Editorials

Leprosy after starting antiretroviral treatment

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Stephen D Lawn, Wellcome Trust research fellow in clinical tropical medicine (stevelawn@yahoo.co.uk)[1], **Diana N J Lockwood, professor of tropical medicine**[2]

Author affiliations

An increasingly reported clinical problem but not a serious public health risk

Recent media reports have highlighted a “startling and worrisome new link” between antiretroviral treatment and leprosy.**1** Some people infected with HIV who have started such treatment in countries where leprosy is endemic have developed florid leprosy lesions in the initial months of treatment. What underlies these unusual manifestations and do they have implications for the control of leprosy?

The note of alarm is understandable—leprosy and HIV are both greatly feared diseases. The manifestations described, however, are a well recognised complication of antiretroviral treatment known as immune reconstitution disease or immune reconstitution inflammatory syndrome (IRIS).**2** This presents with the manifestation (or “unmasking”) of a previously subclinical coinfection or the deterioration of an opportunistic infection that had been responding to treatment. These effects are due to antiretroviral treatment causing the rapid recovery of cell mediated immune responses, which trigger host immune responses to foreign antigen. Such reactions typically occur during the first four months of treatment—the most rapid phase of immune recovery.

The HIV pandemic has had surprisingly little effect on the epidemiology and clinical features of leprosy.**3** However, immune reconstitution disease is a new and unexpected clinical interaction between these diseases in patients who have just started treatment. The first published case of leprosy associated immune reconstitution disease occurred in 2003 in a Ugandan living in London.**4** More cases have been described since, mostly in patients living in South America.**3 5 6** In most cases, immune reconstitution disease triggered the initial presentation of leprosy, often with a reactional state—acute inflammation within the leprosy lesions that may result in rapid loss of nerve function. Some reactions have been unusually severe with skin ulceration, protracted cutaneous inflammation, and neuropathy.**3 4 5 6**

Antiretroviral treatment has been available since 1996 in countries with high average incomes. Immune reconstitution disease has been well characterised in this setting and is associated with a predictable range of opportunistic infections.**2** Antiretroviral treatment is increasingly being used in resource poor countries where different coinfections exist; which of these infections have the potential to be associated with immune reconstitution disease is not yet clear. Immune reconstitution disease has, for example,

recently been described in association with the parasitic infections leishmaniasis, strongyloidiasis, and schistosomiasis.[7] Many of these cases were in immigrants receiving antiretroviral treatment in countries with higher incomes. Leprosy has joined this growing list of tropical infections associated with immune reconstitution disease.[4 5 6 7]

Antiretroviral treatment is now more accessible in resource poor countries where leprosy is still endemic, such as South America, India, and Africa; not surprisingly, reports of leprosy associated with immune reconstitution disease are increasing.[1] This disease is most likely to be seen in India, where the HIV epidemic is growing and where 161 457 new cases of leprosy were diagnosed in 2005 alone.[8] From the patient's perspective, HIV infection and leprosy are both highly stigmatising diseases, and having both is understandably distressing. This distress may be heightened by the patient's perception that the leprosy was caused by the antiretroviral drugs. Frequent cases of this disease could make patients less enthusiastic about antiretroviral treatment programmes. Importantly, some lesions seen in leprosy associated with immune reconstitution disease are unusually florid, and severe neuropathy triggered during antiretroviral treatment might lead to permanent disability.

Medical staff who provide antiretroviral treatment to patients in (or originating from) countries where leprosy is endemic need to be aware that leprosy may present as immune reconstitution disease. The diagnosis of leprosy is often missed or delayed in immunocompetent people, and the likelihood of diagnostic confusion and delay is even greater in patients infected with HIV who start antiretroviral treatment. Immune reconstitution disease should be considered in patients who present during the initial months of antiretroviral treatment with erythematous and oedematous skin lesions or loss of peripheral nerve function (as shown by anaesthesia or muscle weakness). Missed or delayed diagnoses may lead to the development of permanent disability. The clinical spectrum of manifestations needs to be defined, and surveillance is needed to determine the frequency of leprosy associated with immune reconstitution disease. A key question is how best to manage reactional states triggered by antiretroviral treatment because immunosuppressant therapy in patients with HIV may have greater risks than in patients without HIV. Prolonged and robust immunosuppressive therapy may nevertheless be necessary in some cases.[4]

From a public health perspective, we have less cause for alarm. Leprosy presenting as immune reconstitution disease represents the manifestation of previously subclinical disease and not the development of new infections. Increased numbers of leprosy diagnoses due to immune reconstitution disease therefore do not indicate a deterioration in leprosy control. Moreover, such disease usually manifests itself with the non-infectious borderline forms of the disease.[3] These cases are unlikely to pose a risk of infection to people in antiretroviral treatment clinics or in the community. Furthermore, whereas immune reconstitution disease associated with tuberculosis or cryptococcal meningitis has an appreciable risk of mortality,[9 10] disease associated with leprosy is not life threatening.

These facts need to be put into perspective. Immune reconstitution disease associated with leprosy has been reported in a relatively small, albeit increasing, number of patients. Meanwhile, it is estimated that in 2005 alone between 250 000 and 350 000 deaths were prevented by antiretroviral treatment in low and middle income countries.[11] Antiretroviral treatment will continue to save hundreds of thousands of lives each year, but unusual manifestations of immune recovery including leprosy will inevitably occur.

Footnotes

- **Competing interests:** None declared.

- **Provenance and peer review:** Commissioned, externally peer reviewed.

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