)	0.954
Adolescent	5 (62.5)	3 (37.5)	0.725[c]
Adult	49 (55.1)	40 (44.9)	0.716
Older adult	5 (41.7)	7 (58.3)	0.382
Type of lesion (n=205) [a]			
Ulcerative	71 (47.7)	78 (52.3)	0.059
Nodular	18 (62.1)	11 (37.9)	0.229
Infiltrative	6 (54.5)	5 (45.5)	1.000
Verrucose	2 (100)	0 (0.0)	0.498[c]
Scabbed	0 (0.0)	2 (100)	0.232[c]
Polymorphic	9 (75.0)	3 (25.0)	0.137[c]

[a] p-value calculated by comparing the proportion with the category complement.
[b] Chi-square test
[c] Fisher's exact test

62 patients used chemicals to manipulate their lesions; the most commonly used were antibiotic or antifungal creams and hydrogen peroxide (Table 3). Patients also reported having used the following plants: *Plantago major* (llantén), *Piper aduncum* (matico), *Chamaemelum nobile* (chamomile), *Oenothera rosea* (chupasangre), among others. 29 patients manipulated their lesions with plants, llantén was the most used, followed by matico and chamomile. Only 6 patients used thermal burns and another 6 used products such as beef liver, pig fat, honey, urine and excreta.

Finally, the most reported change was increased size with 35.8% (24/67), followed by increased inflammation with 28.4% (19/67). No change in lesions was reported by 31.3% (21/67) (Table 4).

Table 2. Smear results according to manipulation and time of disease in patients with cutaneous leishmaniasis who were treated at the Institute of Tropical Medicine of the Universidad Peruana Cayetano Heredia.

Manipulation	Time of illness		p-value
	≤3 months	>3 months	
Manipulated			0.003[a]
Positive smear test	25	21	
Negative smear test	3	18	
Non-manipulated			0.003[a]
Positive smear test	30	15	
Negative smear test	2	10	

[a] Fisher's exact test

DISCUSSION

In this case series, manipulation of CL ulcerative lesions with traditional treatments significantly reduced parasite observation effectiveness. This practice prevents definitive diagnosis, which is necessary for a patient with CL to receive free treatment, as specified by the Ministry of Health's national standard for the treatment of leishmaniasis [8].

More than half of the patients with CL (54.0%) came to consultation with history of having handled their lesions; most of them with multiple products, usually chemicals (92%). However, literature shows higher frequencies of manipulation (71.2%) in populations from long-standing

Table 3. Products used in cutaneous leishmaniasis lesions by patients treated at the Institute of Tropical Medicine of the Universidad Peruana Cayetano Heredia (n=67)

Product	n (%)
Chemicals	62 (92.5)
Antibiotic cream	16 (23.9)
Hydrogen peroxide	14 (20.9)
Antimycotic cream	9 (13.4)
Antibiotic tablet	7 (10,5)
Topical corticoid	5 (7.5)
Lemon	4 (6.0)
Salt	4 (6.0)
"Blue stone"	3 (4.5)
Battery acid	3 (4.5)
Gentian violet	3 (4.5)
Others	37 (55.2)
Plants	29 (43.3)
Plantago major (llantén)	13 (19.4)
Piper aduncum (matico)	8 (11.9)
Chamaemelum nobile (manzanilla)	5 (7.5)
Oenothera rosea (chupasangre)	3 (4.5)
Croton lechleri (sangre de grado)	3 (4.5)
Others	12 (17.9)

Table 4. Changes observed in manipulated lesions of cutaneous leishmaniasis by patients treated at the Institute of Tropical Medicine of the Universidad Peruana Cayetano Heredia (n=67)

Characteristic	n (%)
Type of change	
Increased size	24 (35.8)
Increased inflammation	19 (28.4)
Decreased inflammation	7 (10.5)
Decreased size	2 (3.0)
No change	21 (31.3)
Most frequent changes	
Only plants	
No change	2 (3.0)
Increased size	1 (1.5)
Increased inflammation	1 (1.5)
Only chemical substances	
Increased size	15 (22.4)
Increased inflammation	10 (14.9)
No change	9 (13.4)
Decreased inflammation	2 (3.0)
Decreased size	1 (1.5)
Only thermal	
Increased size	1 (1.5)
Plants and chemical substances	
No change	10 (14.9)
Increased inflammation	6 (9.0)
Increased size	5 (7.5)
Decreased inflammation	3 (4.5)
Chemical and thermal	
Decreased inflammation	1 (1.5)

leishmaniasis endemic areas [3] and in studies from Latin American countries [10-12]. In rural populations located in CL-endemic areas it is common to use traditional medicine, even in communities with health services [3]. The origin of this cultural habit is attributed to the lack of information or distorted perceptions about the disease, the desire to prevent its progression, or the lack of an adequate diagnosis [10,12].

Most patients in the study were male, probably because they have a higher risk of transmission [13,14]. Similar findings have been reported in Guatemala and Ecuador [10,12], where infection is associated with occupational risks (agriculture, livestock). However, there are areas where children under 15 are the most vulnerable, especially when transmission occurs within the household [13].

Lesion manipulation often occurs before seeking health care [3,12], which affects diagnosis negatively. Not only does it decrease the probability of detecting the parasite with the smear test, but it alters the morphology of the lesions, making clinical diagnosis by health personnel with limited training difficult. Based on the experience of the Cayetano Heredia Hospital, it is relatively common for any chronic ulcer in patients from rural areas to be classified as leishmaniasis, corresponding in many cases to other diseases such as sporotrichosis, pyogenic infections, insect bites, skin cancer, and skin tuberculosis, among others. Likewise, the handling of lesions delays and makes the diagnosis of CL more expensive. The usual procedure at the Cayetano Heredia Hospital is to obtain the result of the smear test within a few hours for non-manipulated lesions and to begin treatment the following day. However, in patients with manipulated lesions, the diagnosis exceeds one week and additional tests are required, such as cultures, pathological anatomy or polymerase chain reaction (PCR). This implies increased costs for patients (prolonging their stay in Lima) and for the health system.

The time of illness is known to affect parasitological diagnosis, especially the classic diagnostic methods [15,16]. In this study, it was found that the lesions with the longest time of illness (three months or more), independently of the presence of manipulation, had a lower proportion of positive smears, due to reduction of the parasitic load as a result of the immune response [15].

Inhabitants of endemic communities manipulate their lesions mainly with caustic products; most of them used chemicals (92%) and less than half (43%) used plants. At least a third of those who manipulated their lesions recognized that there was an increase in the size of the lesion or inflammation. Lesion manipulation frequently results in inflammation, superinfection, necrosis [3] and first- to third-degree burns [12]. Damage magnitude depends on the product used; the use of sulfur or acids generates more damage, which causes extensive subcutaneous tissue infection. The plants used caused less adverse effects on the lesions. In Colombia, it was found that people initially used "strong" treatments (burns, caustics) followed by "soft" treatments (plants) to heal [11].

Patients who come to the Cayetano Heredia Hospital recognize that handling their lesions with these substances causes pain and burns, but they hope the injury will heal. In some cases, they succeed; but most fail, because the burn is not regulated and causes many damaged tissues (dermal and lymphatic) to remain with parasites that later help lesion growth. Thermotherapy has used this knowledge to produce a regulated second-degree burn at a temperature below 52 °C with a time limit of 30 seconds [17].

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As for study limitations, the time between the last manipulation and the first contact with the referral center was not considered, which generates a confusing bias due to the chronicity of the injury. In addition, there could be a bias from the interviewer to adequately obtain the information since the population initially tends to deny the manipulation, underestimating its prevalence. The *Leishmania* species was not typified, therefore it could not be assessed whether it constitutes a confounding variable. Future studies with a prospective design and access to molecular methods could evaluate the effect of manipulation of CL lesions on parasite load, PCR results and *Leishmania* species identification.

In conclusion, manipulation of cutaneous leishmaniasis lesions could determine a negative effect in the smear result of ulcerative lesions and also distort their morphology, which makes the clinical diagnosis difficult. This would prevent timely and free treatment provided by the Ministry of Health, which requires parasitological demonstration. First-level healthcare usually lack the clinical experience found in referral hospitals. Therefore, the greatest impact would be felt at first-level health care, where the main diagnostic method is light microscopy. This is why it is necessary to implement educational programs in endemic areas to reduce leishmaniasis lesions manipulation.

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