CASE REPORT

Borderline tuberculoid leprosy with upgrading Type 1 reaction in a HIV seropositive patient, after antiretroviral therapy: an Immune Reconstitution Inflammatory Syndrome

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Summary A case of borderline tuberculoid (BT) leprosy with upgrading Type 1 reaction, in a HIV seropositive patient, 7 weeks after starting highly active antiretroviral therapy, as an immune reconstitution inflammatory syndrome (IRIS), is reported.

Introduction

With increasing availability of highly active antiretroviral therapy (HAART) in more and more leprosy endemic areas, an increasing number of patients of leprosy-HIV co-infection are being reported, who present as IRIS following institution of HAART. The case definition of IRIS should include (1) leprosy and/or leprosy Type 1 reaction presenting within 6 months of starting HAART, (2) advanced HIV infection, (3) low CD4 count before starting HAART and (4) CD4 count increasing after start of HAART. IRIS in the form of upgrading Type 1 leprosy reaction in the borderline spectrum of leprosy, has been documented in many patients co-infected with leprosy and HIV. We report a case of borderline tuberculoid leprosy with upgrading Type 1 reaction, in a HIV seropositive leprosy adult female patient, occurring 7 weeks after the initiation of HAART.

Case Report

A 32 year-old Indian female was referred to the dermatology unit on 26th November 2006 from the HIV/AIDS outpatient clinic, complaining of a single reddish raised rounded lesion on the left side of the front of the neck, for about 2 weeks. She had earlier presented to the hospital in 2002 with painful blisters on the left side of the chest wall, diagnosed as herpes...
zoster. At that time she was found to be HIV-1 seropositive by ELISA method using two different antigens/methods, as per the national HIV testing policy of India. Her husband died in 1992, probably of AIDS, suggesting that she acquired HIV infection before 1992. In October 2005, she reported itchy papular eruptions over her back, face and extremities; pigmentations over the oral cavity and all her nails. Her CD4 count was 366 cells/mm$^3$ and she was counselled to come regularly for follow up examinations. In October 2006 her CD4 count had dropped to 125 cells/mm$^3$ and she was started on HAART, Stavudine, Lamivudine and Nevirapine in standard doses. Seven weeks later, on 26th November, she returned with a reddish patch that had developed on her neck over the previous week. Examination revealed a coin shaped erythematous, edematous, tender plaque 3.5 cm $\times$ 2.7 cm on the left front of her neck just below the mandible (Figure 1).

The surface of the plaque was smooth and shiny and warm to touch. Both light touch and pain sensations were impaired. There was no thickening of localised cutaneous nerves or peripheral nerve trunks. A clinical diagnosis of borderline tuberculoid (BT) leprosy with upgrading (reversal) Type 1 reaction was made. A slit-skin smear examination for $M. leprae$ did not reveal any acid-fast bacilli (AFB). A skin biopsy confirmed the diagnosis, showing perineural and periadenexal granulomas composed of lymphocytes, a few epithelioid cells and occasional giant cells. The dermis showed oedema and scattered chronic inflammatory cells. Fite-Faraco stain revealed a single intra-neural fragmented bacillus (Figure 2). Her CD4 count was now 333 (a 2.7 fold rise from the pre-HAART level).

**Discussion**

IRIS is a phenomenon that can occur in HIV infected people at an advanced stage of the disease (CD4 lymphocyte counts $< 200/mm^3$) where clinical signs of inflammation appear, mostly in association with opportunistic infections, following triggering of a generalised immune activation by HAART, associated with a fall in viral load and rise in CD4 cells. The infectious agent may have been treated previously or may have been present in a latent state, but is always present in the patient’s body before the introduction of HAART.
Immunopathology under such situations is usually triggered via cell-mediated Type 1 cytokine secreting immune responses. In the present case, the immune recognition of *M. leprae* antigen after HAART, probably initiated the development of an active clinical BT leprosy with a Type 1 upgrading reaction.

Over the past 4–5 years, several cases of HIV & leprosy co-infections presenting as IRIS have been documented. A report from Brazil describes a 35 year-old patient with HIV who developed BT leprosy with Type 1 reaction following 3 months of HAART. He had been treated for BL leprosy for 5 years, till smear negativity at the age of 10 years. Another report describes two HIV and leprosy co-infected patients who developed Type 1 reaction even before HAART or anti-leprosy treatment (ALT) was instituted. The clinical reaction of leprosy in HIV co-infected patients, whether it occurs after HAART, or ALT or, for that matter, in the absence of either, is clinically indistinguishable, thus suggesting some common underlying immunological mechanism. The possible explanations underlying leprosy IRIS could be that HAART may provide the immunological ‘trigger’ to the antigens present leading to the development of sub polar tuberculoid form of disease. Secondly, there could be a sudden unexplained switching-on of Th1 type responses to *M. leprae*, induced by HAART, (akin to the mechanism underlying Type 1 leprosy reaction) even though HIV may not impair immune responses to *M. leprae*. Thirdly, HIV co-infection could result in a degree of suppression of host responses to *M. leprae* infection which is reversed after commencing HAART.

In countries where both HIV & leprosy are endemic, like India and Brazil, from where the majority of leprosy IRIS cases have been reported in co-infected patients, episodes of IRIS will occur from time to time and dermatologists and leprologists should remain vigilant.

References


Figure 2. Photomicrograph showing perineural and periadenexal granulomas (GR) (H&E ×400). Inset photomicrograph shows a single fragmented acid fast bacillus inside a nerve (Fite Faraco stain ×1000).


Trindade MA, Valente NY, Manini MI et al. Two patients co-infected with *Mycobacterium leprae* and human immunodeficiency virus Type 1 and naive for antiretroviral therapy who exhibited Type 1 leprosy reactions mimicking the immune reconstitution inflammatory syndrome. *J Clin Microbiol*, 2006; 44: 4616–4618.

