CASE REPORT

Borderline leprosy presenting as immune reconstitution inflammatory syndrome: Two cases

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Summary The introduction of highly active anti-retroviral therapy (HAART) in HIV-infected leprosy patients has led to the emergence of a new clinical syndrome known as immune reconstitution inflammatory syndrome (IRIS). We reported the first cases in two Malians: a male of 31 and a female of 22 years old respectively diagnosed with borderline lepromatous and borderline tuberculoid leprosy. Both were known HIV-1 positive and treated with HAART. IRIS occurred respectively 3 and 4 months following HAART. All patients received WHO multi-drug therapy (MDT) without any complication.

Introduction

The interaction between Mycobacterium leprae (M. leprae) and human immunodeficiency virus (HIV) has been of interest to the leprosy community since the description of the original case of leprosy and HIV infection by Lamfers. Co-infection raised various questions about the clinical presentation of leprosy in HIV co-infected patients, disease outcomes and the prevalence of relapse and reaction. Several studies were conducted including in Mali but were not conclusive. The improvement in access to highly active antiretroviral therapy
(HAART) was accompanied by the recognition of leprosy as an immune reconstitution inflammatory syndrome (IRIS). Lawn et al. reported the first case in a Ugandan man in the United Kingdom in 2003. To date, only one case has been reported in west Africa. Here, we report two cases of borderline leprosy presenting as an IRIS in HIV infected patients following HAART in Mali, West Africa.

OBSERVATIONS

Case 1

A 31 year old man was referred to our Dermatology clinic with a skin eruption that had been present for 5 months. He was known to be HIV-1 positive and had been on HAART with zidovudine, lamivudine and nevirapine for 10 months. Three months following the HAART initiation he observed hypopigmented patches on his anterior abdominal wall but he did not seek advice. At the 6 month follow up, a drug eruption was suspected and the initial HAART was replaced by the combination of abacavir, lamivudine, indinavir and ritonavir. After 2

Figure 1. Case 1: Infiltrated and erythematous plaques over the trunk.
months’ therapy with this second line regime, his condition worsened and he developed more skin lesions associated with fever and joint pain. The physical examination revealed many infiltrated and erythematous plaques located over the trunk, back and genitalia (Figures 1, 2, 3).

There was hyperthrophy of the ulnar, radial and greater auricular nerves and impairment of sensation over palm and plaques. The motor function was normal. The CD4 count was 190 per µl before the initial HAART and 315 per µl 6 months later. After 12 months’ therapy this had increased to 410 CD4 per µl. The viral load was not performed. Slit-skin smear demonstrated a bacteriological index of 4+ at various sites. Histological examination of a skin lesion demonstrated diffuse infiltrate of the dermis involving the sweat glands and

Figure 2. Case 1: hypertrophy of the left great auricular.

Figure 3. Case 1: annular and erythematous lesions with dry skin.
nerves. This infiltrate comprised foamy macrophages, plasma cells and numerous lymphocytes along with oedema confirming the diagnosis of borderline lepromatous leprosy with Type 1 reaction (T1R). The patient received corticosteroid therapy with prednisone 40 mg per day. WHO multibacillary (MB) multi-drug therapy (MDT) was introduced after the patient was clinically stabilised 2 weeks later. The prednisone was reduced gradually and stopped after 4 months without complication. The clinical and biological findings of case 1 are summarised in Figure 4.

**Case 2**

A 22 year old woman consulted our clinic because of a skin eruption of 2 months duration. She was HIV-1 positive and had been started on zidovidune, lamivudine and efavirenz 6 months before when her initial CD4 count was 205 per μl. Four months after the initiation of HAART, she developed a single plaque on the forehead with others appearing on her trunk and limbs. The physical examination demonstrated numerous infiltrated hypopigmented patches 2–3 cm in diameter on the forehead, cheek, arm and back (Figure 5).

There was thickening of the ulnar nerve. The rest of the examination was normal. The CD4 count was 450 per μl. The bacteriological index was negative. The histological examination revealed epithelioid granulomas in the dermis involving sweat glands and nerves consistent with the borderline tuberculoid leprosy. The patient was prescribed WHO MB MDT for 12 months without any complication. The clinical and biological findings of case 2 are summarized in Figure 6.

**Discussion**

In this study, we report the first cases of borderline leprosy presenting as IRIS in HIV infected patients in Mali. The clinical presentation and investigations of our patients were consistent with the diagnostic criteria of IRIS as defined in previous studies. These include: (1) patients with AIDS; (2) a significant increase in CD4 lymphocyte count following antiretroviral therapy; (3) reconstitution of the immune system, accompanied by the detection of a latent infection (borderline leprosy in our cases) and (4) symptoms not consistent with the expected progression of a previously diagnosed opportunistic infection, the expression of

![Figure 4. Clinical summary and evolution of case 1.](image-url)
a newly acquired infection, or the manifestation of undesirable effects of the HAART. Although a cutaneous adverse drug reaction was suspected in one patient but not confirmed, there was no evidence of any other opportunistic infections. Our patients also met the Type 1 classification of IRIS as defined by Deps et al.\textsuperscript{8}
Several cases of IRIS due to leprosy with T1R were reported in the United Kingdom, India and French Guiana; only one case was reported from West Africa in Senegal. Many of these patients presented with tuberculoid or borderline leprosy and had clinical evidence of T1R. In one of our cases, the onset of leprosy was initially misdiagnosed as an adverse drug reaction, which resulted in a change in HAART. IRIS associated with leprosy usually occurs within a few months (1–6 months) of HAART introduction. In our patients, the symptoms of leprosy were present for about 5 months and 2 months respectively before the disease was diagnosed. This indicates that leprosy may occur early in the course of the disease but it is often only recognised when reaction occurs. T1R is common in borderline leprosy; this could be upgrading or downgrading reaction respectively linked to the reinforcement or the degradation of the host defense against \( M. leprae \). Even in the absence of the viral load in our patient, the increase of CD4 count together with clinical manifestations (infiltrated lesions, fever and joint pain) particularly in case 1 is consistent with a reversal reaction and a regaining of immunity against \( M. leprae \).

Reversal reaction may occur in HIV-infected leprosy patients before the initiation of HAART. In a cohort study by Lienhart et al., four of the six asymptomatic patients presented with Type 1 reaction and none were receiving HAART. Making comparisons about the frequency of T1R in HIV and non-HIV infected patients is difficult because T1R is the commonest complication of borderline leprosy, occurring in at least 30% of patients in most cohort studies, and only very small numbers of patients with leprosy as IRIS have been described.

IRIS has been reported with other pathogens like herpes simplex virus, Mycobacterium tuberculosis and granulomatous diseases such as sarcoidosis. However, given the increasing number of patients on HAART and the prevalence of leprosy particularly in sub-Saharan Africa, the number of leprosy as IRIS tends to be rare. Therefore, it is possible that some cases might consult leprosy management clinic without providing their HIV status. This should prompt physicians to consider performing an HIV test in all patient newly diagnosed with leprosy.

**Conclusion**

IRIS is a rare inflammatory syndrome associated with leprosy and HIV whose prevention and good management should prompt dermatologist to propose a systematic HIV test to all patient newly diagnosed with leprosy. Clinicians who are managing HIV infected patients should be aware of the possibility of leprosy as IRIS when facing a patient with a skin eruption within 6 months following HAART introduction.

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**References**

IRIS and leprosy in Mali


