New World Cutaneous Leishmaniasis in a Traveler: the First Documented Case in the Philippines

Katerina T. Leyritana,[1] Mediadora C. Saniel,[1,2] Beatriz G. Carpo[3] and Henry W. Murray[4]

[1] *Department of Medicine, College of Medicine and Philippine General Hospital, University of the Philippines Manila*
[2]*Infectious Disease Practice and Innovations, The Medical City, Pasig*
[3] *Department of Dermatology, Makati Medical Center, Makati*
[4]*Department of Medicine, Weill Cornell Medical College, New York, USA*

ABSTRACT

We describe New World cutaneous leishmaniasis (*Leishmania amazonensis*), a disease not endemic in the Philippines, in a 45-year-old man with ulcerating lesions on his hand and leg after returning from South America. The patient responded to treatment with liposomal amphotericin B. This imported case of leishmaniasis highlights the importance of obtaining a detailed travel history in patients with chronic, non-healing skin lesions which should lead to earlier recognition and treatment.

Key Words: Leishmania, endemic, travel, cutaneous, New World, treatment

Case Report

A 45-year-old Filipino reported a boil-like bleeding lesion on the dorsum of his left hand after it was accidentally hit by a badminton racquet. This event was followed by the appearance of a similar lesion on his anterior left leg. In the span of four months, both enlarged into deep tender ulcers with erythematous inflamed borders accompanied by multiple subcutaneous nodules in a lymphangitic distribution along the left arm proximal to the ulcer. He was initially treated for pyoderma gangrenosum with oral prednisone and topical tacrolimus, which resulted in incomplete and temporary reepithelialization.

Biopsy of the hand ulcer and a nodule showed superficial and deep dense nodular infiltrates of lymphohistiocytes with plasma cells in the dermis. Numerous amastigotes were present within these histiocytes (macrophages) (Figures 1a & 1b). A preliminary diagnosis of leishmaniasis was made, consistent with patient's exposure to places endemic for leishmaniasis during his travels. Diagnosis was confirmed by the Leishmania Diagnostic Laboratory of the Walter Reed Army Institute of Research (WRAIR), Washington, DC, USA, by culture of biopsy tissue and real-time polymerase chain reaction amplification demonstrating *Leishmania* DNA. The species was identified by cellulose acetate electrophoresis and isoenzyme analysis results, as *L. Amazonensis*, which the patient most probably acquired eight months prior, during a trip to Colombia, South America.

Initial treatment with oral fluconazole (400 mg per day) for 3 weeks resulted in a decrease in the size and number of the subcutaneous nodules on the arm. However, there was progressive increase in the size of both the hand and leg ulcers. A 7-day course of intravenous liposomal amphotericin B (LAmB) was then given at 3 mg/kg/day with no adverse reactions. Granulation and decrease in ulcer depth were noted as early as the 4th day of LAmB treatment. There was progressive epithelialization of the ulcers and decrease in size and number of nodules nine days after discontinuation of LAmB. Six months after LAmB treatment, only residual scars were evident. (Figure 2)

Discussion

Leishmaniasis is not endemic to the Philippines. New World cutaneous leishmaniasis (NWCL) has been seen among returning travelers in other countries owing to increasing travel to Latin America, but this has not yet been documented locally.[1]

A search through Pubmed using the search terms "leishmaniasis", "visceral leishmaniasis", "cutaneous leishmaniasis", "diffuse cutaneous leishmaniasis", "mucocutaneous leishmaniasis" and "Philippines" yielded one case report of an Austrian man who was diagnosed with visceral leishmaniasis and had history of travel to Sicily and the Philippines.[2] A search through the WRAIR database did not yield other cases or isolates from the Philippines. A search in local medical libraries and inquiries from the Philippine General Hospital and the Research Institute for Tropical Medicine's Dermatology departments resulted in

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Corresponding author: Katerina T. Leyritana, MD
Section of Infectious Diseases
Department of Medicine
Philippine General Hospital
University of the Philippines Manila
Taft Avenue, Ermita, Manila 1000 Philippines
Telephone: +632 5548400 local 3235
Telefax: +632 5251062
Email: kateleyritana@yahoo.com

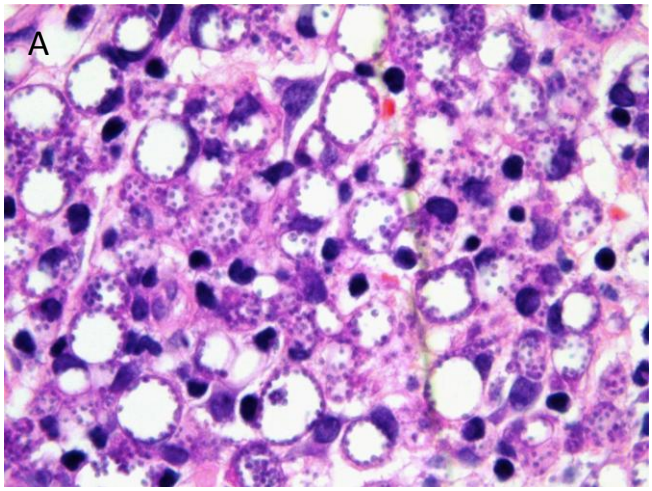

Figure 1a. Lymphocytes and macrophages, within which are clusters of innumerable round basophilic amastigotes (biopsy of hand ulcer, H&E, x 1000)

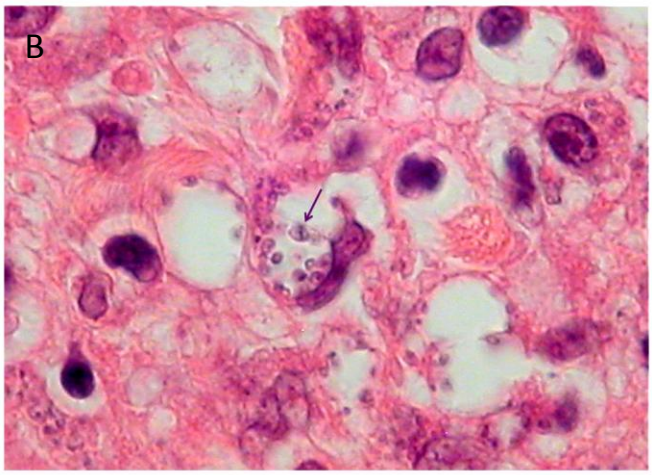

Figure 1b. Characteristic amastigote form with its rod-shaped kinetoplast (arrow) (biopsy of hand ulcer, H&E)

documentation of 5 other known cases of leishmaniasis, all presumed to be acquired in Old World regions (Table 1). The first published case in 1986 was in a 34-year-old male overseas Filipino worker (OFW) who, after staying in Abu Dhabi for two years, returned to the Philippines with fever of unknown origin. Visceral leishmaniasis was found at autopsy.[3] Other local cases were among OFWs who developed cutaneous infection while working in Saudi Arabia. The first case was a 30-year-old man with small ulcerating nonpruritic papules and several non-tender nodules in a lymphangitic distribution proximal to the original lesions.[4] *Leishmania* amastigotes were found in both the primary papular lesions and a subcutaneous nodule. Treatment with one month of daily oral itraconazole resulted in healing with scarring and pigmentation of the ulcers and clearance of the subcutaneous nodules. The second case was a 50-year-old man with a 12-year work history abroad who presented with ulcerating bite-like lesions on the chest.[5] He was diagnosed with leishmaniasis recidivans, and was treated with various regimens including combinations of pentavalent antimony (sodium stibogluconate), rifampicin, liquid nitrogen cryotherapy, oral ketoconazole and isoconazole cream. There was eventual resolution of lesions after recurrence. The two other

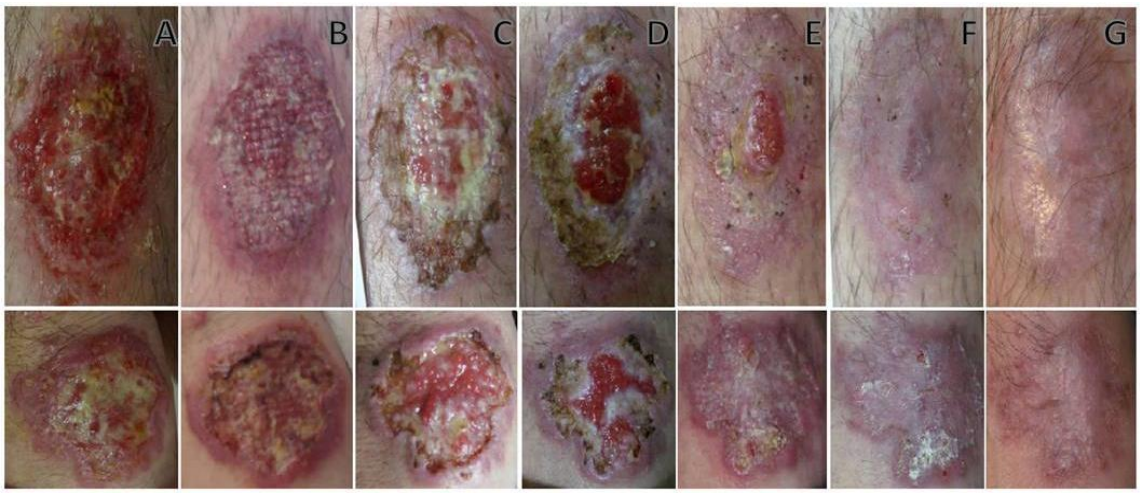

Figure 2. Appearance of skin lesions and response to treatment.
Upper row, lesion on anterior left leg; bottom row, lesion on dorsum of left hand. A , 1 year-old lesions after 23 days of fluconazole and 9 days of prednisone, prior to initiation of LAmB treatment. B, 4th day of LAmB therapy, beginning granulation over ulcers. C, 9 days after LAmB, epithelialization of ulcer borders. D, 15 days after LAmB, further granulation of ulcers and decrease in size of lesions. E, 30 days after LAmB, full reepithelialization of hand ulcer. F, 46 days after LAmB, full reepithelialization of leg ulcer. G, 6 months after treatment, residual scarring.

Table 1. Known cases of leishmaniasis ocurring in Filipinos

AGE/ SEX	EXPOSURE PLACE	EXPOSURE TIME (years)	INITIAL PRESENTATION	TYPE OF INFECTION	TREATMENT	OUTCOME
34/M	Abu Dhabi	2.5	hematochezia	VL	no treatment	died
30/M	Saudi Arabia	2	sporotrichoid distribution of papules, arm	OWCL; sporotrichoid	itraconazole	resolved
50/M	Saudi Arabia	12	ulcerating bite-like lesions	leishmania recidivans	1. sodium stibogluconate 2. rif + LNC 3. keto, iso 4. sodium stibogluconate + keto, iso 5. sodium stibogluconate , keto	resolved
36/M	Saudi Arabia	5	verrucous plaque, arm	OWCL; localized	sodium stibogluconate	resolved
34/M	Saudi Arabia	unknown	erythematous plaque, neck	OWCL; localized	no treatment	lost to follow-up
45/M	Colombia	~ 1-2	ulcer on l hand	NWCL; *L. amazonensis*	liposomal amphotericin B	resolving

VL – visceral leishmaniasis, OWCL – Old World cutaneous leishmaniasis, NWCL – New World cutaneous leishmaniasis, rif – rifampicin, LNC – liquid nitrogen cryotherapy, iso – isoconazole cream, keto - ketoconazole

cutaneous cases were patients seen at the Philippine General Hospital's Department of Dermatology, both of whom presented with localized verrucous erythematous plaques mainly on the arm and neck. One patient had resolution of lesions after receiving sodium stibogluconate (imported from abroad), while the other patient was lost to follow-up.

L. amazonensis may present as localized, as in this particular case, or as diffuse cutaneous form. The latter presents with extensive cutaneous macules, papules, nodules or plaques, without ulcerations and mucosal involvement, and does not heal spontaneously. Relapse commonly occurs, and is unresponsive to further treatment.[6]

Despite evidence of self-healing in cutaneous infections caused by some *Leishmania* species, treatment is indicated in patients with multiple (> 5), large (> 4–5 cm) or chronic lesions (present for six months or more) or for those located over joints. Treatment enables faster control, reduces scarring and is thought to prevent dissemination or relapse.[7-11] The management of leishmaniasis in non-endemic countries poses a challenge for physicians, owing to lack of awareness of the disease and the variety of clinical presentations.[12] The World Health Organization recommends pentavalent antimonials for *L. amazonensis* infection and for cutaneous disease caused by most other species. Amphotericin B deoxycholate, pentavalent antimonials with topical imiquimod or LAmB is recommended for relapses.[6] Oral agents such as miltefosine and the azoles have variable efficacy.[13] Local patients in the Philippines with leishmaniasis were treated with azoles or sodium stibogluconate brought in from the Middle East. [4-5] LAmB, an approved mode of treatment in visceral infection, has been demonstrated to be effective for NWCL in limited trials, but is not locally available.[13] With successful treatment, lesion size is expected to diminish by at least two-thirds after 6 weeks and complete healing is anticipated by 6-12 months.[14] Persistence of an active-appearing lesion more than 3 months after treatment may call for retreatment which may involve a change in therapeutic regimen.[14]

Acquisition of cutaneous leishmaniasis by OFWs or travelers may be avoided by awareness of endemicity in geographical areas, places of particularly high risk exposure, modes of transmission and preventive measures. OFWs in the Middle East should be briefed prior to departure and given advice as to protective clothing, insect repellent, avoidance of sandy areas and animal shelters, going outside from dusk to dawn, the presence of dogs and rodents next to sleeping quarters, and vector control in situations where exposure is unavoidable. If infection occurs while in the country of exposure, familiarity with signs and symptoms is necessary to prompt consultation with and treatment by local health officers. If the infection manifests itself upon return to the Philippines, a high index of suspicion for leishmaniasis is needed for patients with history of travel. Lack of availability of medications locally would require importing them from nearby countries, thus limiting easy access to appropriate treatment.

There is great diversity of imported leishmaniasis in terms of region of acquisition, etiologic agent, clinical presentation, treatment options and outcome.[15] With an increasing number of Filipinos working abroad and opportunities for world travel, we expect to see more cases locally. If a history of travel is not obtained by the physician, the diagnosis may be delayed, and a more complicated form of the disease may develop.

Conclusion

This report describes the first documented case of NWCL in the Philippines. The value of an exhaustive history, including travel and exposure to animals, should be emphasized when presented with an unusual or nonhealing skin lesion case that does not respond to usual modes of treatment. A case-to-case basis for choosing the best mode of anti-leishmanial treatment is recommended as no single treatment approach fits all possible clinical presentations.[6]

Ethical Considerations

Patient's informed consent for written and photographic documentation of the case and course of treatment was obtained through formal written means.

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