

## Leprosy presenting as immune reconstitution inflammatory syndrome - report of three cases

Ravi Munsing Rathod, Pradeep Vittal Bhagwat, Chandramohan Kudligi, Mohan Shendre, Suman Gurunathgouda Odugoudar

Department of Skin & STD Karnataka Institute of Medical Sciences, Hubli, Karnataka

**Abstract** The introduction of highly active antiretroviral treatment (HAART) has led to the emergence of a new clinical syndrome, immune reconstitution inflammatory syndrome (IRIS). This syndrome affects human immunodeficiency virus (HIV)- positive patients at an advanced stage of the disease (CD4 lymphocyte counts  $200/\mu\text{L}$ ). In these patients, clinical signs of inflammation appear mostly in association with opportunistic infection, when HAART triggers a generalized immune activation during the transition phase of viral load suppression and CD4 lymphocyte counts increase. 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 antiretroviral treatment. In the first situation, the opportunistic infection, which is initially improved by specific treatment, then leads to generalized or localized inflammation. In the second situation, the opportunistic infection is first detected when the CD4 lymphocyte count increases. In the first reported cases of IRIS, in 1998, the infectious agents were mycobacteria (*Mycobacterium avium* complex and *M tuberculosis*). The syndrome has since been described in association with more than a dozen different infectious conditions, with herpes zoster (41 cases), *M tuberculosis* (37 cases), *M avium* complex (32 cases), and cytomegalovirus (22 cases) in 73% of the first 182 published 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 first case of leprosy diagnosed after HAART initiation was reported in 2003.<sup>1</sup> We herewith report three cases of leprosy presenting as IRIS as the first manifestation.

**Key words**

Highly active antiretroviral treatment (HAART), immune reconstitution inflammatory syndrome, leprosy.

**Case 1**

A 45-year-old male, diagnosed HIV positive two years back, presented with asymptomatic red colored patches all over the body since 5 months duration. The skin lesion first appeared over the right lower limb, gradually he noticed it over the

upper limbs, trunk and left lower limb. Initially the lesions were small in size, gradually increased in size. There was no history of fever. No other significant history was elicited. On examination, patient had multiple asymmetrically distributed erythematous, tender plaques of varying sizes with average size 5x5cm over back, chest and both limbs (**Figure 1**). Sensation to pain and temperature were normal. Bilateral ulnar and common peroneal nerves were enlarged and nontender. Slit-skin smear from the earlobe did not reveal acid-fast

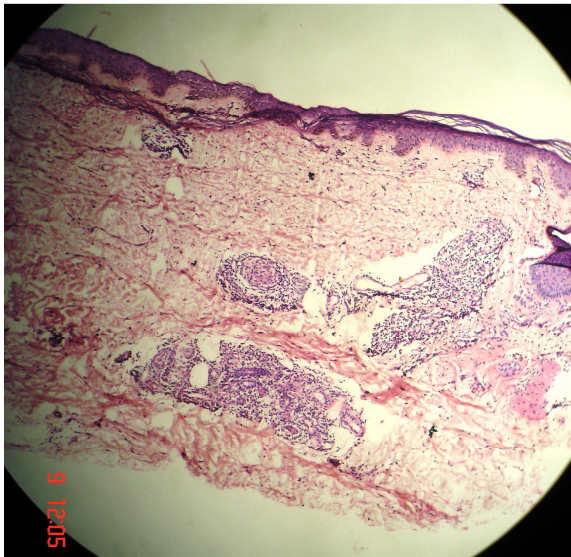
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**Address for correspondence**

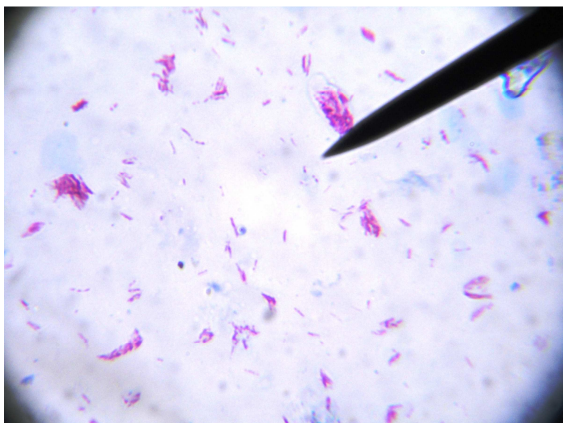
Dr. PV Bhagwat, Associate Professor,  
Department of Skin & STD,  
Karnataka Institute of Medical Sciences,  
Hubli, Karnataka  
Email: sharadapbhagwat@yahoo.com



**Figure 1** Clinical photograph of patient 1.



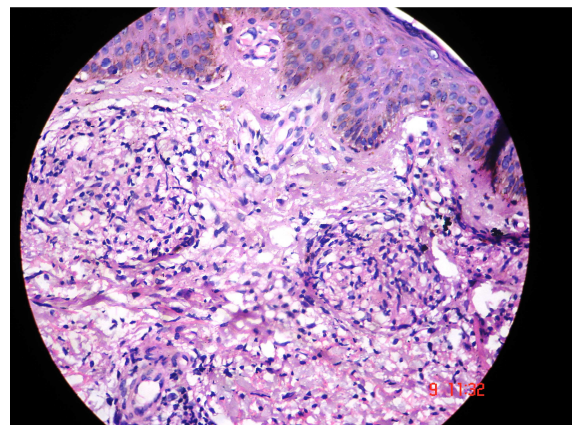
**Figure 2** Histopathology of the skin lesion of patient 1.



**Figure 3** Slit-skin smear of the patient 2.



**Figure 4** Clinical photograph of patient 3.



**Figure 5** Histopathology of the skin lesion of patient 3.

bacilli. A biopsy was done from the skin lesion and subjected to histopathological examination which revealed features of borderline tuberculoid leprosy, in type 1 lepra reaction (**Figure 2**). Fite Faraco stain was negative.

### Case 2

A 43-year-old female, HIV-positive since 2 years, on ART since 3 months, presented with history of skin lesions all over the body associated with minimal itching of 15 days duration following initiation of ART (Nevirapine based regimen). Skin eruption first appeared over the trunk, gradually spread to involve the limbs. There was no history of fever. There was no other significant history. On examination-patient had erythematous papules and plaques 1x1 cm to 5x6 cm, distributed all over the body. Right ulnar nerve, right and left common peroneal nerves were thickened and nontender. Slit-skin smear from the earlobe revealed numerous acid-fast bacilli with globi (**Figure 3**). We were in a dilemma whether it was nevirapine-induced drug rash or leprosy presenting as IRIS. We resorted to treat the patient with systemic corticosteroids. Meanwhile we did skin biopsy from the lesion and sent for histopathological examination. After two weeks, lesions persisted but erythema reduced. Diagnosis was revived. We concluded that it was leprosy presenting as IRIS. The Histopathological examination revealed features of borderline tuberculoid leprosy with type 1 lepra reaction. Fite Faraco stain revealed numerous acid-fast bacilli and globi.

### Case 3

A 48 years old, HIV positive male, on ART since 5 years, presented with asymptomatic persistent patches over face, arms, back, legs of 6 months duration. There was no other significant history available. Examination revealed multiple, normoesthetic, erythematous, tender plaques, distributed over face, trunk and limbs (**Figure 4**). Bilateral ulnar and common peroneal nerves were thickened. Biopsy from the lesion revealed features of BT Hansen's with

type 1 lepra reaction (**Figure 5**). Fite Faraco stain was negative.

### Discussion

Immune reconstitution inflammatory syndrome (IRIS) is defined as the occurrence or worsening of clinical/or laboratory parameters despite a favorable outcome in HIV surrogate markers (CD4 counts and viral load). Earlier, it was believed that, unlike tuberculosis, the course of leprosy was not significantly affected by HIV. However, we now know that immune suppression caused by HIV can suppress the clinical manifestation of leprosy, which can then be unmasked with ART, often as a reversal reaction. There are some case reports of leprosy presenting as IRIS.<sup>2,3,4</sup>

Several case reports have demonstrated that the immune reconstitution inflammatory syndrome induces reversal reaction in HIV and leprosy co-infected patients. Although HIV infection has been reported to have little impact on leprosy, initiation of antiretroviral treatment has been associated with activation of subclinical *M leprae* infection and exacerbation of existing leprosy lesions. A study involving 10 patients demonstrated that leprosy reaction is a manifestation of immune reconstitution.<sup>3</sup> We are reporting these cases because all of our patients, who were on ART, presented with skin eruptions, which, at the first instance, misled us towards some other diagnosis. Only after detailed workup, we could diagnose that these were leprosy presenting as IRIS. With increasing incidence of HIV and resurgence of leprosy, diagnosis of IRIS requires a high index of suspicion. These cases reflect that a careful and thorough examination is required in HIV patients to rule out rare IRIS conditions including leprosy and lepra reaction. We would like to highlight that leprosy, along with reversal reaction, should be included in the list of

differential diagnosis of other opportunistic infections presenting as IRIS.

### References

1. Couppie' P, Abel S, Voinchet H *et al*. Immune reconstitution inflammatory syndrome associated with HIV and leprosy. *Arch Dermatol*. 2004;**140**:997-1000.
2. Mehta S, Padhiar B, Shaw B. Leprosy presenting as immune reconstitution inflammatory syndrome. *Indian J Sex Transm Dis & AIDS*. 2008;**29**:96-7.
3. Kharkar V, Bhor UH, Mahajan S, Khopkar U. Type I lepra reaction presenting as immune reconstitution inflammatory syndrome. *Indian J Dermatol Venereol Leprol*. 2007;**73**:253-6.
4. Daps P, Lockwood DNJ. Leprosy presenting as immune reconstitution inflammatory syndrome: proposed definitions and classification. *Lepr Rev*. 2010;**81**:59-68.
5. Menezes VM, Salesa AM, Illarramendia X *et al*. Leprosy reaction as a manifestation of immune reconstitution inflammatory syndrome: a case series of a Brazilian cohort. *AIDS*. 2009;**23**:637-43.