Cutaneous Leishmaniasis: A Report of Two Cases Seen at a Tertiary Dermatological Centre in Singapore

H H Tan, S S Wong, B H Ong

ABSTRACT

Cutaneous leishmaniasis (CL) is not common in South-East Asia and often presents as a granulomatous plaque on the exposed areas, with a high index of suspicion required for diagnosis. Two such cases were seen at the National Skin Centre recently, and both were Gurkha men with a history of travel to Belize. They were treated with intravenous sodium stibogluconate with success. A discussion on CL and its management follows.

Keywords: skin, stibogluconate, tropical infection

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INTRODUCTION

Tropical infections can present diagnostic problems both to the physician, as well as the dermatologist. When considering a cutaneous lesion of possible infective cause, the common differentials would include mycobacterial and deep Ringal aetiologies. Two cases of cutaneous leishmaniasis were seen at the National Skin Centre in March 1997 and were imported from Belize, in Central America.

Case 1

A previously well, 38-year-old man of the Gurkha contingent of the Singapore Police Force, attended a jungle combat course in Belize from April to December 1996. He presented with a non-healing ulcer on the left ear 6 weeks after retuning to Singapore in the middle of December 96. The lesion started as an itchy red papule which slowly enlarged into an ulcerated plaque. He remembered being bitten by sandflies during his stay in Belize. There were no systemic symptoms. The ulcer failed to heal despite several courses of systemic antibiotics, including septrim and cloxacillin. There was no past medical or drug history of note.

When he was seen at our centre in March 1997, he was noted to have a 2 cm x 1.8 cm crusted, ulcerated plaque on the upper, inner aspect of the left ear (Fig. 1). There were no regional or generalized lymphadenopathy and no muco-cutaneous changes. Systemic examination was unremarkable. A clinical diagnosis of cutaneous leishmaniasis was made. A skin biopsy showed ulcer with chronic inflammation and clusters of histiocytes with pale cytoplam containing small organisms. These organisms had tiny dot-like nuclei and scanty cytoplasm. Culture taken from the ulcer grew streptococcal group A organisms for which he was treated with a course of cephalosporins. Culture to identify the species of leishmaniasis was also taken, but was subsequently negative. He was admitted to the ward for treatment in April 97 with injection of intravenous sodium stibogluconate (850 mg daily) daily for 20 days. The ulcer healed after the course of treatment.

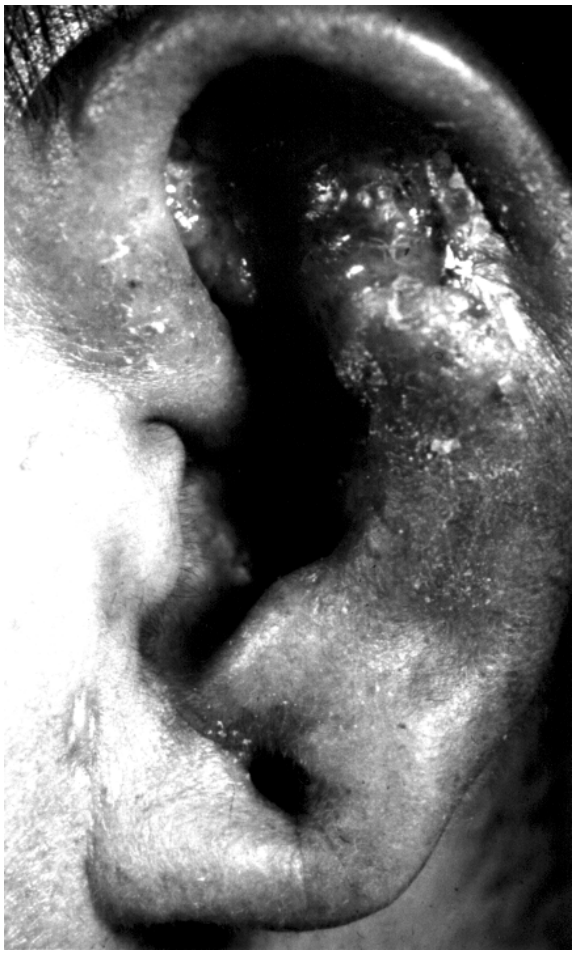

Fig. 1 Ulcerative plaque on the left ear.

National Skin Centre
I Mandalay Road
Singapore 308205

H H Tan, MBBS, MRCP (UK)
Associate Consultant

S S Wong, MBBCh, MRCP (UK)
Consultant Dermatologist

Department of Pathology
Singapore General Hospital
Outram Road
Singapore 169608

B H Ong, MBBS, DCP (Lond)
Senior Consultant

Correspondence to:
Dr H H Tan

Case 2

A previously well, 35-year-old man of the Gurkha contingent of the Singapore Police Force, attended a jungle combat course in Belize from August to December 1996. While in Central America, the patient recalled being bitten by sandflies during his stay in Belize. Three weeks after commencing the jungle training course, he noticed an asymptomatic red plaque on the inner aspect of his left thigh. It began to slowly enlarge, but the patient did not experience any systemic symptoms. He sought medical advice in Belize, and was told that he had cutaneous leishmaniasis (CL). He was commenced on ketoconazole 200 mg/day for four weeks.The patient was subsequently seen at the National Skin Centre on March 1997 and a biopsy of the lesion was performed.

On examination, the patient had a 2 cm by 3 cm erythematous plaque with central ulceration on the inner aspect of the left thigh (Fig. 2). There was no regional or generalised lymphadenopathy and no muco-cutaneous changes. Systemic examination was unremarkable. A clinical diagnosis of CL was made.

Biopsy showed epidermal hyperplasia, with foci of necrosis and a dense infiltrate of lymphocytes and plasma cells in the dermis. There were multiple epithelial granulomas and numerous dot-like organisms present in the cytoplasm of histiocytes as well as lying free in the tissue (Fig. 3). This was compatible with a diagnosis of cutaneous leishmaniasis.

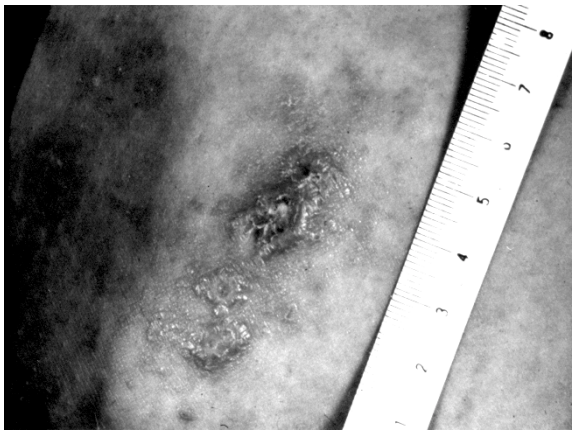

Fig. 2 Ulcerated plaque on the thigh.

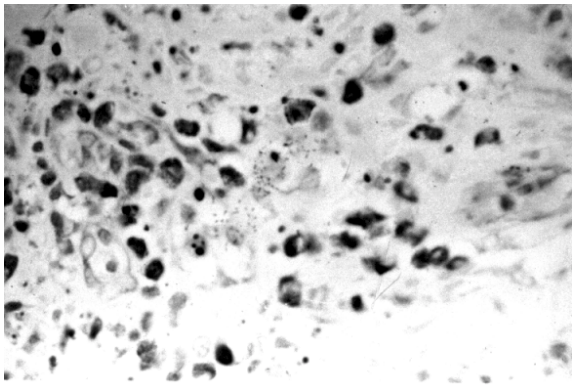

Fig. 3 Biopsy of Case 2 showing multiple epithelial granulomas and dot-like organisms in the cytoplasm of histiocytes as well as lying free in the dermis.

The patient was given intravenous sodium stibogluconate 600 mg BD for 2 weeks with slow but definite improvement of the lesion, and remains on follow up.

DISCUSSION

The leishmaniases are a group of parasitic diseases caused by several species of the genus *Leishmania*. Each species tends to occupy a particular zoo-geographical zone. They are transmitted by the bites of female sandflies, which are of the genus *Phlebotomus* in the Old World and *Lutzomyia* in the New World[1]. About 30 species of sandfiies are proven vectors; the usual reservoir hosts include humans and domestic/wild animals.

The geographical distribution of leishmaniasis is extremely wide; it is prevalent on four continents and considered to be endemic in 88 countries, including Bangladesh, Brazil, Afghanistan, Iran, Saudi Arabia, Peru, Sudan and India[2].

Human leishmaniasis is usually classified as cutaneous or visceral. Visceral leishmaniasis (VL) or 'kala-azar' is caused by *L. donovani*, *L. infantum* and *L. chagasi*. These species, in contrast with the other species of leishmania that infect man, are normally viscerotropic, and cause a severe systemic infection, often accompanied by gross splenomegaly, anemia, diarrhoea, hepatomegaly, lymphadenopathy and signs of malnutrition[3]. Cutaneous leishmaniasis (CL) is caused mainly by *L. tropica*, *L. major* and *L. aetiopica*. CL is discussed further as this was the diagnosis in both patients.

The incubation period in CL is usually measured in months but ranges from a few days to over a year. In our patients, the lesions appeared 3 weeks after they began jungle training in Central America. The face, neck and arms are the commonest targets, although the location of the lesion in a covered area such as the inner thigh in the case of the second patient is not unusual. There are four clinical types of CL, reflecting the different natural histories caused by the different organisms as well as variety in host response:

(1) acute CL

This is the most common clinical form of cutaneous leishmaniasis. It can be caused by any species that causes CL. It is defined as a lesion that does not last beyond 1 year, and can present in a variety of morphologies, including an ulcerated nodule, eczematoid or verrucoid plaques and a zosteriform pattern[4].

(2) chronic CL

An infection that lasts for more than one year is considered to be chronic CL, and is more likely to be due to *L. tropica*. It usually presents as a boggy erythematous plaque surrounded by distinct coalescing papules.

(3) leishmaniasis recidivans

In this form, a new papule develops around the apparently healed lesion. There is clinical overlap with chronic CL.

(4) diffuse CL

In this form, the initial nodule does not ulcerate, and new nodules develop on the face and trunk, resembling lepromatous leprosy clinically.

Differential diagnoses include infective granulomas such as lupus vulgaris, deep fungal infections and leprosy. A high index of suspicion is required, and histology is necessary.

Treatment of CL is often difficult. Even though most sores will heal spontaneously, their duration cannot be predicted in an individual case. Our second patient did not respond to oral ketoconazole that was started by the doctors in Belize. Ketoconazole has been shown to have some clinical utility in Central America, where 16 out of 21 patients (76%) treated were cured[5], but results from South America were not encouraging[6]. A randomised double-blind study using itraconazole to treat CL caused by *L. tropica* in Iran showed a poor response rate[7].

Antimonials are still the first line drug in the treatment of CL. Sodium stibogluconate (Pentostam) and meglumine antimonate (Glucantime) are essentially similar drugs which contain pentavalent antimony (Sb). Sodium stibogluconate can be administered intravenously or intramuscularly, while meglumine antimonate should only be given via the intramuscular route. The recommended dose is 20 mg/kg/day for 15 - 20 days[8]. Treatment with antimonials is associated with some side effects such as myalgia, as well as possible liver or cardiovascular toxicity, which fortunately is rare. A recent study using intralesional sodium stibogluconate showed that alternate day or weekly administration of intralesional sodium stibogluconate was effective in the treatment of CL[9].

Dapsone and allopurinol have also been used for the treatment of CL. The mechanism of action is not known, although basic biochemical studies have shown that Leishmania cannot make all of their own nucleic acids and use the host's purines through the purine salvage pathway. Other systemic options include amphotericin B and pentamidine, which are second line drugs used only when treatment fails with antimonials.

Besides systemic treatment, local measures such as cryotherapy, local excision of a small focus and topical treatment using 15% paromomycin ointment has also been shown to be effective in some cases[10]. Vaccines for prophylaxis and immunotherapy have been developed, and are currently undergoing trials in many countries, including Venezuela, Brazil and Iran. The development of molecular biology techniques is also improving knowledge on the structure, evolution and expression of the Leishmania genome, and the study and definition of the mechanisms that regulate the parasite biochemical and molecular features will certainly contribute to the development of new and more effective strategies for leishmaniasis treatment.

These cases emphasize the point that when assessing lesions of possible infective aetiology, a detailed travel history and knowledge of the common infective agents in the location concerned are of great importance in arriving at a diagnosis and appropriate treatment.

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