



Leishmaniasis in Costa Rica- A Pilot Study

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Abstract

Objective: This project was undertaken to estimate the prevalence of leishmaniasis in the Northern region of Costa Rica, to understand the various manners of disease presentation, diagnosis, and responses to treatment, and to understand patients' knowledge about the disease, their treatment preferences, and their sources of Leishmaniasis education.

Design and methods: Prospective study of patients who presented to the Department of Dermatology, Hospital San Carlos with lesions suspicious for Leishmaniasis. We studied all patients over the period Feb 10, 2003 to March 20, 2003. Clinical examination and interview using a standardized survey were performed to determine demographic information, clinical history, and patients' knowledge and beliefs about the disease.

Results: A total of 10 patients presented over this time period with either a known diagnosis of Leishmaniasis or clinical lesions suspicious for Leishmaniasis. 6 out of the 10 patients were diagnosed with Leishmaniasis. Of these 6 patients, 2 (33%) were diagnosed based on clinical examination and history only while 4 (67%) were diagnosed based on clinical and pathological examination. All 6 of 6 patients reported that Leishmaniasis was important to treat, but 5 out of 6 (83%) lacked basic knowledge of this disease, based on questions regarding transmission, prevention, and treatment of the disease.

Conclusions: The results demonstrate that the Northern region of Costa Rica is an area endemic for Leishmaniasis. Based on evaluation of the study population, we know that Leishmaniasis has a fairly consistent presentation of cutaneous ulcers or nodule, but responds variably to treatment. In addition, this study highlights the challenges of relying on pathologic exams to determine diagnosis and the lack of education among the general population about this disease.

Recommendations: Based on the low sensitivities for pathologic tests for Leishmaniasis, we recommend the initiation of appropriate therapy when clinical history and exam are suggestive of Leishmaniasis, but tests are negative. We also recommend improved public health education utilizing physicians and home health nurses as sources of information.

Introduction

Leishmaniasis is a parasitic infection caused by the protozoan *Leishmania* and transmitted by the sandfly. Cases of Leishmaniasis have been reported on every continent except for Australia. The disease is endemic in areas in the tropics and subtropics such as Central and South America, southern Europe, Asia, the Middle East, and Africa. It is estimated that approximately 10% of the world's population or approximately 350 million people are at risk of contracting this infection [6]. Worldwide there are 2 million new cases of Leishmaniasis reported annually. Moreover, worldwide incidence has increased over recent years, thought to be related to the AIDS epidemic, global warming, and other environmental factors [1,6].

Leishmaniasis has three major clinical presentations: cutaneous lesions, which can cause disseminated skin ulcers, mucosal lesions which can result in significant facial disfigurement, and visceral lesions, which if left untreated invariably leads to death. Of the 2 million cases reported annually, an estimated 1.5 million of cases are cutaneous and the other 500,000 are visceral [6].

Leishmaniasis in Costa Rica

According to biostatistics information published by the Costa Rican Ministry of Health, the numbers of Leishmaniasis cases have measured between 481 to 998 cases per year over the period 1996-2000, or approximately 14-26 cases per 100,000 people [3]. Based on epidemiological studies in Central America as well as observations made in Costa Rica, it is felt that the majority of cases in Costa Rica occur in more rural areas, close to forests and farmland

where the parasite reservoirs and vectors reside together [4,13]. However, it is very difficult to accurately estimate the number of cases of Leishmaniasis in Costa Rica. This is related to the natural history of the disease, in which the ulcer frequently resolves on its own. Because the disease is thought to be more common in poorer and more rural communities, failure to seek medical care, lack of access to medical care, and lack of reporting by physicians also play a role in underestimation of cases. Thus, it is believed that numbers published by the Costa Rican Ministry of Health are underestimates of the true incidence of this disease.

Methods

We studied all patients with lesions clinically suspicious for leishmaniasis over the period Feb 10, 2003 to March 20, 2003 who presented to the Department of Dermatology, Hospital San Carlos. This hospital serves the province of Alejuela, an area of approximately XX square miles and population of XX. Letters were sent to 19 EBAIS, or local health clinics, asking physicians to refer patients who had been diagnosed with leishmaniasis or patients with lesions suspicious for leishmaniasis to the regional dermatology clinic. Clinical examination and interview using a standardized survey (Figure 1) were performed to determine demographic information, clinical history (including evolution of lesion, dates of diagnosis, past treatments undertaken), and patients' knowledge and beliefs about the disease. Following the interview, patients were educated on the etiology, symptoms, treatment, and methods of preventing Leishmaniasis. For patients who came to the clinic on first presentation, pathologic confirmation of disease was attempted by scraping the lesion for Gram staining and culture (frotis y cultivo). All patients who had pathologically proven Leishmaniasis or clinical history and lesions consistent with Leishmaniasis were started on meglumine antimoniate (Glucantime).

Results

A total of 10 patients presented over this time period with either a known diagnosis of Leishmaniasis or clinical lesions suspicious for Leishmaniasis. The most common presentation was of a non-healing ulcer or crusted nodule on exposed part of the body (Figure 2 and 3). 4 of 10 (40%) had leishmaniasis confirmed on gram stain of the lesion (Figure 4). Another 2 of 10 (20%) patients had lesions clinically suspicious for leishmaniasis but no organisms were seen on pathological examination. The remaining 4 of 10 (40%) patients were diagnosed with other skin diseases after clinical and pathological exam. These other diagnoses were sporotrichosis (1), bacterial infection (2), and diagnosis pending culture results (1). Demographic and clinical characteristics of the 6 patients with lesions clinically suspicious for Leishmaniasis are shown in Table 1. Of these 6 cases, the average time before initial presentation was 5.7 weeks (range 8 days to 3 months). All lesions were of the cutaneous subtype. Lesions varied in response to meglumine antimoniate (Glucantime), with some lesions almost completely resolving within the first week of injections and other lesions requiring up to 117 injections before adequate resolution took place. During the period that these patients were followed, none prematurely discontinued therapy. However, one patient was lost to follow-up before treatment could be initiated.

Patients were interviewed regarding their knowledge and beliefs about Leishmaniasis.

The study revealed that 3 out of 6 patients (50%) had suspicions that their symptoms were consistent with papalomoyo, the colloquial term for Leishmaniasis. For the majority of patients (5 out of 6, 83%), this was their first time infected with Leishmaniasis. The majority had other family members who had been infected previously (4 out of 6, 67%). All patients believed that it was important to receive treatment to prevent lesions from spreading (6 out of 6, 100%). The majority knew that the disease was caused by an insect (4 out of 6, 67%), but most of these individuals identified the vector as a mosquito (3 out of 4, 75%). None were familiar with the sandfly. The majority of patients did not know how they might be able to prevent infection (4 out of 6, 67%). Two patients identified repellents as an effective method of preventing bites. Other methods of preventing disease, including remaining indoors, wearing long sleeves and pants during the evening when the sandfly usually feeds, using insecticide impregnated, sleeping nets and disposing properly of waste materials were not identified by this population. 3 out of 6 (50%)

patients identified effective medical treatment as some type of injection, but they were not familiar with specifically with meglumine antimoniate. 2 out of 6 (33%) respondents also reported knowledge of home remedies for Leishmaniasis. One patient indicated that the plant *corajillo* is sometimes effective. Another patient applied a mixture of lemons and garlic to her ulcers and drank the mixture as well, recommended by one of her neighbors. The most important sources of information identified were doctors (3 out of 6, 50%) and others in the community (2 out of 6, 33%).

Discussion

Leishmaniasis remains a common skin infection in Costa Rica. This study confirms that a significant number of cases are from northern rural regions of the country, and suggests that the focus of education efforts should be in these areas. We were surprised to find that fewer patients presented with Leishmaniasis during this period than we had expected. We believe that this does not represent a decrease in overall incidence of Leishmaniasis in Costa Rica. Rather, one of the major reasons for the low number of study participants is that patients are often treated in local EBAS and never see a dermatologist. In addition, this result might be attributable to seasonal fluctuations of the disease that result in a decreased incidence of the disease during the dry season, the season during which this study was conducted. Several studies performed in other tropical countries have suggested that Leishmaniasis is less prevalent in the dry season, but cases increase during the wet season [8]. In addition, the natural history of cutaneous leishmaniasis is that of a self-healing ulcer after a variable period. Thus, of the patients who contract Leishmaniasis, a portion may never see a physician if their lesion resolves on its own, making it difficult to estimate the true prevalence and incidence of disease. Furthermore, the localization of Leishmaniasis in poor, rural, and more remote areas of the country made it difficult to recruit patients into this study.

The demographics of patients showed no obvious predilection for sex or age. The most consistent demographic characteristic was that patients were from smaller towns and agricultural areas in the northern lowlands (Figure 5). This is consistent with other studies which have shown that the sandfly vector tends to breed in farming and forest areas where reservoir hosts such as sloths and rodents reside together with the sandfly vector. Proximity to coffee plantations, which are abundant throughout this region of Costa Rica, have been reported to be one of the most important risk factors for contracting Leishmaniasis [13]. The sandfly vector also thrives in the dark, damp cracks of poorly built homes and in piles of construction material and waste which predominate in these smaller and poorer communities [5]. The combination of poverty and the agricultural setting of the Northern Lowland area puts individuals living here at especially high risk of developing Leishmaniasis.

All patients in this study were diagnosed with the cutaneous subtype of Leishmaniasis, either presenting with a non-healing ulcer or crusted nodule as the major clinical symptom. No patients presented with disseminated cutaneous, mucosal, or visceral variants. Despite the similarity in clinical presentations, a wide range existed between the time of initial symptoms and time of presentation to a dermatologist. Usually this was because patients waited until it was clear that the lesion was not going to heal on its own before seeing a physician. In one case, the patient had seen a general physician one year earlier who did not make the correct diagnosis. Time had subsequently been lost undertaking various ineffective therapies with antibiotics. Decreasing the time between the appearance of initial symptoms and presentation to a physician is an important goal of public health efforts. Delay in diagnosis and treatment can increase the risk of cutaneous lesions developing into mucosal lesions which can result in severe facial disfigurement. The risk of mucosal spread is greatest in infections with the *Leishmaniasis viannia braziliensis* subgenus [6]. Since subtyping is not widely done in Costa Rican hospitals, limited information is available regarding the subtypes of Leishmaniasis that predominate in this country. However, case studies confirm the presence of *L.braziliensis* in Central America and most dermatologists in Costa Rica

feel that *L. braziliensis* exists in large enough proportion that all lesions should be diagnosed and treated as quickly as possible [11].

The diagnosis of Leishmaniasis is often difficult and many studies report rather low sensitivities for the various diagnostic tests [5]. In one study of 475 cases due to *L. major* in Saudi Arabia, the parasite was demonstrated by smear in only 50-80% of lesions, by skin biopsy in 70%, and by culture in 50%. When all three methods were combined, the parasite was still not detected in 10-20% of cases [7]. Other studies report that the maximum overall sensitivity even when combining diagnostic tests is only 67-75% and is even lower in chronic or mucosal disease [6,10]. Due to the rather low sensitivities of individual diagnostic tests, some have recommended that the best approach to diagnosis is to simultaneously use several methods. One study recommends taking a full thickness biopsy from the infiltrated margin of the lesion and dividing it into three parts: to prepare an impression for smear, for histologic examination, and for culture [5]. In Costa Rica, physicians do not use multiple diagnostic tests. The test of choice is dermal scraping or slit-skin smear test, obtained by scraping the edge of the lesion with a blade or making a shallow slit in the lesion and scraping the cut edge. The contents are then applied to a slide and culture media. The reported sensitivity of histologic diagnosis using dermal scrapings varies greatly from 14-62% [9,10,14]. Consistent with these numbers, only 4 of the 6 (67%) patients with lesions clinically suspicious for leishmaniasis had a positive slit-skin smear, which presents the challenge of deciding how to treat a lesion when the diagnostic test is negative. We recommended that a "therapeutic test" be initiated and all patients with clinically suspicious lesions should be started on meglumine antimoniate, even if the pathologic exam is negative. This recommendation is based on the importance of treating cases of *L. braziliensis* which have the small but significant risk of progressing into mucosal leishmaniasis. Resolution with meglumine antimoniate would then be presumed to be conclusive for diagnosis with Leishmaniasis. At the time of writing this study, follow-up has not been long enough to determine whether the patients started on meglumine antimoniate based on clinical suspicion will have resolution of their lesions.

This study also confirms the variable response of Leishmaniasis to meglumine antimoniate. All patients in this study who were started on meglumine antimoniate reported being compliant with therapy. However, the number of injections needed before disease resolution ranged between 4 to over 110. This variability is likely related to subtype of leishmaniasis and host factors. Other studies have reported the variance in response to treatment within the same community where different subtypes of *Leishmania* existed. For example, one study compared the responses to meglumine antimoniate in patients with *L. braziliensis* and *L. guyanensis* and demonstrated that the cure rate for the *L. braziliensis* group was significantly higher than in the *L. guyanensis* group (50.8% versus 26.3%) [12].

The results of the survey regarding patients' knowledge, beliefs, and practices suggest that public health education regarding Leishmaniasis in Costa Rica could be greatly improved. The majority of patients (5 out of 6, 83%) had limited knowledge of their disease as measured by their inability to identify the mode of transmission, methods of prevention, or effective treatments for Leishmaniasis. This lack of knowledge likely contributes to delayed presentation to a doctor and not taking precautions to prevent disease. Although patients did not have a great deal of background knowledge about Leishmaniasis, they were all appropriately concerned about their disease. All patients stated that it was important to treat because it could spread to other parts of their skin or become secondarily infected. These results do not differ greatly from larger surveys done in other countries that asked similar questions. For example, an interview of 425 heads of households in Guatemala showed that all participants believed it was necessary to receive treatment for cutaneous leishmaniasis in order to prevent progression of the lesion. Similar to the population reported here, about half (55%) of the respondents in Guatemala knew about injection therapy with meglumine antimoniate. Also similarly, the communication channels reported to be most effective for dissemination of information were the use of radio broadcasts and direct communication via community leaders [2]. The similarity of our interview responses with results

of previous studies suggests that patients in Costa Rica are no more or less educated about their disease in comparison to populations in other countries. One way to improve public health education would be the training of *etaps* to disseminate information about the symptoms, prevention, and control of Leishmaniasis. *Etaps*, who are trained community members that conduct health maintenance home visits to all individuals within a community, are logical choices for public health education campaigns because they come into contact with a large population of both the sick and the healthy and are generally more accessible to the general population than physicians.

Areas for Further Study and Conclusions

This study is a small prospective pilot study designed to obtain more information about the epidemiology, clinical features, and knowledge and beliefs of patients with Leishmaniasis. Given the small sample size, no specific conclusions can be drawn about the epidemiology of this disease in Costa Rica. Future studies will need to involve numerous referral centers and local EB AIS clinics in order to obtain accurate estimates about the disease incidence and prevalence. Nonetheless, this pilot study provides valuable information regarding the varied presentation, clinical history, response to treatment, and knowledge and beliefs of patients with Leishmaniasis. It supports the conclusions of other studies which show that Leishmaniasis is a disease that disproportionately affects rural agricultural populations and has a varied clinical presentation and response to treatment. The study also highlights the challenge of using insensitive diagnostic tests in treatment decisions. The authors recommend that if pathologic examination is negative, treatment still be considered based on clinical history, clinical exam, and ruling out other obvious possible diagnosis such as sporotrichosis, chromomycosis, and bacterial infection. Other possible improvements to diagnostic technique in Costa Rica would be the addition of tissue biopsy rather than exclusively relying on smears and culture as a way of increasing overall diagnostic sensitivity.

The results from patient interviews also suggest that people living in communities most at risk for the development of Leishmaniasis have significant gaps in their knowledge of disease, especially in the area of transmission and prevention of disease. Public health measures that include utilization of doctors, *etaps*, and other community members could be especially effective.

Leishmaniasis is an important disease affecting a significant proportion of the world's population. The psychological distress of chronic skin lesions as well as the risk of progression to physically debilitating mucosal and life-threatening visceral variants underscores the importance of obtaining more information about the epidemiology, diagnosis, treatment, and prevention of this disease. This pilot study attempts to characterize Leishmaniasis in Costa Rica and to provide recommendations regarding areas of future study and ideas for public health interventions. Critical to the success of future studies is the coordination of multiple physicians, hospitals, and EB AIS in order to recruit a representative sample of Leishmaniasis patients. The authors recommend continued follow up of this study population as well as increasing the scope of the project to include other study sites in order to obtain more information about Leishmaniasis in Costa Rica.

References

1. Anis E, et al. Cutaneous leishmaniasis in Israel in the era of changing environment. *Public Health Reviews* 2001; 29(1):37-47.
2. Arana BA. Cutaneous leishmaniasis in Guatemala: people's knowledge, concepts and practices. *Annals of Tropical Medicine and Parasitology* 2000;94(8):779-86.
3. Costa Rican Ministry of Health Biostatistics, 2000 <http://www.netsalud.sa.cr/ms/ministe/memoria/me2000/bioesta.htm>
4. Davies CR, et al. The epidemiology and control of leishmaniasis in Andean countries. *Cadernos de Salud Publica* 2000;16(4):925-50.
5. Hepburn NC. Cutaneous leishmaniasis. *Clinical and Experimental Dermatology* 2000;25:363-70.
6. Herwaldt, BL. Leishmaniasis. *The Lancet* 1999;354:1191-99.
7. Kubba R, et al. Clinical diagnosis of cutaneous leishmaniasis (oriental sore). *Journal of the American Academy of Dermatology* 1987;16:1183-9.
8. Nacher M, et al. Seasonal fluctuations of incubation, healing delays and clinical presentation of cutaneous leishmaniasis in French Guiana. *Journal of Parasitology* 2001;87(6):1495-1498.
9. Palma G, et al. Laboratory diagnosis of Leishmania. *Clinics in Laboratory Medicine* 1991;11(4):909-22.
10. Palmer, RA et al. The management of cutaneous leishmaniasis from Belize. *Clinical and Experimental Dermatology* 2001;26:16-20.
11. Personal communication with Dra. Marta Garcia Palomo.
12. Romero GA, et al. Comparison of cutaneous leishmaniasis due to *Leishmania braziliensis* and *Leishmaniasis guyanensis* in Brazil: therapeutic response to meglumine antimoniate. *American Journal of Tropical Medicine and Hygiene* 2001;65(5):456-65.
13. Sanchez-Tejeda G, et al. Cutaneous leishmaniasis caused by members of *Leishmania braziliensis* complex in Nayarit, State of Mexico. *Memorias de Instituto Oswaldo Cruz*; 2001;96(1):15-9.
14. Weigle KA, et al. Diagnosis of cutaneous and mucocutaneous leishmaniasis in Colombia, a comparison of seven methods. *American Journal of Tropical Medicine and Hygiene* 1987;36(3):489-96.

- IDENTIFICATION
 1. Date
 2. Name
 3. Date of birth

- DEMOGRAPHICS
 1. Sex
 2. City of residence
 3. Occupation

- CLINICAL INFORMATION
 1. Reinfection or new infection
 2. Do you remember what you were doing when you were infected? Do you remember being bitten by an insect?
 3. Time since initial symptoms
 4. Number of lesions, evolution
 5. Type of lesions
 - Subclinical
 - Cutaneous
 - Mucosal
 6. Date that you first saw a doctor
 7. Date of diagnosis

- TREATMENT
 1. Date of initial treatment
 2. Date of final treatment
 3. Total doses received
 4. Home remedies
 5. Reasons, if any, for termination of treatment

- KNOWLEDGE AND BELIEFS
 1. Have you ever been infected with Leishmaniasis in the past? When? On what part of the body?
 2. Has anyone in your family ever been infected with Leishmaniasis? Who? When?
 3. What is the mode of transmission of Leishmaniasis?
 4. What are some ways of preventing infection with Leishmaniasis?
 5. What are the symptoms of infection?
 6. Is it important to treat this infection? Why?
 7. What is the most effective treatment for Leishmaniasis?
 8. Are there any other effective treatments for Leishmaniasis, for example are there any home remedies?.
 9. How have you learned about Leishmaniasis? For example, from doctors, your family, others in your community, TV, or books?
 10. Do you have any major health problems?

Figure 1. Survey used to interview patients referred to the Department of Dermatology with lesions suspicious for Leishmaniasis

Patient Characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age	35	30	14	41	27	46
Sex	F	F	M	F	M	F
Residence	Los Chiles	Pital	Pital	Cano Negro	Ciudad Quesada (but infected in Nicaragua)	Pital
Occupation	Homemaker	Homemaker	Student	Works in national park	Farmer	Homemaker, Farmer
Clinical presentation						
Total #	3	1	1	1	4	2
Location	R forearm, wrist, finger	R ankle	R ankle	R calf	Lower back, foot, ankle, nose	Right arm, left arm
Duration						
Sxs to first presentation	3 months	1 week	1 week	4 days	2 months	2 months
Presentation to diagnosis	1 year 3 months	1 week	1 week	4 days	1 day	1 day
Diagnosis						
Touch smear or culture	negative	positive	positive	negative	positive	positive
Treatment						
Total received	none	4 out of 20	10 out of 20	none	117 doses	7 out of 20
Follow up	Lost to follow-up	Lesion resolving	Lesion resolving	Will start Glucantime based on clinical suspicion	Lesions resolved	Lesions resolving

Table 1. Features of 6 patients diagnosed with leishmaniasis on pathological exam, clinical exam, or both.



Figure 2. An acute ulcer with a raised indurated margin consistent with Leishmaniasis.



Figure 3. Multiple crusted nodules on exposed arms. Many of the lesions resemble a volcano with a central depressed crater, i.e. volcano sign.

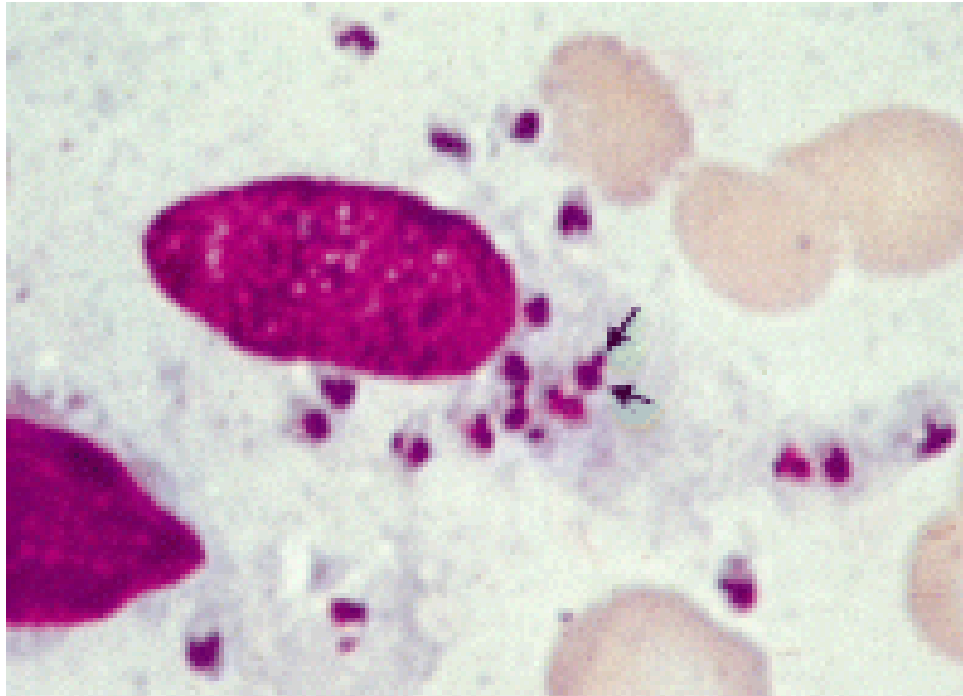


Figure 4. Infected macrophages showing amastigotes, known as Leishman-Donovan bodies. Each amastigote has a nucleus (bottom arrow) and kinetoplast (top arrow). Image taken from Lancet 1999, 354: 1191-99.



Figure 5. Red squares indicate areas of infection of patients diagnosed with Leishmaniasis in this study. Image taken from <https://www.mapquest.com>.