Immune reconstitution inflammatory syndrome: A therapeutic paradox

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ABSTRACT

A 41-year-old HIV positive woman was started on highly active antiretroviral therapy when her CD_4 count was 54/cu mm. Three weeks later, she developed erythematous to skin-colored plaques over the face. Investigations revealed a moderate eosinophilia, raised ESR, elevated 24-hour urinary calcium and hyperglobulinemia. Skin biopsy of the facial plaque revealed prominent epithelioid cell granulomas in the dermis. Reticulin stain showed reticulin fibers within the granulomas. Five months later, all the facial lesions regressed with continuation of HAART, with no specific treatment for facial plaques. Repeat CD_4 count was 104/cu mm. A diagnosis of cutaneous sarcoidosis occurring as a part of immune reconstitution inflammatory syndrome was made. Although systemic sarcoidosis has been reported, the occurrence of cutaneous sarcoidosis as part of immune reconstitution inflammatory syndrome has not been elucidated conclusively.

Key words: Highly active antiretroviral therapy, retroviral therapy, immune reconstitution inflammatory syndrome, cutaneous sarcoidosis

INTRODUCTION

Highly active antiretroviral therapy (HAART) reduces morbidity and mortality in HIV infection and also alters the clinical course of the associated subclinical opportunistic infections or autoimmune diseases. Atypical inflammatory disorders that develop after initiation of HAART and are known as immune reconstitution inflammatory syndrome, immune restoration syndrome, immune reconstitution syndrome or immune restoration inflammatory syndrome.[1] Immune reconstitution inflammatory syndrome is defined by manifestations of HIV disease, which may worsen despite an adequate response to HAART, as measured by an increase in CD_4 cell counts and a decrease or disappearance of serum HIV-RNA.[2]

CASE REPORT

A 41-year-old female detected to be HIV positive 1.5 years ago with a past history of pneumocystis carinii pneumonia (one year ago), was referred to the dermatology department with complaints of reddish to skin-colored raised lesions over the face of one week duration. She was started on HAART three weeks prior as her CD_4 count was 54/cu mm. (Viral load was not done due to lack facilities.) On examination, she was well looking, moderately built and well nourished. There was no pallor or generalized lymph node enlargement. Face showed three hyperpigmented and erythematous plaques 2-3 cm in size over the bridge of nose, left nasal alar cartilage and adjacent right cheek [Figure 1].

In the context of HIV infection with a low CD_4 count, the possibilities of cutaneous lymphoma, Kaposi's sarcoma, insect bite granuloma and cutaneous tuberculosis were considered. From the morphologic appearance of the lesions, cutaneous sarcoidosis and leishmaniasis were also considered. The patient was further investigated for the skin condition.

The positive investigation findings were moderate eosinophilia, raised ESR, elevated 24-hour urinary calcium and hyperglobulinemia.

Skin biopsy from one of the centro-facial plaques showed epithelioid cell granulomas in the dermis with scanty lymphocytes and a few giant cells. There was no necrosis, LD bodies, atypical cells or AFB [Figure 2]. Reticulin stain showed reticulin fibres within the granuloma [Figure 3].

With the above features, a final diagnosis of cutaneous sarcoidosis in advanced HIV infection was made.

As the patient did not show any features of systemic sarcoidosis, she was advised to continue HAART and placed under followup. After five months, all her facial lesions regressed [Figure 4].

DISCUSSION

Acquired immunodeficiency syndrome (AIDS), since its recognition in 1981, has grown to a wide-spectrum disease phenomenon with a multitude of associated conditions. Most of it is attributed to the immune suppression due to a drastic drop in the CD_4 count. Dr. Martin French added a new catchphrase to the HIV/AIDS vocabulary with the introduction of the term immune restoration syndrome,[3] that runs contrary to the usual trend of the immune deficiency associated with this infection.

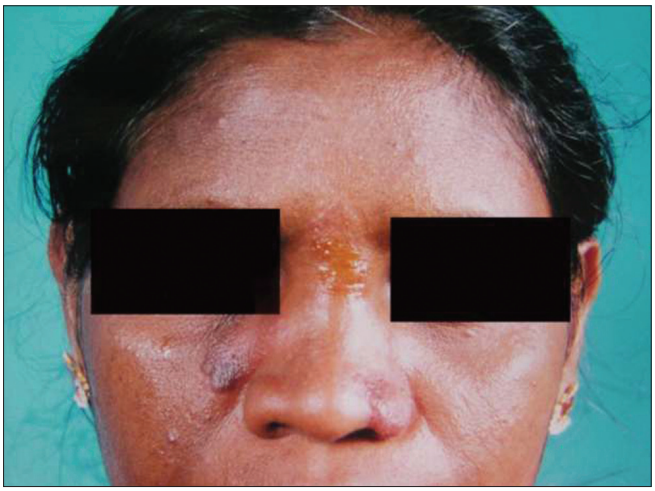

Figure 1: Skin-coloured plaques over the bridge of nose, erythematous and hyperpigmented plaques over the ala of nose and cheek

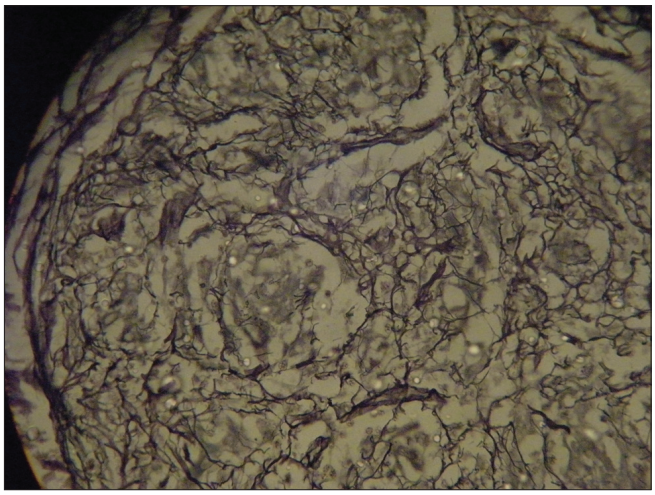

Figure 3: Reticulin stain showing reticulin fibres within the granuloma

Dermatological conditions are often early clues to HIV infection. As the disease progresses, patients develop a progressive depletion of the CD4 cell count and cell mediated immune responses which facilitates the development of a number of skin conditions. With antiretroviral therapy, the Th1 response is restored and some skin problems regress. But, paradoxically, some cutaneous conditions may worsen, such as herpes zoster, mucocutaneous herpes, eosinophilic folliculitis and mycobacterial infections.[4] IRIS is a pathological inflammatory response to preexisting microbial, host, or other antigens that results in clinical deterioration in HIV - infected persons after initiating HAART. The suppression of HIV replication allowing gradual restoration of immune capacity is central to the pathogenesis of IRIS.[5] The symptoms of immune reconstitution inflammatory syndrome may resemble drug side-effects or a flareup of an opportunistic infection. About 25% of the people who have good results with HAART may experience this syndrome, patients and physicians should be aware of this alternative diagnosis.[3]

Shelburne *et al*. had proposed the following set of criteria for the diagnosis of IRIS:[6]

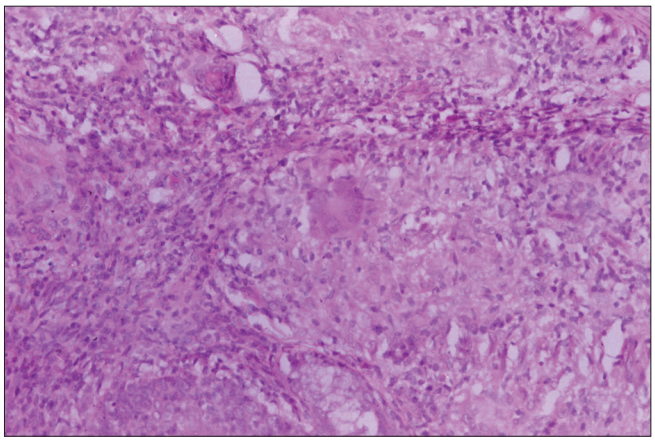

Figure 2: Epithelioid cell granulomas with scanty lymphocytes

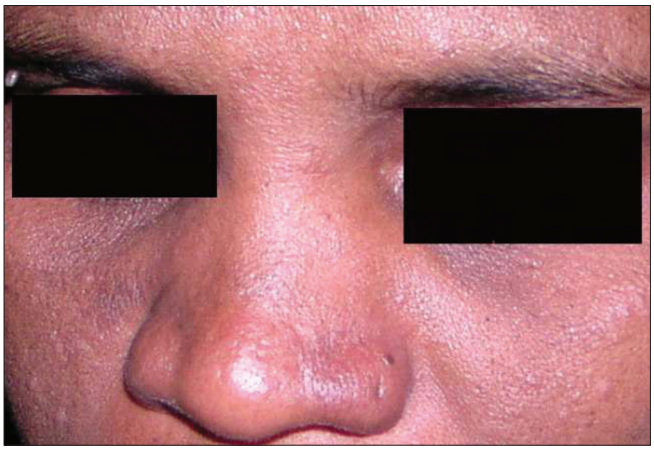

Figure 4: Regressed lesions seen on follow-up

A patient must

- be HIV positive and receiving ART;
- have a decreasing viral load, with or without an increase in the CD4 cell count from baseline;
- have clinical symptoms consistent with an inflammatory process in which the clinical course is not consistent with the expected course of previously diagnosed opportunistic infections (OIs), expected course of newly diagnosed OIs or drug toxicity.

The best approach to the management of immune reconstitution inflammatory syndrome is not clear. Treating the associated condition does not always lead to clinical improvement. As many cases resolve on their own, it is impossible to say what works, without conducting prospective clinical studies.

HIV and sarcoid coexit relatively infrequently, perhaps because of the inability of the depleted CD4 cells to stimulate macrophages and mount the immune response required to form granulomas and manifest sarcoid. So during IRIS the increase in CD4 cells explains the occurrence of sarcoid.[7] From the immunological standpoint cutaneous sarcoid is not distinct from systemic sarcoid, as the underlying pathological phenomenon are the same and only the tissue affected is different. The appearance of cutaneous sarcoidosis following institution of HAART and its regression without specific treatment during follow-up accompanied by a rise in CD_4 count temporally substantiates the linkage of sarcoidosis with immune reconstitution inflammatory syndrome.

REFERENCES

1. Stoll M, Schmidt RE. Immune restoration inflammatory syndromes: The dark side of successful antiretroviral treatment. Curr Infect Dis Rep 2003;5:266-76.
2. Johnson RA. Cutaneous manifestations of human immunodeficiency virus disease. In: Freedberg IM, Elsen AZ, Wolff K, Austen KF, Goldsmith LA, Katz SI, editors. Fitzpatrick's Dermatology in General Medicine. 6th ed. New York: McGraw Hill Medical Publishing Division; 2003. p. 2138-50.
3. Maclean D. Immune restoration disease. CATIE- News: Bite sized HIV/AIDS treatment news bulletins. Created on 1998 February 2. Available from: http://www.catie.ca/catienews.nsf. [Last cited on 2011 Aug 1].
4. Handa S, Bingham JS. Dermatological immune restoration syndrome: Does it exist? J Eur Acad Dermatol Venereol 2001;15:430-2.
5. Lawn SD, Bekker LG, Miller RF. Immune reconstitution disease associated with mycobacterial infections in HIV - infected individuals receiving antiretrovirals. Lancet Infect Dis 2005;5(6):361-73.
6. Anubhav G, Kamath NK. Immune reconstitution inflammatory syndrome in a unique clinical scenario. Indian J Sex Transm Dis 2010;31:128-9.
7. Lehloenya R, Meintjes G. Dermatologic manifestations of the immune reconstitution inflammatory syndrome. Dermatol Clin 2006; 24:549-70.

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