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Human Immunodeficiency Virus and Leprosy Coinfection in Pune, India▽

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We report eight cases and the incidence of leprosy in human immunodeficiency virus (HIV)-infected individuals after initiation of antiretroviral treatment (ART). The incidence of leprosy in patients on ART was 5.22 per 1,000 person-years (95% confidence interval, 2.25 to 10.28). This high incidence suggests that there should be regular examination of HIV-infected individuals for clinical signs of leprosy.

Although there is a declining trend in the global burden of leprosy, there are 15 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 (14). Human immunodeficiency virus (HIV) and leprosy both are feared due to the associated social stigma, and leprosy can manifest as immune reconstitution inflammatory syndrome (IRIS) in HIV-infected individuals (9). 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 (8, 10).

Antiretroviral treatment (ART) for HIV infection is now available in resource-poor regions where leprosy is still endemic, such as South America, Africa, and Asia, including India. India accounts for half of the world's leprosy cases due to its population of more than 1 billion, even though a nationwide prevalence of less than 1 case/10,000 population was reported in 2005 (4). In addition, India also has the third largest burden of HIV-infected individuals (12). In spite of having a large burden of both leprosy and HIV, there are very few published reports of HIV-leprosy coinfection from India. We report eight cases of incident leprosy in HIV-infected patients who were on ART and the incidence of leprosy in HIV-infected individuals on ART.

This report is from the Amrita Clinic of PRAYAS, a nongovernmental organization working on HIV/AIDS in Pune, in the state of Maharashtra, India. We retrospectively analyzed data on HIV-infected patients who initiated ART between January 2003 and December 2006 and we studied their follow-up till December 2007 to evaluate the incident cases of leprosy. ART was provided following the national guidelines for treatment of HIV infection (7).

Diagnosis of leprosy was based on the clinical signs and symptoms and demonstration of acid-fast bacilli in the slit skin smears by Ziehl-Neelsen staining. All patients with leprosy received multidrug treatment per the WHO guidelines (15).

Several definitions of IRIS have been utilized, each incorporating the general concept that cases of IRIS need to have an inflammatory component occurring in the setting of immune reconstitution that cannot be explained by drug toxicity or a new opportunistic infection (1, 6). We have considered leprosy manifestation after starting ART with increase in $CD4^+$ cell count, inflammatory response as seen by neuritis, type I or type II leprosy reaction, or need for the use of steroids for the control of inflammation as a criterion for defining leprosy manifestation as IRIS. Statistical analysis was done using STATA (version 8.0).

Between January 2003 and December 2006, among the 1,002 HIV-infected patients who started ART for HIV infection and were followed up till December 2007, eight incident cases of leprosy were detected. None of them had clinical evidence of leprosy at the time of initiation of ART. Table 1 describes the details of these eight patients. All the patients except for one were males, and the mean age of the patients with leprosy was 33.8 years (standard deviation [SD], 5.1 years; range, 27 to 42 years). Four patients had paucibacillary leprosy, and four patients had multibacillary leprosy. The mean $CD4^+$ cell count of incident leprosy cases was 326 (median, 245; SD, 255.5; range, 99 to 892). Of these eight patients, three had other opportunistic infections such as pulmonary tuberculosis, abdominal tuberculosis, and herpes zoster. The mean number of months to develop leprosy after starting ART was 13.8 months (SD, 14.3 months; range, 2 to 43 months). All eight patients completed their leprosy treatment and recovered completely. Although eight patients developed incident leprosy, six of them developed leprosy within 2 years of starting ART and two patients had delayed manifestations, with one patient developing leprosy after 28 months and the other after 43 months. These 1,002 patients on ART contributed to 1,532.5 person-years, and hence, the overall incidence of leprosy after starting ART was 5.22 per 1,000 person-years (95% confidence interval, 2.25 to 10.28).

To our knowledge, this is the first published report on the incidence of leprosy in HIV-infected patients on ART. ART is now more accessible in resource-poor regions where leprosy is still endemic, and reports of leprosy associated with immune reconstitution disease are increasing. This disease is most likely to be seen in India, where the HIV epidemic is growing and

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TABLE 1. Details of HIV-infected patients on ART with incident leprosy[a]

Patient no.	Age (yr)	Sex	Clinical presentation	Bacterial index	WHO classification	$CD4^+$ cell count (cells/mm^3) before HAART	$CD4^+$ cell count (cells/mm^3) 6 mo after HAART	% rise in $CD4^+$ cell count	$CD4^+$ cell count when leprosy was diagnosed	Time to onset of leprosy (mo)	Other associated opportunistic condition(s)
1	35	M	Hypoaesthetic patch and nodules, ENL	2+	MB	177	316	1.8	892	43	None
2	35	M	Multiple patches in reaction, neuritis	2+	MB	75	170	2.3	170	8	Pulmonary tuberculosis, pericardial effusion
3	40	F	Hypoaesthetic patch, neuritis	0	PB	85	251	3.0	251	6	None
4	31	M	Nodules, ENL	3+	MB	99	338	3.4	99	2	Diarrhea
5	31	M	Nodules	3+	MB	124	239	1.9	239	28	None
6	30	M	Hypoaesthetic patch, ENL, neuritis	0	PB	31	215	6.9	144	4	Abdominal tuberculosis
7	42	M	Hypoaesthetic patch	0	PB	331	548	4.0	374[b]	16	None
8	27	M	Hypoaesthetic patch with inflammation	0	PB	174	436	2.5	436	5	Herpes zoster

[a] Abbreviations: M, male; F, female; ENL, erythema nodosum leprosum; PB, paucibacillary; MB, multibacillary; HAART, highly active ART.
[b] Percent CD4 cell count was similar to what was seen at 6 months.

where 161,457 new cases of leprosy were diagnosed in 2005 alone (2). Vigilance needs to be especially high during the first several months of therapy, when the incidences of IRIS peaks, but cases continue to occur even after 1 or 2 years of therapy. Leprosy may not always manifest as IRIS, and there are a few reports of leprosy-HIV coinfection among patients who were not receiving ART (11). Difficulty in defining IRIS has been reported elsewhere (13), and we have faced similar difficulty in labeling two cases of leprosy as IRIS that developed at 28 and 43 months, respectively, after initiating ART. It is not clear if it was due to immune reconstitution or new infection, and prospective well-planned studies with longer follow-up will help in identifying the longest interval to development of IRIS.

Our report shows a high incidence of leprosy in HIV-infected individuals after initiation of ART. In the same state of Maharashtra, in the general population, the National Leprosy Elimination Programme reported a total of 12,397 new cases of leprosy and the new case detection rate was 11.12 per 100,000 with the prevalence being 0.71 per 10,000 population (3).

To conclude, with the availability of ART in developing countries, more and more incident leprosy cases are likely to be seen in areas where leprosy is endemic and HIV is also highly prevalent. HIV-infected individuals on ART from countries where leprosy is endemic should be regularly examined for cutaneous lesions and nerve thickness, especially during the first 2 years of starting ART, but cases may continue to occur even after 1 to 2 years of therapy.

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