Interactions between leprosy and human immunodeficiency virus: More questions than answers

It has been well-documented that each of tuberculosis (TB) and human immunodeficiency virus (HIV) contributed in the progression of the other as well as their related poor treatment outcomes.[1] However, the interactions between leprosy and HIV have been little studied and poorly understood.[2,3] At the early phase of the HIV epidemic, it was hypothesized that HIV co-infection would undermine leprosy control. Indeed, it was anticipated that it would result in higher rates of lepromatous leprosy cases, faster decline in clinical state, drug-resistant leprosy and overall poor treatment outcomes. None of these however turned out to be the case and this has remained a paradox.[2,3] A number of questions have since remained unanswered regarding leprosy-HIV co-infection. One of such is if HIV infection increases the risk of developing leprosy. This has been difficult to answer largely because prospective studies have never been conducted and the long incubation period of leprosy makes this harder to conduct even in high burden settings.[3] Most published studies assessed the prevalence of HIV in cohorts of leprosy patients and found no significant differences in HIV-1 prevalence between cases and control groups.[2,3]

Another important issue is if HIV co-infection alters the clinical spectrum and features of leprosy. Most reports on the rates of tuberculoid versus lepromatous leprosy in HIV-infected versus HIV-negative patients demonstrate that the spectrum of the disease was not altered by the presence of HIV infection.[3-5] In terms of clinical features, both skin lesions and peripheral nerve damage are common presentations of leprosy. Data that indicate that skin lesions are substantially worse in HIV-infected leprosy patients are lacking.[4,5] Given that HIV itself is neuropathic, it has been forecasted that nerve lesions in HIV-infected leprosy patients will be worse-off, there are however no data that indicate that HIV infection worsens nerve damage.[2,3] A persisting observation in the pathogenesis of HIV co-infected leprosy patients with low-CD4+ T cell count is that the histological features of leprosy remains preserved—this indicates a relative preservation of the ability of HIV co-infected leprosy patients to form granuloma—and has been aptly called the granuloma paradox.[3]

Also, it has been documented that following treatment with both antiretroviral therapy and leprosy multidrug therapy, some lepromatous leprosy patients with HIV co-infection shifts to borderline tuberculoid leprosy—suggesting that in these patients, granuloma formation might be altered by an antiretroviral therapy—induced increase in the CD4+ T cell count.[3,6] This has been suggested to occur due to an improvement in immunity from immune reconstitution inflammatory response syndrome (IRIS).[3,6] Furthermore, the initiation of antiretroviral treatment have been reported to be associated with the activation of sub-clinical *M. leprae* infection—resulting in the manifestation of features of leprosy as a form of IRIS in itself,[7] or more commonly following treatment there is a reversal reaction due to a "switch on" of the cell-mediated immunity resulting in the clinical manifestations of IRIS in HIV-infected leprosy patients.[3]

In this issue of the journal, Yadav and colleagues report on a case of a HIV-infected leprosy patient who developed facial nerve palsy after 3 years on antiretroviral therapy.[8] The clinical presentation of this case suggested an unmasking IRIS where following improvements in the immunity with antiretroviral therapy; the patient's immune system was able to mount an immunological response probably by switching on the cell-mediated immunity resulting in varied clinical features and skin changes after the CD4 count substantially increased. Another important manifestation of this case is the occurrence of facial nerve palsy. Although, facial nerve palsy is a presenting feature of leprosy in HIV-negative persons,[9] its occurrence in HIV-infected leprosy patients have rarely been reported in the literature. However, HIV infection in this case suggests that it does not alter the occurrence of facial nerve palsy in leprosy cases. It will be interesting to compare the response to treatment of this case with other HIV-infected and HIV-negative leprosy patients especially their timing of response to therapy and improvement in clinical status.

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Surprisingly, more than three decades after the onset of HIV/AIDS pandemic the questions on its impact on the epidemiology, clinical presentation, histiopathogenesis and treatment of leprosy remain. However, the data so far has shown that unlike for TB, HIV has not contributed in the persisting burden of leprosy or delay in its elimination strategies.[3] Large epidemiological cohort studies are needed in settings with high prevalence of HIV and leprosy in order to document the detailed epidemiological and clinical associations of these diseases. Given the similarities in the etiologic agent of TB and leprosy, there is also need for studies using molecular techniques to investigate the clinical and immunological differences in interactions between HIV and leprosy on one hand and HIV and TB on the other hand. This may generate answers that will result in newer strategies to contain these diseases.

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