Unwanted souvenirs

A leg ulcer and nasal ulceration in a returned traveller from South America

Commentary by

SHELANAH A. FERNANDO MB BS(Hons), BMedSci
TIMOTHY J. GRAY MB BS(Hons), BMedSci(Hons), MPH&TM
THOMAS GOTTLIEB MB BS, FRACP, FRCPA

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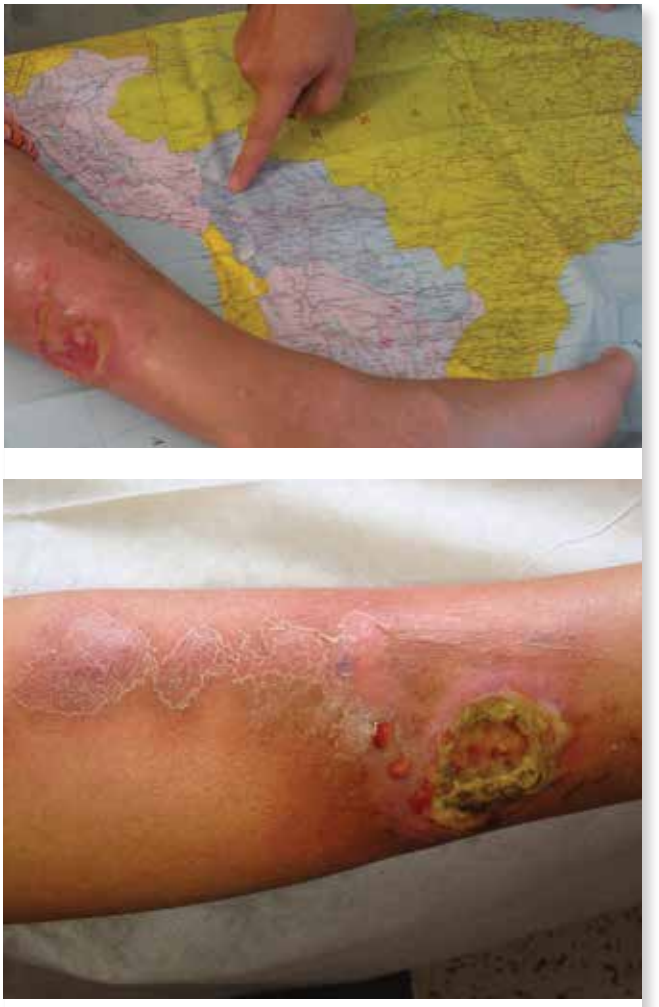
Can cutaneous leishmaniasis acquired in South America involve the oronasopharyngeal mucosa and cartilaginous facial structures?

CASE SCENARIO

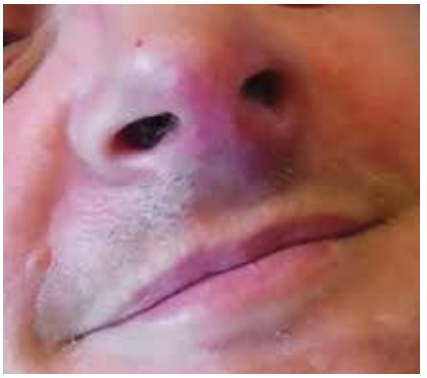
Sam, aged 52 years, initially presented with a persistent leg ulcer 10 weeks after travelling to jungle parts of Bolivia where he recalled having had multiple sandfly bites (Figures 1a and b). He had had recurrent treatment courses of antistaphylococcal antibiotics without any improvement. After advice from an infectious diseases physician, cutaneous leishmaniasis was confirmed on biopsy. Treatment with intravenous liposomal amphotericin B resulted in eventual complete healing of the ulcer.

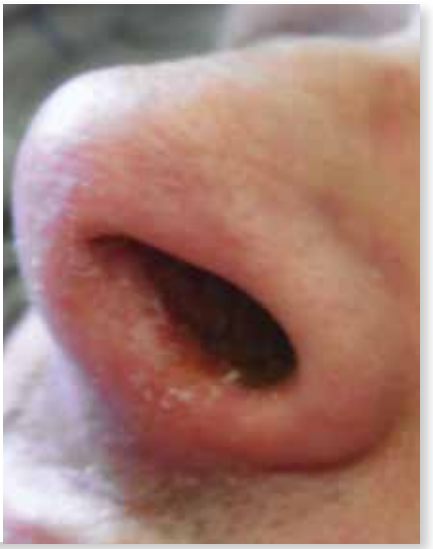
- *Should all persistent skin ulcers after travel to South or Central America be considered due to cutaneous leishmaniasis?*



Figures 1a and b. Cutaneous leishmanial ulceration of the patient's leg. a (top). The well-demarcated ulcer with distinctive heaped margins ('volcano' edges). b (bottom). The ulcer with superimposed bacterial infection.

Dr Fernando is an Infectious Diseases Registrar, Dr Gray is a Microbiology Registrar, and Associate Professor Gottlieb is a Senior Specialist in the Department of Microbiology and Infectious Diseases at Concord Hospital, Sydney, NSW.





Figures 2a and b. a (left). Mucocutaneous leishmaniasis of the patient's left nostril. b (right). Close-up of the nasal tip and septum.

Six months later, Sam presented with new nasal congestion and erythema. Nasal examination revealed erythematous swelling and septal crusting (Figures 2a and b).

- *Could the patient's nasal symptoms be related to his apparently cured leishmaniasis?*

Mucocutaneous leishmaniasis was confirmed on nasal biopsy. Intravenous liposomal amphotericin B and pentavalent antimony (pentostam) were trialled but both were curtailed because of side effects (pancreatitis, hepatitis and renal failure). He was eventually cured, after the nasal congestion worsened, with the new oral antiprotozoal drug miltefosine.

COMMENTARY

The clinical spectrum of leishmaniasis ranges according to the continent of acquisition. Localised disease or diffuse to disseminated skin involvement occurs as part of New World disease acquired in Latin America (Central and South America, Mexico and the Caribbean). Visceral disease and also localised cutaneous lesions are seen with Old World disease acquired in the Middle East, Africa, western Asia and southern Europe.[1] Mucocutaneous involvement can be a specific complication following infection by species of *Leishmania* found in South America.[2]

Chronic ulcers in returned travellers

The initial approach to the nonhealing ulcer in a returning traveller requires a careful assessment of the travel history to determine whether the cause is infectious or noninfectious. As some ulcers that initially heal may relapse months later, even a remote travel history may be relevant.

Features such as failure to improve with standard therapy, the presence of nodular lymphangitis and unusual symptoms in distant sites should all prompt further investigation for an infectious cause. When possible, it is useful to identify the likely vector and the country or region where the infection may have been acquired.

A thorough exposure history outlining details of travel, including occurrence of animal, tick or fly bites, recreational activities, water or soil exposure and sexual contacts, is crucial in differentiating possible causes of nonhealing ulcers and in guiding further investigations. Differential diagnoses for cutaneous leishmaniasis are listed in the Box.

Cutaneous and mucocutaneous leishmaniasis

New World cutaneous leishmaniasis is caused by several species of *Leishmania* and infections are now increasingly seen in traditionally nonendemic regions.[1] Clinical manifestations depend on the species of *Leishmania* and may occur weeks to months after the protozoa are first inoculated by the bite of a sandfly.[1,2]

In most instances, cutaneous leishmaniasis originates as a small macule at the bite site, with progression over weeks to months into a painless, erythematous papule; pruritus may be an associated symptom. Although spontaneous resolution may be seen at any time, some lesions evolve into granulomas and thereafter into well-demarcated ulcers with distinctive heaped margins ('volcano' edges; Figure 1a).[1] Secondary infection with bacteria or fungi may confuse the clinical

DIFFERENTIAL DIAGNOSES FOR CUTANEOUS LEISHMANIASIS

Infectious causes

- Bacterial infection
  - *Staphylococcus aureus* and *Streptococcus pyogenes* infections
  - nontuberculous mycobacterial infections, e.g. *Mycobacterium ulcerans* (Buruli ulcer), *M. marinum*
  - cutaneous tuberculosis
  - nocardiosis
  - endemic syphilis and yaws (endemic treponematoses)
  - tularaemia
- Fungal infection
  - sporotrichosis
  - blastomycosis
  - mycetoma
  - paracoccidioidomycosis

Noninfectious causes

- Pyoderma gangrenosum
- Neoplasms
- Cutaneous T-cell lymphoma
- Sarcoidosis
- Lupus vulgaris
- Kaposi sarcoma (especially in immunocompromised patients)

appearance by distorting classical clinical characteristics and causing the ulcer to become a painful lesion that may be slow to heal (Figure 1b).

Cutaneous leishmaniasis is generally a self-limiting illness but lymphatic dissemination and invasion of the upper respiratory mucosa occurs in approximately 1 to 5% of cases, being more likely in disease caused by species predominant in South America. This may result in the destruction of the oronasopharyngeal mucosa and cartilaginous facial structures.[2] Mucocutaneous leishmaniasis may occur simultaneously with cutaneous leishmaniasis or, as seen in Sam, be a late complication occurring months to years after first infection and successful treatment of the cutaneous ulcer.[3]

Symptoms of mucocutaneous leishmaniasis are typically nonspecific and can range from nasal pruritus to crusting and mucosal bleeding (Figures 2a and b).[2] Nasal ulcers may only be evident on nasoendoscopy, hence it is imperative that the clinician be alert to a potential diagnosis of mucocutaneous leishmaniasis. Early referral to an ENT specialist should be considered for patients who present with rhinorrhoea and epistaxis after having travelled to leishmaniasis-endemic areas, including Brazil, Bolivia and Peru.

Diagnosis and treatment of leishmaniasis

The most useful diagnostic test for leishmaniasis is a punch biopsy, and tissue from lesions should be assessed with routine bacterial, mycobacterial and fungal cultures and by histopathology (which may reveal the typical amastigotes, the nonflagellated intracellular form of *Leishmania*). *Leishmania* promastigotes, the flagellated form of the protozoa and a common morphology in the insect vector, can be detected by specialised culture. These specific tests need to be discussed with the laboratory at the time of referral. Skin scrapings and needle aspirates from the central ulcer are also useful but are less sensitive. Molecular tests (polymerase chain reaction) have become available recently and may become the preferred method of detecting *Leishmania* in biopsy specimens.

Old World localised cutaneous leishmaniasis tends to heal spontaneously over several months with no long-term sequelae, and may not require treatment. Indications for treatment include lesions that are large (more than 4 to 5 cm in diameter), lesions located over joints or in cosmetically important areas and the presence of multiple lesions or nodular lymphangitis.[2] Local treatment may be appropriate in some instances, and regimens involving intralesional antimonials, thermotherapy, cryotherapy and topical aminoglycosides are all of proven efficacy.[2]

Of the *Leishmania* species found in the New World, systemic therapy is indicated for infections with those belonging to the subgenus *Viannia* (the type found in South America), with the aim of eradicating both the local cutaneous parasite load and also disseminated disease, thereby preventing life-threatening mucocutaneous complications.[4] Current therapies are limited by emerging resistance, toxicity and cost. Where possible, *Leishmania* speciation may be useful because cure rates and treatment choice depend on the geographic region of acquisition and the subgenus.[5,6] Liposomal amphotericin B is the recommended therapy for cutaneous leishmaniasis, with average cure rates of approximately 85% in that caused by *L. braziliensis*.[6] Immunosuppression, older age, premorbid comorbidities and larger lesion size are factors predisposing to treatment failure. Pentavalent antimony is the traditional therapy for mucocutaneous leishmaniasis; however, resistance to antimonials is increasing and it may now be less effective.[3]

Miltefosine is a new oral agent largely used for treating visceral leishmaniasis but is not routinely available in Australia. To date, miltefosine has shown variable activity for New World leishmaniasis compared with Old World disease.[5] It is a promising oral rescue therapy with a low toxicity profile.[7]

CONCLUSION

The described case highlights the late presentation of mucocutaneous leishmaniasis following localised cutaneous leishmaniasis and the potential for failure of initial treatments.

Clinicians should always consider leishmaniasis in any patient with persistent skin ulceration after travel to the Americas, North Africa, western Asia and parts of the Middle East. There is a need to be vigilant for concurrent or subsequent mucocutaneous involvement for leishmaniasis acquired in the Americas. Relapse may occur months after apparent healing, and thus close re-evaluation of infection sites for up to one year should be standard care. MT

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COMPETING INTERESTS: None.