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# Unresponsive cutaneous leishmaniasis and HIV co-infection: Report of three cases

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## ABSTRACT

Cutaneous leishmaniasis (CL) is a vector borne disease caused by various species of *Leishmania* parasite. CL is endemic in the Thar desert of Rajasthan state and Himachal Pradesh in India. Immune suppression caused by human immunodeficiency virus (HIV) infection is associated with atypical clinical presentation of CL which responds poorly to the standard treatment and causes frequent relapses. We are reporting three cases of localized and disseminated CL due to *Leishmania tropica* which failed to respond to conventional intralesional/intramuscular sodium stibogluconate (SSG) injections. Initially, we did not think of HIV infection because CL is endemic in this region. When patients did not respond to SSG injections, we performed enzyme-linked immunosorbent assay (ELISA) tests for HIV and they turned out to be HIV positive. Our report showed that CL is emerging as an opportunistic infection associated with HIV/AIDS and may be the first manifestation in HIV positive patients in an endemic area.

**Key words:** Human immunodeficiency virus infection, sodium stibogluconate, unresponsive cutaneous leishmaniasis

## INTRODUCTION

Cutaneous leishmaniasis (CL) is a protozoan disease caused by various species of *Leishmania* and transmitted by *Phlebotomus* sandfly in Old World. The Thar desert of Rajasthan state, Bikaner, located in the northwestern part of India, is one of the endemic areas for CL, where it is caused by *Leishmania tropica*.[1] In 2005, Sharma *et al*.[2] also reported a new endemic zone of CL from sub-alpine valley along Satluj River in Kinnaur district of Himachal Pradesh. CL manifests as single or multiple non-itchy, painless papules, nodules or plaques, with or without ulceration, usually over exposed areas of body. Once an individual is infected with CL, it is unlikely that he or she will be re-infected by the same species of *Leishmania* due to development of lifelong immunity.[3]

Immune suppression caused by human immunodeficiency virus (HIV) infection is usually associated with multiple disseminated and atypical cutaneous lesions which respond poorly to the standard treatment and causes frequent relapses.[4,5] Various studies have reported association of CL and HIV/AIDS from different countries in the last two decades.[6-8] Chaudhary *et al*,[9] and Mehta *et al*,[10] published single case reports of co-infection from India. The recommended treatment of CL is intralesional or systemic antimonials in immuno-competent patients.[3] HIV co-infected patients are also treated successfully with antimonials[6,8] and resistance is reported rarely.[11] We are reporting three cases of CL who did not respond to sodium stibogluconate (SSG) injections and were later found to be suffering from HIV infection.

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## CASE REPORTS

Clinical details, investigations done and treatment given before and after detection of HIV infection in all three cases are described in Tables 1 and 2.

### Case 1

A 40-year-old male farmer presented with numerous painless, non-itchy, discrete, non-tender nodules and plaques of variable size, distributed asymmetrically over limbs and face for last 1 year [Figures 1 and 2]. Past, personal and family history was insignificant. General and systemic examination did not reveal any abnormality. Because of endemicity in this region, we provisionally diagnosed him as a case of disseminated CL, which was confirmed by skin smear and biopsy. Skin biopsy showed mononuclear infiltrate and macrophages laden with LD bodies [Figure 3]. Species characterization was done by restriction fragment length polymerization (RFLP) and kinetoplast DNA (kDNA) polymerase chain reaction (PCR) tests, which established *L. tropica* as the causative species. Routine hemogram, renal and hepatic functions, serum amylase and serum venereal disease research laboratory (VDRL) test were normal. Patient was treated with intramuscular injection of SSG but there was no improvement even after 21 injections and new lesions kept on appearing. Because of unresponsiveness, HIV infection was suspected and confirmed by different enzyme-linked immunosorbent assay (ELISA) methods. On close inquiry, the patient revealed history of extramarital sexual contact 5 years back. HAART (zidovudine, lamivudine, and nevirapine) was started along with second course of intramuscular injection of SSG in the same dosage. After 8 days, the patient developed severe pain abdomen radiating to back with vomiting and fever. Serum amylase was raised from 45 units/L to 650 units/L; the patient was diagnosed as a case of pancreatitis which was confirmed by computerized tomography (CT) scan. Injection SSG was stopped but the patient died in the next few days.

### Case 2

A 34-year-old male laborer presented with well-defined, non-tender lesions of different size for the last 6 months [Figure 4]. Clinically, the patient was diagnosed as CL which was confirmed by skin smear, biopsy and species identification by PCR test. He was

**Table 1: Clinico-epidemiological data and investigations of patients before treatment**

| Data | Case 1 | Case 2 | Case 3 |
|---|---|---|---|
| Initial number of lesions | 38 | 5 | 1 |
| Site of lesions | Scattered | Left hand, wrist, neck and chin | Right leg |
| Size of lesions | 1–4 $cm^2$ | 1–3 $cm^2$ | 3 $cm^2$ |
| Type of lesions | Nodules and plaques (crusted) | Ulcerated and crusted plaques | Ulcerated plaques |
| Associated systemic illness | None | None | None |
| Skin smear for LD bodies | Positive | Positive | Positive |
| Skin biopsy | Abundant intracellular and extracellular bodies seen | Few intracellular LD bodies seen | Abundant LD bodies seen |
| PCR test for *Leishmania* (RFLP-PCR, kDNA-PCR methods) (ICMR, New Delhi) | *L. tropica* | *L. tropica* | Not done |

**Table 2: Initial treatment and its response, follow-up investigations, and treatment after detection of HIV infection**

| Data | Case 1 | Case 2 | Case 3 |
|---|---|---|---|
| Initial treatment | Inj. SSG (IM) | Inj. SSG (IL) | Inj. SSG (IL) |
| Dose of SSG | 20 mg/kg/BW/day | 50 mg/$cm^2$ of lesion/TW | 50 mg/$cm^2$ of lesion/TW |
| Number of injections | 21 | 10 | 12 |
| Response to treatment | No improvement | No improvement | No improvement |
| Test for HIV (Tridot, TMB Micro-ELISA, Comb AIDS) | Reactive | Reactive | Reactive |
| CD4+ count (cells/$mm^3$) | 290 | 380 | Refused |
| Viral load count (copies/mL) | 155,400 | 75,640 | Refused |
| Treatment after HIV was detected | Inj. SSG (IM) with HAART | Rifampicin without HAART | Rifampicin, no HAART |
| Final outcome | Died | Improved | Not improved |

SSG: Sodium stibogluconate, IM: Intramuscular, IL: Intralesional, TW: Twice a week, BW: Body weight

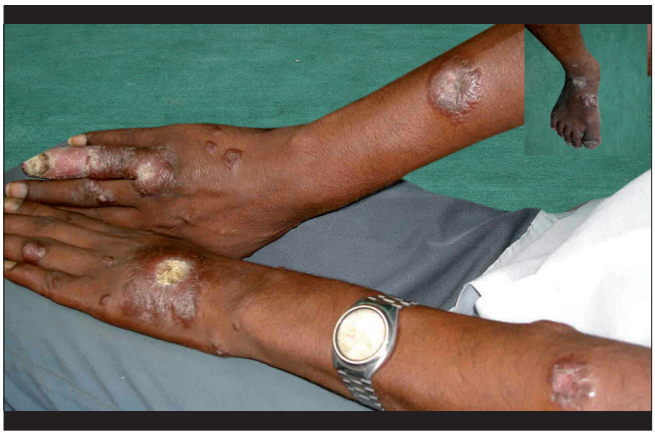

**Figure 1: Nodules and plaques of cutaneous leishmaniasis over forearms, hands and right foot (Inset) in HIV positive patient (case 1)**

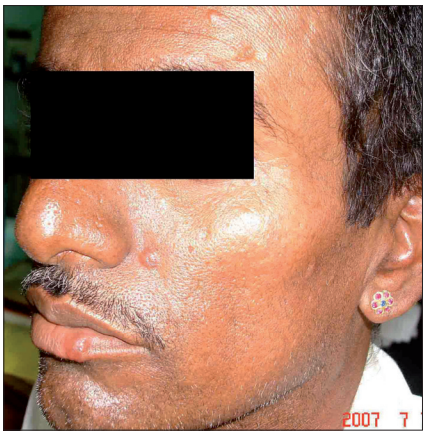

**Figure 2: Nodules over lower lip, naso-labial fold and forehead in case 1**

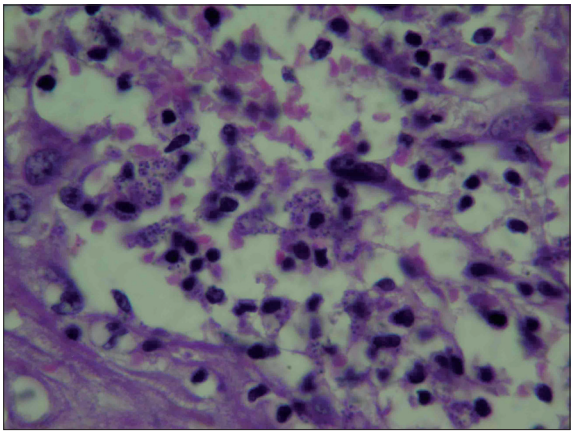

**Figure 3: Microphotograph showing intracellular and extracellular amastigote form of Leishmania (LD bodies) in biopsy specimen of case 1 (H and E, ×100)**

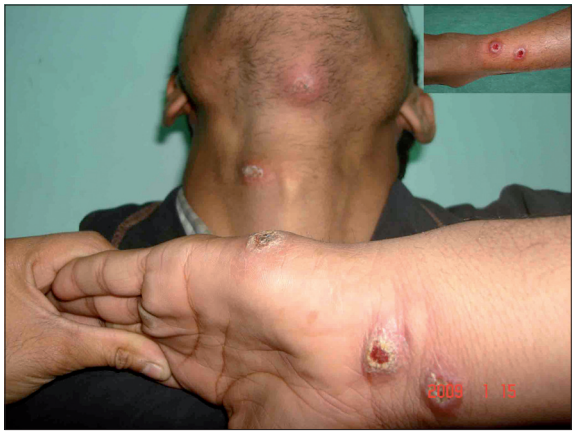

**Figure 4: Plaques over left hand and neck in case 2. Two lesions developed over right leg (Inset) even after treatment**

treated with twice weekly intralesional injection of SSG. Lesions did not improve clinically even after 5 weeks and two more lesions appeared over left leg within 3 months [Inset of Figure 4]. Observing unresponsiveness to treatment and development of new lesions, ELISA test for HIV was performed and found to be positive. Later, he gave history of blood transfusion for some kind of abdominal surgery for abdominal pain 3 years ago. After all the investigations, oral Rifampicin was started at a dose of 1200 mg/day for 6 weeks. HAART was not started because CD4+ count was more than 350 cells/mm$^3$. Lesions healed completely in 12 weeks, after which the patient did not return for further follow-up.

### Case 3

A 28-year-old laborer presented with single asymptomatic, non-tender lesion for the last 6 months [Figure 5]. Diagnosis was confirmed microscopically and the patient was treated with intralesional injections of SSG. Lesion did not improve clinically even after 6 weeks, rather three new lesions [Inset of Figure 5] developed within a period of 2 months. Tests for HIV were done which came out to be reactive. Patient refused for viral load, CD4+ count and HAART. After all routine investigations, he was treated with oral Rifampicin 1200 mg/day for 6 weeks. Patient did not respond to treatment and refused for further management.

## DISCUSSION

In the Old World, CL is caused by *Leishmania. tropica, Leishmania major, Leishmania infantum* and *Leishmania aethiopica*.[3] Multiple lesions scattered over different anatomical areas can occur due to

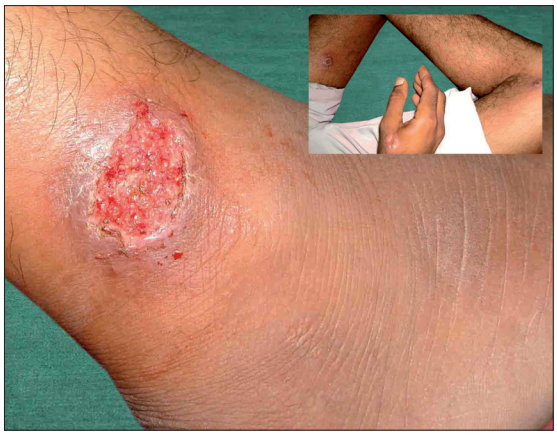

**Figure 5: Single ulcerated plaque over right leg in case 3. Three lesions developed (Inset) even after intralesional SSG treatment**

multiple bites of sandfly in an immuno-competent person but usually occurs secondary to an underlying deficiency in cellular immunity. In the past, several authors have reported CL in known cases of HIV/AIDS.[5,7,8] Chaudhary *et al*,[9] simultaneously diagnosed a case of co-infection. Our cases were having typical papulo-nodulo-ulcerative lesions of CL without any systemic symptoms; we diagnosed them as cases of localized or disseminated CL which is endemic in this region. When they did not respond to treatment satisfactorily and even new lesions appeared, we thought of HIV infection and found them to be positive. CL usually responds well to systemic or intralesional antimonials and relapses are not frequent in immuno-competent patients.[3] In co-infected patients also, antimonial treatment is effective and resistance is very rarely reported.[11] Niamba *et al*,[4] and Rosatelli *et al*,[8] reported successful treatment with antimonials in co-infected patients of HIV with *L. infantum* and *Leishmania braziliensis*, respectively. Unresponsiveness to SSG in our cases may be due to difference in species of *Leishmania* or host immunological factors. The co-infection causes complex immunological disturbances in the patients,[11] both by HIV and *Leishmania*, which may be the reason of unresponsiveness in the cases presented. Our report indicates that CL may be the first manifestation of HIV infection, particularly in endemic areas.

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