

## CASE REPORTS

Borderline Tuberculoid Leprosy with Type 1  
Reaction in an HIV Patient—A Phenomenon of  
Immune Reconstitution<sup>1</sup>Tarun Narang, Sunil Dogra, and Inderjeet Kaur<sup>2</sup>

The course of leprosy in patients with HIV infection has been a controversial issue for a long time. It is still a matter of debate whether the HIV status of an individual has any impact on the natural history of leprosy and response to anti-leprosy treatment. Though various effects on immune system can be expected in a case of co-existent leprosy with HIV infection, epidemiological studies failed to establish any such bearing in the clinical course of leprosy. A World Health Organization (W.H.O.) meeting in 1993 concluded that there is no convincing evidence for an association between HIV and leprosy (<sup>14</sup>). A case control study held in South India among leprosy patients also confirmed these findings (<sup>11</sup>). Individuals with profound immunosuppression due to HIV infection may have active coinfections that are subclinical because of the lack of host inflammatory responses. Reconstitution of the immune system during the initial months of antiretroviral treatment, however, may result in the development of overt clinical manifestations of these coinfections (<sup>1,3</sup>), as restoration of CD4<sup>+</sup> T lymphocytes permits inflammatory responses to be mounted (<sup>8,9</sup>). Immune reconstitution or immune restoration phenomenon is now a

well-recognized complication of highly active antiretroviral treatment (HAART) and has been described in individuals infected with *Mycobacterium tuberculosis*, nontuberculous mycobacteria, cytomegalovirus, and hepatitis B and C viruses (<sup>1,3</sup>).

## CASE REPORT

A 28-year-old married man was referred to our department for evaluation of erythematous plaque on his left thigh, observed 5 weeks back. He had become aware of his HIV status 4 months back when he was being evaluated for prolonged fever and intractable diarrhoea. His wife was also seropositive. At the time of presentation the patient had advanced immunosuppression, with a blood CD4<sup>+</sup> lymphocyte count of 125/ $\mu$ L and a plasma virus load of 150,000 HIV-1 RNA copies/mL. He was started on HAART (zidovudine, lamivudine, and efavirenz) and after 2 months of triple drug therapy, the patient noticed an erythematous plaque on his left thigh. Over the next week, the lesion enlarged, became swollen and smaller lesions appeared in its periphery (The Figure) along with symptoms of pain and paraesthesias in the left leg. Clinical examination revealed well-demarcated, erythematous, edematous tender plaque with complete loss of sensation. Left lateral popliteal nerve was thickened and tender. A clinical diagnosis of borderline tuberculoid (BT) leprosy with reversal (type 1) reaction was made. Skin biopsy confirmed the diagnosis, showing noncaseating granulomas, marked nerve destruction, and no acid-fast bacilli (AFB). At the time that the cutaneous lesions developed, the patient's plasma viral load had declined to 1750 HIV-1 RNA

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copies/mL, and his CD4<sup>+</sup> lymphocyte count had increased to 280/ $\mu$ L.

The patient was started on W.H.O. multi-drug therapy (M.D.T.) PBR. He was also started on prednisolone 40 mg once daily for the reversal reaction, which was gradually tapered and stopped in 12 weeks. He responded favorably to the treatment.

### DISCUSSION

HIV has generally not been found to have a significant impact on the clinical course of treated and untreated leprosy. However, it has been reported that the neuritis in co-infected people can be more severe and the reversal reaction may be more frequent after therapy. In endemic areas with HIV disease and leprosy, there does not appear to be a greater incidence of leprosy among HIV patients. It may be because of the very slow proliferation of the bacilli or the prolonged incubation period, or perhaps a particular cellular mechanism involved in its pathogenesis.

HIV-infected patients responding to HAART can show a diverse spectrum of symptoms caused by immune reconstitution and subsequent inflammatory reactions. The pathogenesis of this phenomenon, called immune restoration disease (IRD)/Immune reconstitution inflammatory syndrome (IRIS) is unclear. IRIS is an unusual inflammatory reaction to an opportunistic infection that occurs in a HIV-positive patient with profound immunosuppression during the reconstitution of the immune system in the initial months of HAART (<sup>2</sup>). A variety of manifestations of IRIS have been described, most prominently including *Mycobacterium avium* complex lymphadenitis, paradoxical exacerbations of pulmonary and CNS *Mycobacterium tuberculosis* infection (<sup>8</sup>), paradoxical exacerbations of *Cryptococcus neoformans* meningitis, herpes zoster and cytomegalovirus uveitis (<sup>12</sup>). Reactions in leprosy, especially the type 1/reversal reaction, should be recognized as an IRIS-associated manifestation with a possibility of atypical presentation.

Our patient may well have harbored latent infection with *Mycobacterium leprae* for many years or had ill defined lesions which escaped his attention. He developed clinically apparent leprosy within a span of two months, and the timing of the presenta-



THE FIGURE. Well defined plaque with satellite lesions on left thigh.

tion was related to his immune status. The temporal association between the development of skin lesions and the HAART-induced changes in plasma HIV-1 load and CD4<sup>+</sup> lymphocyte count strongly suggests that leprosy manifested clinically as a result of immune reconstitution. Immune reconstitution either resulted in the development of active leprosy per se or triggered the reversal reaction leading to presentation of previously unrecognized disease. Indeed, many patients with BT leprosy present only when a reversal reaction develops. The onset of immune reconstitution phenomena often occurs within 1 to 6 months of HAART, even prior to substantial increase in the blood CD4<sup>+</sup> T lymphocyte count (<sup>1,3</sup>).

Studies have shown that HIV-1 infection is not a risk factor for leprosy (<sup>4,6</sup>). Although a shift in the spectrum of leprosy from the tuberculoid to the lepromatous form might be expected, studies have shown that HIV-1 co-infection does not alter either the clinical or histological spectrum of the disease (<sup>6,9</sup>). The development of borderline tuberculoid (BT) leprosy in this patient (indicating strong cell-mediated immunity), after increase in CD4<sup>+</sup> T lymphocyte counts is, therefore, consistent with previous observations (<sup>2,5</sup>). However, the presentation of leprosy as an immune reconstitution phenomenon does suggest that HIV-1 associated immunosuppression masked the patient's disease before the start of HAART. There are few case reports of this phenomenon in leprosy (<sup>2,5</sup>), and it is possible that the incidence of clinically overt leprosy may be decreased among HIV-infected individuals who are profoundly immunosuppressed.

Type 1 (reversal) reactions occur most

frequently among patients with BT leprosy, causing acute inflammation in cutaneous lesions and nerves harboring *M. leprae* antigens. Such reactions result from an increase in cell-mediated immunity and typically occur during the early stages of leprosy treatment. Paradoxically, such reactions are observed more frequently among those with HIV-1 coinfection<sup>(13)</sup>.

The increasing availability of HAART in areas where both HIV and leprosy are prevalent may well reveal latent leprosy cases as a result of an IRIS in patients starting antiretroviral treatment. Differentiation of IRIS from an opportunistic infection is important because IRIS indicates a successful, albeit undesirable, effect of HAART. It is also important to differentiate it from drug toxicity to avoid unnecessary cessation of HAART.

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