CASE REPORT

Immune reconstitution inflammatory syndrome in an HIV seropositive leprosy patient

ARCHANA SINGAL, SHILPA MEHTA & DEEPIKA PANDHI
Department of Dermatology and STD, University College of Medical Sciences & Guru Teg Bahadur Hospital, Shahdara, New Delhi 110095, India

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Introduction

The natural course of leprosy co-infected with human immunodeficiency virus (HIV) is not clearly understood. This is important because of the high and increasing prevalence of HIV infection in many leprosy endemic populations.1–3 The introduction of highly active antiretroviral therapy (HAART) has led to the emergence of a new clinical syndrome known as immune reconstitution inflammatory syndrome (IRIS).4 This syndrome has been described in association with diseases such as herpes zoster, Mycobacterium tuberculosis, M. avium, cytomegalovirus and sarcoidosis.5,6 Recent reports have described IRIS in four patients with leprosy. We report an HIV positive borderline lepromatous leprosy patient developing IRIS following institution of HAART.

Case report

A 32-year-old male reported with numbness over upper and lower limbs in a glove and stocking pattern for the last 2 years. Over the last 6 months, he had had intermittent fever associated with multiple crops of red raised painful evanescent lesions on the face and the limbs. He also developed spontaneous blistering, slippage of footwear and difficulty in doing fine work with his hands. He had progressive weight loss over the past 2 years without persistent diarrhoea, cough or other systemic complaints. He denied high risk behaviour towards the acquisition of HIV infection.

The patient was febrile with multiple discrete submandibular, axillary and inguinal non-tender and mobile lymph nodes. Cutaneous examination revealed marked seborrhoea over face and chest with diffuse infiltration of the forehead and ears. Multiple erythematous tender...
papules and nodules varying in size from 0·4 to 2 cm were present over the forehead, cheek, chin, earlobes and extensor aspect of upper and lower limbs. Multiple lesions of molluscum contagiosum were present on the face. Hypopigmented atrophic scars over the extensor aspect of bilateral upper and lower limbs were also seen.

There was atrophy of the bilateral thenar and hypothenar eminence along with glove and stocking pattern of anaesthesia. Right greater auricular, bilateral ulnar, radial cutaneous, lateral popliteal and posterior tibial nerves were thickened and non-tender. Systemic examination revealed no abnormality.

Haematological examination revealed microcytic hypochromic anaemia (Hb 7·6 g%), neutrophilic leucocytosis (TLC 12,500/mm$^3$) and raised erythrocyte sedimentation rate (81 mm in the first hour). Slit skin smear examination for $M$. leprae revealed a bacteriological index of 4 along with a morphological index of 40%. Histological examination of a biopsy taken from the lesion on the right cheek demonstrated diffuse infiltrate of foamy macrophages, plasma cells and lymphocytes along with concentric perineural infiltration, validating the clinical diagnosis of borderline lepromatous leprosy. On Fite–Faraco staining, acid-fast bacilli were seen both singly and in clumps within Schwann cells and macrophages. Histological examination of a biopsy taken from a painful nodule on the arm demonstrated neutrophilic abscesses superimposed on a diffuse infiltrate of foamy macrophages and lymphocytes, along with evidence of leucocytoclastic vasculitis, confirming a diagnosis of erythema nodosum leprosum (ENL). ELISA for HIV by Retroquick, Capillus and Immunocomb was reactive, with a CD4 count of 108/mm$^3$. Stool examination for Cryptosporidium and Isospora, and sputum examination for Pneumocystis jiroveci and $M$. tuberculosis were negative.

The patient was started on rifampicin (600 mg monthly), minocycline (100 mg daily), ofloxacin (400 mg daily) and clofazimine (100 mg thrice daily). Standard WHO MDT regimen including dapsone was not prescribed, as the patient had moderate anaemia with a haemoglobin of 7·6 g%, which is a relative contraindication for the drug. A combination of trimethoprim (80 mg) and sulphamethoxazole (400 mg) twice a day for Pneumocystis jiroveci pneumonia prophylaxis was also started. ENL lesions and fever subsided within 4 weeks. Ofloxacin and minocycline were discontinued after 4 weeks and the patient was continued on rifampicin and clofazamine. After 3 months of anti-leprosy treatment (ALT), HAART comprising zidovudine (600 mg), lamivudine (300 mg) and nevirapine (400 mg) daily was started. One month following HAART, the patient developed erythema, edema and pain over pre-existing lesions, eruption of multiple new lesions, bilateral posterior tibial neuritis and foot drop (Fig. 1). He was diagnosed to have type I leprosy reaction and was treated with oral prednisolone (40 mg daily), which was subsequently tapered. The neuritis subsided with no improvement in dorsiflexion at ankle joints. Currently the patient is continuing HAART, ALT and physiotherapy. His current CD4 count is 224/mm$^3$.

**Discussion**

HIV infection has been shown to be strongly associated with development of active tuberculosis and diseases caused by other mycobacteria, but its association with leprosy is much less clear. An association between HIV and leprosy has been described from Zambia and Tanzania, while reports from Ethiopia and other African countries have not found such a correlation. A study conducted on 4025 leprosy patients in India described only five HIV
coinfected patients. This may be due to the fact that HIV positive patients in the tropics do not live long enough to develop infections such as leprosy, which has a prolonged incubation period.

The course of *M. avium* and *M. tuberculosis* in HIV infected individuals tends to be more rapid and fulminant, since HIV infection compromises the cell-mediated immunity. The cellular immune response is of particular importance in the clinical manifestation of infection with *M. leprae*. It is expected that when an HIV positive individual becomes infected with *M. leprae*, the lepromatous disease would predominate. Despite the expected association of lepromatous leprosy with the underlying immunosuppressed state, studies conducted in Agra (India) found that HIV infection is commonly associated with the tuberculoid form of leprosy and none of these patients progressed to a more severe form of disease.

![Figure 1. Marked seborrhoea and diffuse infiltration over the face and bilateral ears along with necrosis over the left eyebrow and both the cheeks.](image-url)
Many studies have attempted to show the HIV infection as a risk factor for various complications in leprosy. Gebre et al. suggested a positive association of HIV co-infection with erythema nodosum leprosum, recurrent reversal reaction and increased risk of seroconversion and mortality but no association with neuritis. In contrast, Vreeburg et al. reported fulminant neuritis in a relatively short span of time with co-infection. Further, in a recent case report, four out of five leprosy patients who were coinfected with HIV developed type I leprosy reaction following initiation of HAART therapy.

Our patient presented with ENL and developed neuritis as a part of IRIS. IRIS most commonly occurs in HIV positive patients, at an advanced stage of disease when their CD4 count is less than 200/mm³. Clinical signs of inflammation appear in opportunistic infections, when HAART triggers a generalized activation during transition phase of viral load suppression and the CD4 lymphocyte count increases. The syndrome has since been described in association with a number of different infectious conditions, including herpes zoster (41 cases), M. tuberculosis (37 cases), M. avium complex (32 cases) and cytomegalovirus (22 cases). In some cases, IRIS appears in the absence of opportunistic pathogens and manifests itself as an autoimmune or granulomatous disease, of which sarcoidosis is the most frequent (10 cases). The criteria for diagnosis include: (1) patients with full blown AIDS; (2) a significant increase in CD4 lymphocyte counts following antiretroviral therapy; (3) reconstitution of the immune system, accompanied by the detection of a latent infection (leprosy in the present case) and (4) symptoms not consistent with the expected progression of a previously diagnosed opportunistic infection, the expression of a newly acquired infection, or the manifestation of undesirable effects of the HAART.

IRIS with leprosy was first reported by Lawn et al. in 2003, and recently Couppie et al. have reported three patients, of whom two developed a severe ulcerating form of type 1 lepra reaction, responding to corticosteroids. The present case with BL leprosy developed IRIS syndrome in the form of type 1 lepra reaction manifesting as erythematous edematous lesions and polyneuritis with bilateral foot drop, following the onset of HAART. His CD4 count increased from 108 to 224/mm³ after 3 months of HAART, thus fulfilling the criteria for the IRIS phenomenon.

Systemic corticosteroids are indicated in severe leprosy reaction with neuritis, as in the present case. In HIV positive patients, use of high dose corticosteroids is associated with the development of accelerated Kaposi’s sarcoma, avascular necrosis of bone, activation of latent cytomegalovirus and M. avium. Therefore these patients should be closely monitored.

As access to HAART is increasing in leprosy endemic countries, the number of IRIS cases due to M. leprae is likely to increase in future. Therefore, in India, where the number of HIV positive cases has already crossed the 5 million mark, it is important to recognize leprosy as an IRIS associated condition.

References