

Case Report

Atypical disseminated cutaneous leishmaniasis in a patient with HIV infection

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Abstract This is an atypical case of disseminated cutaneous leishmaniasis in a 40-year-old HIV-positive man. He presented with 4-month history of a progressive maculopapular eruption of the skin. The diagnosis of diffuse cutaneous leishmaniasis was established by skin biopsy. This atypical form responded to miltefosine. This clinical form may be confused with other diseases like molluscum, leprosy, tuberculosis etc.

Key words

Disseminated cutaneous leishmaniasis, HIV.

Introduction

Leishmaniasis is a major world health problem, which is increasing in incidence¹ and is very common in Pakistan. The protozoa is transmitted by sandflies and may produce a variety of clinical syndromes varying from a simple ulcer to fatal systemic disease. The clinical situation becomes more complex in patients who are coinfecting with HIV.² A majority of co-infected cases show features of visceral leishmaniasis (VL) but may also show other features like atypical location, parasitic dissemination to skin and reticulo-endothelial system, a chronic and a relapsing course, poor drug response and lack of anti-leishmania antibodies. These are due to decreased cell-mediated immunity.³ The cutaneous presentation can vary a lot in morphology and number.⁴

Case report

A 40-year-old man, known HIV, on HAART (highly active antiretroviral therapy) reported to Dermatology OPD with 4-month history of progressive eruption of non-itchy, painless papules over whole body which started from hands and gradually involved the arms, face, trunk and legs (**Figures 1-3**). He was otherwise healthy apart from the symptoms of fatigue and weight loss which were due to HIV.

Examination showed skin-colored papules with central umbilication on an erythematous base present on trunk, back, arms and hands. These resembled lesions of molluscum contagiosum. Some macular hyperpigmented lesions were also present on the back. Sensations were intact. The surrounding skin was normal and there were no signs of excoriation. There was no lymphadenopathy or hepatosplenomegaly.

Laboratory investigations were unremarkable except for a mild anaemia (Hb

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Figure 1 Skin-coloured molluscum like lesions on an erythematous base on the palm



Figure 2 Molluscum contagiosum-like lesions over elbow.



Figure 3 Maculopapular lesions on the chest.

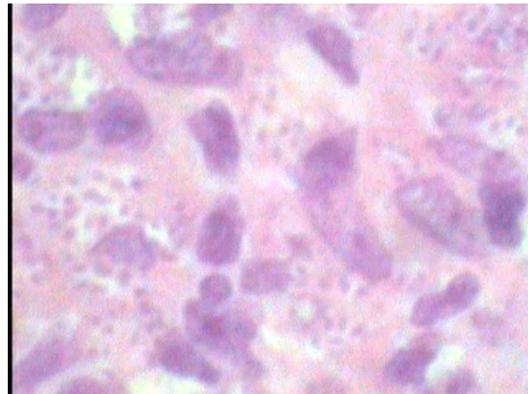
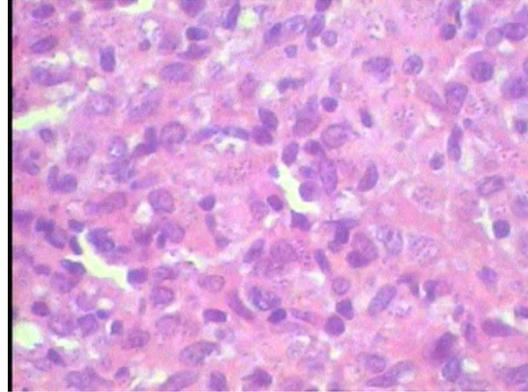


Figure 4 Histopathology showing Leishman-Donovan bodies



Figure 5 Lesions after 1 month of treatment with miltefosine.

9g/dL) but CD4 T cells were low (127/mm³, normal range 500-1000/mm³). Skin biopsy revealed a massive dermal plasma cell infiltrate with Leishman-Donovan (LD) bodies (**Figure 4**). Examination of bone marrow and hepatic aspirates was normal. A diagnosis of diffuse cutaneous leishmaniasis

was made. He was treated with miltefosine, 50mg twice daily for 3 months. A dramatic improvement was noted (**Figure 5**).

Discussion

Cutaneous leishmaniasis, first descriptions of which can be traced back to the 9th century (Balkh sore), remains a major world health problem in the 21st century.¹ There are 12 million people infected with leishmaniasis worldwide. Every year, up to 2 million new infections occur, almost two thirds of these in the cutaneous form.⁵ It is caused by different species of genus *Leishmania*, a protozoon that is transmitted by sandflies. The result of infection varies from a cutaneous ulcer, to erosive mucosal disease with severe facial disfigurement, to a life threatening systemic infection, depending upon the interaction between *Leishmania* and the genetic and immunological status of the host.¹

There is a broad spectrum of clinical manifestations of cutaneous leishmaniasis. The usual lesion is a small, red papule which over several weeks becomes darker, crusts in the center and eventually ulcerates. After about 3-6 months, the ulcer heals, leaving a raised border.⁶ A rare form is the disseminated (diffuse) cutaneous leishmaniasis, in which lesions are disseminated, resembling lepromatous leprosy. The disease usually begins with an initial primary lesion and then disseminates to involve other areas of the skin. The lesions are nonulcerative nodules full of parasites, and are often scattered over the limbs, buttocks, and face. The disease does not invade internal organs.⁷

Although people are often bitten by sandflies infected with *Leishmania* protozoa, most do not develop the disease. However, among persons who are immunosuppressed e.g. as a result of advanced HIV infection, immunosuppressive treatment for organ transplants, haematological malignancy, autoimmune diseases, quickly evolve to a full clinical presentation of severe leishmaniasis.² An overview of 15 documented cases showed that all HIV patients with leishmaniasis were significantly immunosuppressed.⁵

Leishmania/HIV co-infection is emerging as an extremely serious, frequent and new disease. It is anticipated that its number will continue to rise in the coming years and there is evidence that cases are no longer restricted to endemic areas.² Visceral leishmaniasis is the fourth most common opportunistic parasitic disease in HIV-positive individuals in Spain after pneumocystosis, toxoplasmosis, and cryptosporidiosis.⁴ VL and HIV are locked in a vicious circle of mutual reinforcement. VL quickly accelerates the onset of AIDS (with opportunistic diseases such as tuberculosis or pneumonia) and shortens the life expectancy of HIV-infected people.² On the other hand, HIV infection increases the risk of developing VL by 100-1000 times in endemic areas.⁴ Both diseases exert cumulative deficiency of the cellular immune response since both agents destroy the same cells, exponentially increasing disease severity and consequences. Increased plasma HIV viral load is associated with leishmaniasis and decreases following its treatment. Pre-treatment HIV viral load influences the response to antileishmanial chemotherapy. It supports

the idea that concomitant infections play an important role in disease progression of either infection.⁸

The majority of *Leishmania*-HIV co-infection displays clinical features of visceral leishmaniasis. Cutaneous leishmaniasis is uncommonly described in these patients.⁷ The special clinical characteristics are⁴:

- a. Parasitic dissemination to the skin in cutaneous leishmaniasis, or throughout the reticuloendothelial system in visceral disease. Almost every organ containing phagocytic cells may eventually become infected.
- b. Atypical locations
- c. A chronic and relapsing course
- d. Poor response to standard therapy.
- e. Lack of antileishmania antibodies

There is a variable spectrum of lesions of cutaneous leishmaniasis in HIV patients which may occur simultaneously with visceral involvement and can be papular, maculopapular or nodular. *Leishmania* amastigotes have been also found in apparently normal skin, infecting sweat ducts, or co-existing with other cutaneous lesions like Kaposi's sarcoma, herpes simplex, herpes zoster, dermatofibromas, psoriasis, Reiter's syndrome, bacillary angiomatosis, cryptococcosis and oral aphthae, although its presence does not imply a causative role. Leishmaniasis also appears as a dermatomyositis-like eruption, mucocutaneous and mucosal leishmaniasis, generalised cutaneous leishmaniasis, and post-kala-azar dermal leishmaniasis.⁴ So, *Leishmania*/HIV co-infections impose specific difficulties in terms of diagnosis and

treatment. The usual clinical features (fever, weight loss, liver and spleen enlargement, inflammation of the lymph nodes) are not always present. The clinical diagnosis can also be made difficult by associated diseases. The serological diagnosis is falsely negative in 42.6% of co-infected patients. HIV-positive patients have difficulty in producing antibodies against new infectious agents. Although, parasitological diagnosis can be difficult, bone marrow aspirate remains the safest and most sensitive technique, but spleen aspirate and liver biopsy are also used.²

Treatment has proven to be very problematic⁵ in co-infected patients and is aimed at clinical and parasitological cures and prevention of relapses. Unfortunately, in such patients treatment failure, relapses due to drug resistance and drug toxicity are very common.² Before HAART was extensively used, VL was associated with HIV infection relapse.⁹ The advent of HAART has modified the natural history of HIV and its related opportunistic infections and neoplasms and has permitted a partial but substantial recovery of many immune functions in HIV-infected patients.⁴ HAART also prevents the development of symptomatic VL in individuals with subclinical VL.⁹ HAART is very expensive and beyond the means of poor patients. There is a dire and urgent need to develop cheaper and effective methods for diagnosis and management of both VL and HIV infection.³

Overall, treatment approaches are comparable to those of HIV-negative patients with the important difference of prolongation of the duration of antimonial

therapy to 4 weeks rather than 21 days. Pentavalent antimonials remain the treatment of choice for HIV-associated VL because their therapeutic efficacy and the rate of adverse events are comparable to those of amphotericin with less cost. Whenever used, allopurinol and IFN- γ should be combined with antimonials except in patients suspected of having Kaposi's sarcoma, since IFN- γ could promote the progression of KS lesions. Oral miltefosine is a promising alternative and its efficacy is being evaluated.⁴ Besides treatment of VL and administration of HAART, other secondary infections like tuberculosis of the chest, oral candidiasis, CMV infections, *Pneumocystis carinii* pneumonia, toxoplasmosis, Kaposi's sarcoma also need to be treated.³ Pentamidine should only be used when no other options are available.

At present, there is no role for primary prophylaxis against *Leishmania* infection in HIV-infected patients. Secondary prophylaxis employs monthly administration of antimonials.⁴ Patients should be monitored until the lesions have fully resolved. Most relapses occur within 3-6 months after single course of treatment, so follow up at 6 months is appropriate. Thereafter patient should be warned about relapse.¹ Prognosis depends on nutritional and overall immune status of the host and on the precise species of infection.⁶

The lack of local literature about this condition means either non occurrence in Pakistan or clinician's ignorance about this condition. So a high index of suspicion of atypical leishmaniasis should be present

while examining HIV patients. In fact, all infections in HIV patients can present in atypical form. It is necessary to identify them at early stage in order to avoid the complications.

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