CASE REPORT

Leprosy and HIV co-infection in five patients

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Summary In a retrospective study, five patients are reported who suffered from a Mycobacterium leprae/HIV co-infection and were treated for their HIV infection with HAART. In four patients, this revealed their leprosy and induced a type I leprosy reaction. Two patients who were lepromin negative at diagnosis were retested after about 1 year of anti-retroviral treatment, and found to be positive.

Introduction

The clinical course and therapeutic response of a Mycobacterium leprae and HIV co-infection have been the subject of some debate. Most reports suggest that HIV immunodeficiency has little influence on the evolution of leprosy as a disease.1–3 In an immunological and immunopathological study on 12 leprosy patients, Nery et al.4 concluded that an HIV co-infection did not seem to change the natural course of the disease, or cause difficulties in diagnosis and treatment. Lucas5 considered that leprosy was a missed disease in AIDS. Naafs6 proposed that the HIV epidemic could lead to an increase in the number of leprosy patients among the HIV-uninfected population. HIV patients concomitantly infected with leprosy may not show any sign of that disease, due to diminished cell-mediated immunity (CMI), but could well be a source of infection to the healthy community.

Since most clinical signs of leprosy are CMI dependent, it has been postulated that when HIV infected patients with a latent leprosy infection received anti-retroviral treatment (HAART) and their immune system recovered, M. leprae antigens would be recognized and

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clinical disease would develop.6 Opromolla et al. reported an HIV infected leprosy patient who developed a type I reaction after the start of retroviral therapy.7 A similar patient was discussed at the AIDS symposium in Durban, South Africa.8 At the 16th International Leprosy Congress in Salvador, Bahia, Brazil, a number of patients with both leprosy and HIV infection were reported.9–13 Recent publications mention borderline tuberculoid leprosy as a reconstitution phenomenon14 and increased inflammation of leprosy lesions after initiation of HAART.15

In Brazil, both AIDS and leprosy are highly endemic and considered to be important public health problems.16 The present study reports five patients with an M. leprae/HIV co-infection diagnosed at the Division of Hansenology and Sanitary Dermatology (DHDS) in Sao Paulo.

Methods and results

Manual searching from the archives of the DHDS revealed five patients who were co-infected with HIV when leprosy was diagnosed and were receiving HAART treatment, four of them more than 1 month before their leprosy was diagnosed. The data on their HIV infection were extracted from the medical reports in the reference centres for AIDS.

The data from the patients concerning leprosy, HIV treatment and disease progression during treatment are presented in Table 1.

Four of the patients were women. Three patients were in their 50s when leprosy was diagnosed, two were in their 30s. All presented with a history of skin lesions with loss of sensation for at least 6 months. Four patients were clinically and histologically borderline leprosy (BT: 1, BB: 2, BL: 1), one patient was classified indeterminate according to the Ridley–Jopling classification. In all five patients, Fite-Faraco (FF) histological staining was positive for acid-fast bacilli; two also had a positive Ziehl-Neelsen (ZN) stained smear.

One patient showed signs of a type I leprosy reaction at diagnosis of leprosy, having received 2 months of anti-retroviral therapy. Two developed a reaction when on leprosy treatment, after 10 months and 14 months, respectively, of anti-retroviral therapy. One developed neuritis, most likely a type I leprosy reaction, 6 months after leprosy therapy was discontinued, while still on HAART.

The lepromin Mitsuda reaction was positive in one patient at diagnosis and negative in three; in one, it was initially not performed, but it was positive at the 7th month. Mitsuda became positive in two patients retested, in one (912) when she was re-tested after 10 months of anti-retroviral and leprosy treatment, in the other (960) after 12 months of anti-leprosy and 14 months anti-retroviral treatment when she was retested after developing a type I reaction, and the histopathology showed BT features.

Two patients received WHO-MDT for their leprosy. Three patients received an alternative treatment, because it was believed that an interaction between rifampicine and antiretrovirals could lead to adverse reactions.

All patients showed clinical, histological and bacteriological regression at the time of discontinuation of leprosy treatment.

Discussion

The first patient with an M. leprae/HIV co-infection at the Division, the reference centre for leprosy in Greater Sao Paulo, was diagnosed in 1987. The patient had lepromatous leprosy,
Table 1. Data on five patients with leprosy and HIV co-infection. ZN = Ziehl-Neelsen (smear) and FF = Fite-Faraco (histopathological) *M. leprae* stains, diag = time of diagnosis of Hansen’s disease, dose = Hansen’s disease treatment dose, – = not recorded.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Clinical</th>
<th>Histo-pathology</th>
<th>Bacteriology ZN</th>
<th>FF</th>
<th>Mitsuda reaction</th>
<th>Treatment monthly dose</th>
<th>Type I reaction</th>
<th>Associated disease</th>
<th>Treatment month</th>
<th>CD4</th>
<th>Viral load</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>29</td>
<td>BB</td>
<td>BB</td>
<td>+++</td>
<td>++</td>
<td>+++ diag</td>
<td>9th ofloxacin, clofazimine, dapsone</td>
<td>6th diag, 10th dose</td>
<td>–</td>
<td>–</td>
<td>6th month, zidovudine, didanosine, indinavir</td>
<td>87 diag</td>
</tr>
<tr>
<td>F</td>
<td>27</td>
<td>BB</td>
<td>BL</td>
<td>–</td>
<td>+++</td>
<td>– diag</td>
<td>17th rifampicin, clofazimine, dapsone</td>
<td>Neuritis, 6th month after discharge</td>
<td>–</td>
<td>Hepatitis</td>
<td>1st month, zidovudine, didanosine, indinavir</td>
<td>417, 4 years after discharge</td>
</tr>
<tr>
<td>F</td>
<td>40</td>
<td>BT</td>
<td>BT</td>
<td>–</td>
<td>+</td>
<td>– diag +10th dose, 10th month</td>
<td>3rd rifampicin, clofazimine, dapsone +; 9th ofloxacin, clofazimine, dapsone</td>
<td>–</td>
<td>Pneumonia, syphilis</td>
<td>1st month, zidovudine, lamivudine, abacavir</td>
<td>223 diag, 436, 6th dose</td>
<td>23.000 diag, &lt;50 6th dose</td>
</tr>
<tr>
<td>M</td>
<td>44</td>
<td>BT</td>
<td>BB</td>
<td>+</td>
<td>+ nerve</td>
<td>+7th dose</td>
<td>13th rifampicin, clofazimine, dapsone</td>
<td>Diag, 3rd dose Pulmonary tuberculosis</td>
<td>2nd month, zidovudine, lamivudine, efavirenz</td>
<td>291, 7th dose</td>
<td>Not detected, 7th dose</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>49</td>
<td>I</td>
<td>Non-specific</td>
<td>–</td>
<td>+ nerve</td>
<td>Diag ++++, 12th dose, 14th month</td>
<td>2nd rifampicin, clofazimine, dapsone +; 17th rifampicin, ofloxacin, minocycline</td>
<td>12th dose Catsarrhal bronchitis</td>
<td>2nd month, zidovudine, didanosine, sulfame-taxazol</td>
<td>430 diag</td>
<td>&lt;400 diag</td>
<td></td>
</tr>
</tbody>
</table>
and is not reported in this study. Since that time, five more co-infected patients have been diagnosed. These patients are reported in this study.

The fact that all of them had a history of skin lesions with loss of sensation at least 6 months before the time of diagnosis suggested that they had been infected with *M. leprae* several years before. It seems likely that the immunological changes caused by the HIV infection and the HAART triggered new manifestations that brought the patients for diagnosis.

Two patients with a negative Mitsuda at diagnosis were found to have converted when tested 10 and 14 months, respectively, into retroviral treatment, by which time the HAART would have led to a fall in viral load and immunological recovery. This recovery may have led to a type I reaction in four patients, in one of whom the histopathology also changed from I to BT and in another who developed neuritis 13 months after the start of antiretroviral treatment. Naafts had previously postulated that this could happen. The observations are similar to those reported by Opromolla et al., Lawn et al., and Pignataro et al.

The histories of these five patients suggest that in HIV infected patients, leprosy is diagnosed when new signs (reactions) developed during recovery of the CMI.

Leprosy reactions may be triggered: 1) by an instable immune system early in the development of HIV immunosuppression, 2) by introduction of treatment for AIDS-associated diseases such as tuberculosis (drugs like rifampicin, which kill *M. leprae*, may expose antigenic determinants with an immunological reaction as a result), and 3) as suggested by our data, by the introduction of antiretrovirals.

Health authorities and health workers in countries in which leprosy and HIV infections are endemic should be aware that a latent leprosy infection can be present in an HIV infected patient, and that this infection can be revealed when HAART is introduced. Moreover, that an immunological reaction may occur leading to loss of nerve function.

In the absence of information on the optimum duration of treatment or the value of chemoprophylaxis, we suggest that HIV/leprosy co-infected patients should be treated with standard MDT together with the HAART. Standard MDT seems sufficient. Despite the relatively small number of reported cases with double infections, it would be interesting to cross check epidemiological databases for leprosy and AIDS in order to gain a better understanding of this joint infection. However, this should be discussed with local ethical committees.

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