CLINICAL CASE REPORT: DENGUE HEMORRHAGIC FEVER IN A PATIENT WITH ACQUIRED IMMUNEDEFICIENCY SYNDROME

WELLINGTON DA SILVA MENDES,* MARIA DOS REMÉDIOS FREITAS CARVALHO BRANCO, AND MARIA NILZA LIMA MEDEIROS
Pathology Department, Federal University of Maranhao, Sao Luis, Maranhao, Brazil; Municipal Health Secretary of Sao Luis, Sao Luis, Maranhao, Brazil

Abstract. A person diagnosed with acquired immunodeficiency syndrome in 2000 and who received highly active antiretroviral therapy developed co-infection with dengue virus in 2003. In the course of the co-infection, he developed fever, thrombocytopenia (13,700 cells/mm³), petechia, and hypoalbuminemia, which are compatible with the World Health Organization criteria for a case of dengue hemorrhagic fever. Human immunodeficiency virus was not detected 30 days before co-infection and 10 days afterwards. His CD4 cell count did not show significant alterations in the two periods evaluated. He continued his course of treatment without arterial hypotension, serious hemorrhage, or other life-threatening complications.

INTRODUCTION

The association between human immunodeficiency virus (HIV) infection and endemic diseases has been frequently described, especially, in regions with a tropical climate. Tropical diseases have a relevant pathogenicity and can cause illness irrespective of the immunity of the HIV-seropositive person. In many circumstances, co-infection causes a modification of the natural history of the tropical pathology, frequently with aggravation of its clinical form, as observed in cases of malaria, leishmaniasis, and Chagas’ disease. Sao Luis, the capital of Maranhao State in northeastern Brazil, has had successive dengue epidemics that involved dengue virus serotypes DEN-1, DEN-2, and DEN-3. In 2003 and 2004, there were 555 confirmed cases of dengue in this city and 7 fulfilled the World Health Organization (WHO) criteria for dengue hemorrhagic fever (DHF). We report a case of DHF in a person with acquired immunodeficiency syndrome (AIDS) who received antiretroviral therapy.

CASE REPORT

On May 23, 2003, a 56-year-old man sought treatment at the Unidade de Diagnóstico por Imagem Hospital (a tertiary hospital within the municipal district of Sao Luis). He reported high fever, headache, myalgia, arthralgia, retro-orbital pain, and nausea that began two days earlier. He came to the hospital with an axillary temperature of 39°C and petechia in the lower limbs. His total leukocyte count decreased from 232,000 to 13,700 cells/mm³, and his lymphocyte count decreased from 2,590 to 946 cells/mm³. His hematocrit ranged between 38% and 45.1%. Serum albumin levels decreased from 4.9 to 3.1 g/dL. He remained in the hospital for five days and had a fever for three days. His only hemorrhagic manifestation was petechia in the lower limbs. Vascular leak syndrome was indicated by significant hypoalbuminemia and a 16% variation in hematocrit values. Dengue-specific IgM was detected by an antibody capture enzyme-linked immunosorbent assay seven days after the onset of symptoms.

The patient was infected with HIV-1 subtype B, which was diagnosed 39 months earlier during hospitalization for disseminated tuberculosis. At that time, his CD4 cell count (measured by flow cytometry) was 266 cells/mm³, but virus was not detected. He was classified as having an HIV Category C2 infection according to the revised classification system for HIV infection and expanded AIDS surveillance case definition for adolescents and adults (Centers for Disease Control and Prevention, Atlanta, GA).

He had begun antiretroviral therapy with zidovudine, lamivudine, and efavirenz. Because of the development of serious anemia, zidovudine was substituted for stavudine. He was asymptomatic at a checkup 30 days before onset of the dengue symptoms. At that time, he was taking stavudine, lamivudine, and efavirenz and had a CD4 cell count of 412 cells/mm³, but virus was not detected by a polymerase chain reaction technique with a detection limit of 400 copies/mL. Ten days after the onset of the dengue symptoms, he had a CD4 cell count of 466 cells/mm³, but virus was not detected.

DISCUSSION

Little has been published on co-infection with HIV and dengue virus. Our patient showed five criteria for defining a case of DHF, according to WHO guidelines (fever < 7 days with myalgia, arthralgia, and headache; thrombocytopenia less than 100,000 cells/mm³; hypoproteinemia compatible with plasma leakage; hemorrhagic manifestations in the skin; and laboratory confirmation with identification of IgM antibodies against dengue virus). He did not have arterial hypotension, serious hemorrhage, or other life-threatening complications. His CD4 cell count showed a slight alteration 30 days before he developed dengue compared with that 10 days after co-infection. However, this evaluation was not conducted at the most critical time of lymphopenia when the total lymphocyte count was 946 cells/mm³. It is unlikely that the CD4 cell count was stable at that time (Table 1). Virus was not detected 10 days after the onset of dengue symptoms or 30 days before onset of the dengue. However, whether antiretroviral therapy could have had a protective effect against the increase in HIV virus was not determined. It has been
suggested this protection may be caused by protease inhibitors that blocked certain pro-inflammatory cytokines. It is uncertain if the risk of DHF would be the same, greater, or lower in AIDS patients. Although DHF seems to be immunologically mediated, it is more closely related to heterologous immunity than to cell mediated immunity. In our case, the patient did not have marked immunosuppression when he developed DHF (his CD4 count was greater than 400 cells/μm³), which would suggest that slightly immunocompromised AIDS patients would have the same risk of developing DHF as immunocompetent persons.

The incidence of co-infections with HIV and so-called tropical diseases is frequent and the impact of one on the other can be significant. Severe forms of meningoencephalitis associated with reactivation of infection with Trypanosoma cruzi have been observed in HIV patients with low CD4 cell counts. Atypical clinical presentations of leishmaniasis, such as visceral leishmaniasis with a chronic course and frequent relapses and cutaneous leishmaniasis with an uncommon location, have been described in association with elevations of viral load with HIV.

Studies have demonstrated that co-infection of HIV with acute infections can lead to cellular activation, resulting in a significantly increased viral replication of HIV. An increase in Plasma virus associated with acute co-infections has also been observed in individuals receiving antiretroviral therapy, although without significant alterations in the CD4 cell count. In these individuals, levels of HIV returned to levels before co-infection within 2–4 weeks.

It has not been determined if dengue virus has no effect on or reduces the amount of HIV. One study reported a case with a transitory reduction in HIV during co-infection with dengue virus and demonstrated that samples of serum from patients in the acute phase of dengue are capable of inhibiting the infectivity in vitro of HIV-1. A reduction in HIV-1 was associated with scrub typhus co-infection in HIV-infected subjects and included a transitory decrease below the limit of detection.

Ten HIV-1-infected subjects who were not taking antiretroviral drugs received plasma from donors with mild scrub typhus. The median viral load was reduced for eight weeks in seven recipients. In two recipients, a three-fold or greater reduction in copy number was observed. A reduction in HIV has also been demonstrated during co-infection with measles. A transient suppression of HIV replication early during the course of measles was observed in the 33 co-infected children at the time when levels of several plasma markers of immune activation were elevated.

The potential effects of infection with HIV on dengue manifestations have yet to be determined. Conversely, if dengue has an inhibitory effect on viral load of HIV, the nature of this effect remains known.

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Authors’ addresses: Wellington da Silva Mendes, Rua Mitra, 11, Quadra 31, Apartamento 1402, Edificio Costa Marina, Renascença II, CEP 65075-770, Sao Luis, Maranhao, Brazil, Telephone: 55-98-3227-4750, Fax: 55-98-3235-7477, E-mail: w.mendes@elo.com.br. Maria dos Remédios Freitas Carvalho Branco, Rua Baranga, 107, Bloco Ómega, Apartamento 203, Vinhais II, CEP 65074-193, Sao Luis, Maranhao, Brazil. Maria Nilza Lima Medeiros, Rua 98, Quadra 68, Casa 6, Vinhais, CEP 65074-690, Sao Luis, Maranhao, Brazil.

REFERENCES


### Table 1

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<tr>
<th>Date</th>
<th>Total leukocytes (cells/mm³)</th>
<th>Total lymphocytes (cells/mm³)</th>
<th>CD4 No. (%) (cells/mm³)</th>
<th>Viral load</th>
<th>Hematocrit (%)</th>
<th>Serum albumin (g/dL)</th>
<th>Platelets (cells/mm³)</th>
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<td>6,500</td>
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