IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 12 Ver. VII (Dec. 2015), PP 89-92
www.iosrjournals.org

Leprosy Presenting As Immune Reconstitution Inflammatory Syndrome (IRIS) In A HIV Infected Soldier on HAART

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Abstract: *A case of 43 year old male, HIV infected soldier started on HAART (ZLN) presented with a large anesthetic patch in Rt elbow and Lt sole with tingling sensation and numbness in Rt forearm . On examination there was large anesthetic and hypo pigmented patch with erythematous border over Rt elbow area and similar patch in Lt sole and also a hypo pigmented scaly plaque on Lt buttock with thickened Rt ulner nerve . Slit skin smear for AFB was Negative, Skin biopsy shows numerous well epitheloid granulomas with Langhan's giant cells. Features are of chronic granulomatous lesion consistent with Hansen's disease – tuberculoid type . Wade fite faraco stain shows no acid fast bacilli. He was diagnosed as a case of BT leprosy and in the background of HAART and increasing CD4 it was considered as a case of IRIS (Immune Reconstitution Inflammatory Syndrome)*

Key words*: Leprosy ,HIV, IRIS, HAART, MDT*

I. Background

Leprosy, or Hansen disease (HD), is chronic infectious disease caused by Mycobacterium leprae which is associated with inflammation that may damage the skin and the peripheral nerves [1]

Although there is a declining trend in the global burden of leprosy, Leprosy remains an important public health problem in Southeast Asia, the Americas and Africa[2].There are fifteen countries in Asia and Africa which account for 94% of the global total of the new-case detection rate. India is one of the countries where 1,000 new cases of leprosy were reported during 2006.[3]

leprosy can manifest as immune reconstitution inflammatory syndrome (IRIS) in HIV-infected individuals[4]. The first case of leprosy-associated immune reconstitution disease was reported in 2003 for a Ugandan living in London, United Kingdom[5]. Later leprosy was described as a manifestation of IRIS in many instances [6,7].

In addition, India also has the third largest burden of HIV-infected individuals[8]. In spite of having a large burden of both leprosy and HIV, there are very few published reports of HIV-leprosy confection from India. Vinay et al. reported an incidence of leprosy in patients on HAART of 5.22 per 1000 person-years in Pune, India [9].

II. Case Report

A 43 year old male, HIV infected soldier with CD4 count of 32 cells/cmm started on HAART (ZLN) presented with a large anesthetic patch in Rt elbow and Lt sole with tingling sensation and numbness in inner area of Rt forearm. 8 months back he was detected HIV1 (Rapid/ELISA +ve) , was thoroughly evaluated and no opportunistic infections were detected at that time including any clinical evidence of leprosy .His CD4 count was 32 cells / cmm and was started on first line ART (Zidovudine 300 mg BD , Lamivudine 150 mg BD and Nevirapine 200 mg BD) along with OI s Porphylaxis of cotrimoxazole .

After 3 months of start of ART he was again reviewed at this centre and was doing well on ART with his CD4 count increased to 169 cells / cmm. During 8 th month of his HAART, he noticed anesthetic patch over the Rt elbow and Lt sole along with tingling sensations in Rt forearm

On examination there was large anaesthetic and hypopigmented patch with erythematous border over Rt elbow area (Fig 1) and similar patch in Lt sole (Fig 2). on detailed examination there was also a hypopigmented scaly plaque on Lt buttock (Fig 3). On peripheral nerve examination , Rt ulner nerve was found to be thickened . There was no any lymphadenopathy and other significant systemic finding. Routine haematological investigations , biochemistry and Imaging were within normal limit .This time CD4 again increased and reached to 293 cells /cmm. Slit skin smear for AFB was Negative ,Skin biopsy from anesthetic patch of Rt elbow , Lt sole and Lt buttock shows numerous well epitheloid granulomas with Langhan's giant

cells. The stroma shows mild lymphocytic infiltration. Features are of chronic granulomatous lesion consistent with Hansen's disease – tuberculoid type . Wade fite faraco stain shows no acid fast bacilli. He was diagnosed as a case of BT leprosy .In the background of HAART and rising CD4 it was considered as a case of IRIS (Immune Reconstitution Inflammatory Syndrome). .

The patient was started on WHO multi drug therapy (MDT) regime (Rifampicin: 600 mg once a month Dapsone: 100 mg daily Clofazimine: 300 mg once a month and 50 mg daily Duration= 12 months.) and ART switched from ZLN (Zidovudine 300 mg BD , Lamivudine 150 mg BD and Nevirapine 200 mg BD) to ZLE(Zidovudine 300 mg BD , Lamivudine 150 mg BD and Efavirenz 600 mg OD) . Patient responded well with MDT and HAART combination and presently doing well with symptomatic improvement as well as improvement in skin lesions .

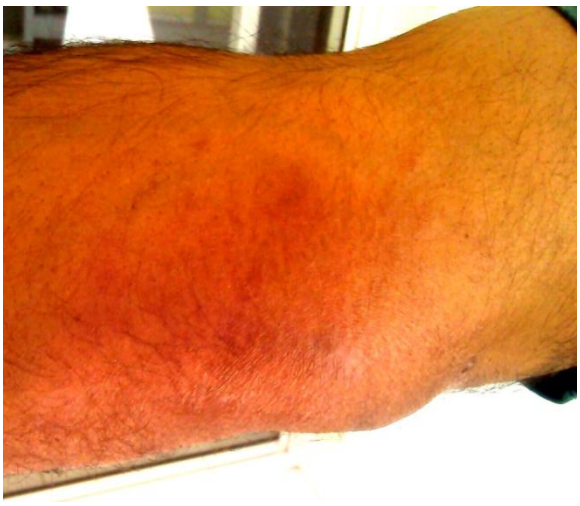

FIG 1

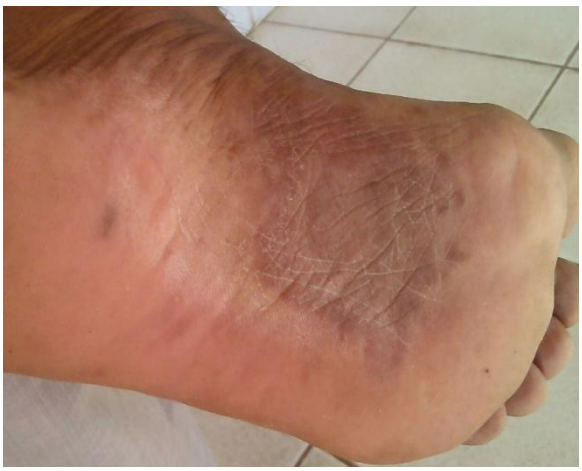

FIG-2

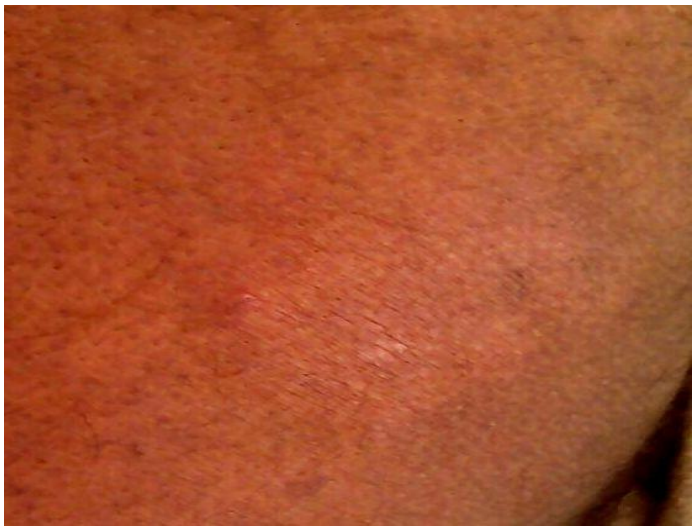

FIG-3

III. Discussion

IRIS is an unusual inflammatory reaction to an opportunistic infection that occurs in HIV positive patients with profound immunosuppression during the reconstitution of the immune system in the initial months of highly active antiretroviral treatment[10].

Patients with tuberculoid leprosy have good cell mediated immune response to M leprae, resulting in a few skin lesions, which histologically have well organized lymphocyte (CD68+, CD3+, CD8+, CD4+)- rich granulomas with predominantly CD4 T cells. In contrast, patients with LL have a strong humoral response but poor or absent cell medicated immunity, resulting in uncontrolled growth of the bacilli and disseminated skin lesions. Histologic examination of biopsies from their lesions reveals that the granulomas are comprised of macrophages and small numbers of CD8 T cells[11].

HIV affects cell-mediated immunity, and it was initially expected that, just as in M. tuberculosis infection, the decrease in CD4 cells would result in decreased capacity for mycobacterial containment and thus an increase in disseminated disease. But studies have shown that the HIV coinfected patients with low CD4 count had borderline tuberculoid lesions with well formed granuloma and normal CD4 cells numbers. In contrast, coinfected patients with LL lesions showed loose infiltrates comprised of macrophages and a small number of almost exclusively CD8 lymphocytes[12,13].

Since the introduction of highly active antiretroviral therapy (HAART) in the management of HIV, especially in regions endemic for leprosy, coinfected patients are also developing tuberculoid leprosy with active lesions, and ulceration of lesions is seen in leprosy type 1 reactions. Leprosy is being increasingly reported as part of the immune reconstitution inflammatory syndrome (IRIS).

IRIS is a paradox deterioration in clinical status after starting HAART, a deterioration that is attributable to the recovery or reactivation of someone's immune response to a latent or subclinical process.

The HAART regimes currently used increase production and redistribution of CD4+T cells and improve pathogen-specific immunity, both to HIV and other pathogens. While improved immunity to HIV is the required effect from HAART, improved immunity to other opportunistic pathogens or development of autoimmunity can result in IRIS. The prevalence of IRIS in cohort studies of HIV positive patients ranges from 3% to more than 50%, varying greatly with acquired immunodeficiency syndrome (AIDS)- defining illness affecting the patient at the start of HAART therapy[14].

Risk factors for the development of IRIS include advanced HIV disease with a CD4+ T cell count under 50 cells/mm, unrecognized opportunistic infection or high microbial burden, and the number and presence of prior opportunistic infections. HAART triggers overt clinical manifestations of coinfection with tuberculosis, cytomegalovirus, herpes zoster, C and B hepatitis virus, and now leprosy. Since 2003, 23 reports of patients developing leprosy as IRIS have been published [9,12-17]. A study involving 10 patients demonstrated that leprosy reaction is a manifestation of immune reconstitution[18]

The onset of immune reconstitution phenomena often occurs within 1 to 6 months of HAART, even prior to substantial increase in the blood CD4 + T lymphocyte count [19,20].

IV. Conclusion

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. Many more reports from India are now coming from different part of india [18,21].

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.

HIV infected individuals on ART from leprosy endemic countries should be regularly examined for cutaneous lesions and nerve thickness especially during the first two years of starting ART but cases may continue to occur even after 1 to 2 years of therapy It is also important to differentiate it from drug toxicity to avoid unnecessary cessation of HAART.

The prevalence of leprosy is falling in our country and many states reach elimination levels. We should not miss out on these patients as there prompt recognition and treatment is important for the community in general and patient in particular.

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