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CASE REPORT

Shifting of the clinical spectrum of leprosy in an HIV-positive patient: a manifestation of immune reconstitution inflammatory syndrome?

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Introduction

The introduction of combination drug regimens, known as highly active antiretroviral therapy (HAART), has led to a significant decrease in AIDS-related morbidity and mortality.[1] However, a subgroup of human immunodeficiency virus (HIV)-positive patients under HAART have clinical deterioration even during improvement of CD4 count and decrease of HIV viral replication. These patients probably acquire a capacity to mount exuberant inflammatory responses towards opportunistic pathogens that had been present in a latent state before they started HAART.[2] This new clinical syndrome has been named immune reconstitution inflammatory syndrome (IRIS).[1–3]

IRIS was initially observed in cases of coinfection with mycobacteria (*Mycobacterium avium complex* and *Mycobacterium tuberculosis*).[4] Following the initial description, associations with cytomegalovirus, *Cryptococcus neoformans*, hepatitis B and C virus and *Histoplasma capsulatum*, have been reported.[2] In other reported cases, however, the target antigen remains unknown, as with sarcoidosis.[5]

Recently, IRIS has been also described in association with leprosy.[3,6–11] We report an HIV-positive patient with shifting of the clinical spectrum of leprosy after starting HAART.

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Case report

A 35-year-old Brazilian male presented in January 2003 with a 6-month history of severe pain in his lower limbs associated with a sensation of numbness and difficulty in walking. In March 2002, with recurrent lesions of molluscum contagiosum, he had been diagnosed with HIV-1 infection with a CD4 count of 92 cells per μl. HAART (indinavir, stavudine and didanosine) was initiated in April 2002. At the age of 10, the patient had been diagnosed with borderline lepromatous (BL) leprosy with multiple acid-fast bacilli (AFB) on histopathological examination. He received treatment with dapsone, rifampicin and clofazimine for 5 years until the skin smear became negative (then the standard criterion of World Health Organization (WHO) for treatment withdrawal).

Clinical examination revealed a patient in poor physical condition with hypoaesthetic and hypopigmented patches on the buttocks (Figure 1). Both ulnar and posterior tibial nerves were enlarged and tender. Routine laboratory tests were within normal ranges, CD4 count of 426 cells per μl and viral load of 8·300 copies per ml. Electroneuromyography demonstrated multiple peripheral neuropathies. Skin biopsy revealed epithelioid granulomas surrounded by dense lymphocytic infiltrate. Multinucleate giant cells were present in both superficial and reticular dermis. There were no signs of necrosis. Wade–Fite staining was negative for AFB. Based on the clinical and histopathologic findings a diagnosis of borderline tuberculoid (BT) leprosy was established.

In accordance with WHO recommendations, the patient was given dapsone (100 mg) daily and rifampicin (600 mg) monthly for 6 months. Prednisone (1 mg/kg per day) was introduced for neuritis and antiretroviral treatment was maintained. There was progressive improvement of pain and numbness of the lower limbs and cutaneous lesions. Prednisone was continued for 8 months, tapering the dose after the 4th week. The patient is still receiving HAART and has shown no disability during a 26-month follow up.

Comments

According to WHO, leprosy is still a public health problem in nations such as Angola, Brazil, Central African Republic, Democratic Republic of Congo, India, Madagascar, Mozambique,

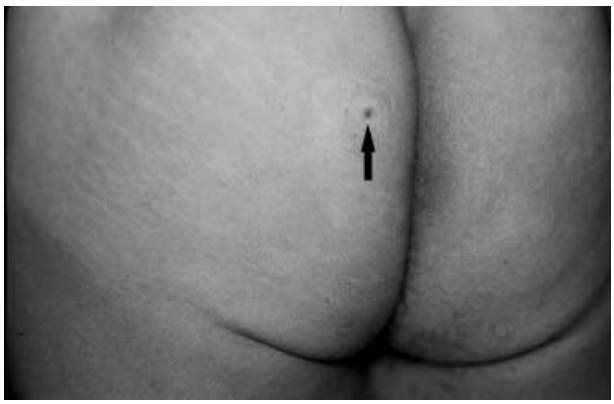

Figure 1. Hypochromic patches on the buttocks. The arrow indicates the site of biopsy.

Nepal and the United Republic of Tanzania.[12] Since HIV-1 prevalence is high in many of these countries[13] it would be reasonable to expect that AIDS might have a major impact on the clinical course of treated and untreated leprosy. However, contrary to these early expectations and unlike other mycobacterial diseases such as tuberculosis, the clinical and pathological spectrum of leprosy in HIV-positive patients seems to be unaltered.[3]

After the initial description of leprosy-associated IRIS by Lawn *et al.*,[7] other cases have been described.[8–11] The reported cases meet the following criteria for IRIS: (1) a clinical picture of AIDS; (2) HAART followed by a significant increase in CD4 lymphocyte count; (3) reconstitution of the immune system accompanied by the detection of a latent infection of leprosy; and (4) symptoms not consistent with the expected progression of a previously diagnosed opportunistic infection, the expression of a newly acquired infection or adverse effects caused by HAART.[1,3,9] Interestingly, our patient fulfilled all the criteria for leprosy-associated IRIS and also displayed a shift of the clinical spectrum of leprosy, upgrading from BL to BT.

The immunological basis of the polar lepromatous (LL) leprosy is not fully elucidated. However, possible explanations include immune deviation of the CD4 lymphocyte response, deletion of T cells reactive to *M. leprae* and the presence of regulatory or suppressor T cells.[14] In any event, patients with LL and BL leprosy show T-cell unresponsiveness. Moreover, since borderline forms are unstable, downgrading from BT to BL would be expected, not the opposite.[14] We believe that the shifting of the clinical spectrum of leprosy presented by our patient may be due to the immune reconstitution induced by HAART. It is known that patients with advanced HIV-1 infection undergoing HAART show an increasing number of CD4 lymphocytes.[2] Therefore, the CD4 cells may have played an important role in promoting a new and adequate cellular immune response to *M. leprae* in our patient. However, it must be pointed out that our case may as well represent a delayed relapse or reinfection. Further studies in a larger group of patients are necessary for the better understanding of leprosy-IRIS correlation.

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