

Case Report

Dual infection with dengue virus 3 and human immunodeficiency virus 1 in Havana, Cuba

Daniel Gonzalez¹, Daniel Limonta², Juan Francisco Bandera¹, Jorge Perez¹, Gustavo Kouri², Maria G. Guzman²

¹Department of Medicine, Pedro Kouri Tropical Medicine Institute

²Virology Department, Pedro Kouri Tropical Medicine Institute

Abstract

Although dengue virus (DEN) endemic regions overlap with human immunodeficiency virus 1 (HIV) high incidence areas, little has been documented on HIV and DEN mixed infection. Here we report DEN/HIV concurrent infections recorded during the DEN-3 epidemic in 2001-2002 in Havana. Serologic-confirmed DEN is described in two HIV-infected subjects with dengue fever symptoms. Although patients had dengue disease, the CD4+ cells remained within normal levels and no accelerated progression of HIV disease was observed. To our knowledge, DEN cases caused by DEN-3 in HIV-infected individuals have not been reported previously. Further research is needed to diagnose this likely underreported mixed viral infection in DEN endemic areas.

Key words: dengue, HIV, coinfection, concurrent, dual, Cuba

J Infect Dev Ctries 2009; 3(4):318-320.

Received December 15 2008 – Accepted February 25 2009

Copyright © 2009 Gonzalez *et al.* This is an open-access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Dengue is caused by four closely related viruses (DEN-1 to -4) within the *Flaviviridae* family and is found in the tropical/subtropical areas of the world. Classical dengue illness, dengue fever (DF), is self-limited and involves fever, headache, myalgia, arthralgia, and rash. However, the severe form, dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS) can be life-threatening [1]. Human immunodeficiency virus 1 (HIV), which belongs to the *Retroviridae* family, is a human retrovirus that causes the acquired immune deficiency syndrome (AIDS) pandemic. Frequently the natural history of HIV infection includes a long period of latency followed by the development of opportunistic complications [2].

From June 2001 to March 2002, a dengue epidemic caused by a DEN-3 was reported in Cuba. There were 14,524 cases confirmed serologically in the country with most of them in Havana city (88,7%). Eighty-one DHF/DSS cases were recorded during the epidemic [3].

Here, we report the two DEN/HIV concurrent infections, after informed consent was obtained, that were recorded during the epidemic.

Case Report

Two male subjects were admitted during the DEN-3 epidemic at the Pedro Kouri Tropical Medicine Institute. Neither patient had a history of recent travel. Fever, malaise, headache, arthralgia, and myalgia were reported in both cases. No hemorrhagic manifestations, abdominal pain, or shock signs were found (Table 1). Their medical history comprised an asymptomatic HIV-1 infection (confirmed by Western Blot tests) during ten years (patient A) and four years (patient B), and CD4+ T cell counts were within normal limits.

White blood cells (WBC) counts showed neutropenia in both cases, lymphocytosis in patient A and leukopenia in patient B. Platelets counts were normal. In both patients, transaminases were slightly elevated and immunoglobulin M (IgM) against DEN was detected through an IgM antibody-capture enzyme-linked immunosorbent assay (MAC-ELISA).

Both patients remained asymptomatic after discharge. Two weeks after the WBC counts, liver function tests of patient A were normal. Four months later, patient A's CD4+ T cell count was 29% (899 cells/mm³) and considered normal over the next 5

Table 1 Clinical and laboratory data of patients coinfecting with DEN-3 and HIV

Patients	Age/Sex	Clinical symptoms	WBC count (cells X 10 ⁹ /L)/ differential	Platelets (cells X 10 ⁹ /L)	Days of illness	CD4+ T cell count (cells X mm ³)
A	32/M	Fever, malaise, headache, arthralgia, myalgia, vomits, diarrhea	7.0 (17% neutrophils, and 72% lymphocytes)	190	6	730 ^a
B	24/M	Fever, malaise, headache, arthralgia, myalgia	4.3 (18.4 % neutrophils, and 24 % lymphocytes)	209	3	396 ^b

WBC: white blood cells.

^a 9 months previous to dengue illness.^b 75 days previous to dengue illness.

years. Patient B showed normal CD4+ T cell counts 22 months after dengue illness (12%-369 cells/mm³) which persisted for three years afterwards. Both individuals, A and B, classified as AIDS patients after five and three years, respectively.

Discussion

Dengue is the most widely spread arthropod-borne virus [1] and HIV has caused an astonishing pandemic [2]; nevertheless, only three studies have documented HIV and DEN mixed infection [4-6]. Here, we report two HIV-infected subjects with DF. DEN infection was confirmed by the specific IgM detection. No hemoconcentration, hemorrhage, or thrombocytopenia were recorded to fulfill the DHF case definition according to the World Health Organization (WHO). However, hematological and liver test abnormalities described often in DF were found [1].

This report presents the two DEN/HIV concurrent infections that were recorded during the Cuban DEN-3 epidemic in 2001-2002. It is probable that HIV and DEN-3 coinfections were not found more frequently because of the low HIV prevalence in our population [7].

Interestingly, although acute viral diseases may cause accelerated progression of HIV disease [2], we did not observe this event in the HIV-infected subjects studied after they suffered from dengue illness (DF). In this context, Watt *et al.* showed previously that HIV load was transiently reduced during DF caused by DEN-1 in an HIV case from Thailand and that DF acute phase serum (DEN-1) from an uninfected HIV individual suppressed HIV infectivity *in vitro* [5]. Similarly, a very recent and interesting study showed DEN-2 NS5 protein inhibits HIV replication in CD4+ T cells expressing this viral protein *in vitro* [8]. Additionally, in another recent work, five HIV patients treated with Highly Active Antiretroviral Therapy (HAART) had an uncomplicated DF course [6].

However, taken into account the lack of evidence on DEN/HIV coinfection [4-6] and *in vitro* work [5, 8], it is not possible to assure that DEN/HIV coinfecting individuals are not at increased risk of HIV/AIDS disease acceleration.

Three previous reports have documented DEN/HIV coinfections [4-6]: in a Thai HIV patient with DF caused by DEN-1 [5]; in a Brazilian AIDS patient suffering from DHF in which the DEN serotype was not determined [4]; and in five Singaporean HIV patients with either positive dengue

serology (MAC-ELISA) or positive generic dengue (not DEN serotype specific) reverse-transcriptase polymerase chain reaction (RT-PCR) [6]. However, our DEN/HIV coinfection cases were caused by DEN-3. As far as we know, DEN-3 disease in HIV-infected individuals has not been reported previously.

Although a recent study in South India showed lack of evidence of HIV infection in 34 individuals with anti-DENV IgM [9], it is possible DEN/HIV coinfections might be underappreciated if we take into consideration that endemic DEN regions [1] overlap with HIV high incidence areas [2].

In summary, we report two cases of DEN/HIV concurrent infections caused by DEN-3. No DHF/DSS or accelerated progression of HIV disease was observed. Further effort is needed to diagnose this likely underreported coinfection in DEN endemic areas. Additional research might also elucidate possible immunopathological interactions between DEN and HIV and their implications in the dual infection outcome.

Acknowledgements

We are grateful to the Department of Medicine from the IPK hospital for providing the clinical data.

References

1. Guzman MG, Kouri G (2002) Dengue: an update. *Lancet Infect Dis* 2:33-42.
2. Simon V, Ho DD, Abdool Karim Q (2006) HIV/AIDS epidemiology, pathogenesis, prevention, and treatment. *Lancet* 368:489-504.
3. Gonzalez D, Castro OE, Kouri G, Perez J, Martinez E, Vazquez S, Rosario D, Cancio R, Guzman MG (2005) Classical dengue hemorrhagic fever resulting from two dengue infections spaced 20 years or more apart: Havana, Dengue 3 epidemic, 2001-2002. *Int J Infect Dis* 9:280-285.
4. Mendes Wda S, Branco Mdos R, Medeiros MN (2006) Clinical case report: Dengue hemorrhagic fever in a patient with acquired immunodeficiency syndrome. *Am J Trop Med Hyg* 74:905-907.
5. Watt G, Kantipong P, Jongsakul K (2003) Decrease in human immunodeficiency virus type 1 load during acute dengue fever. *Clin Infect Dis* 36:1067-1069.
6. Siong WC, Ching TH, Jong GC, Pang CS, Vernon LJ, Sin LY (2008) Dengue infections in HIV patients. *Southeast Asian J Trop Med Public Health* 39:260-265.
7. de Arazoza H, Joanes J, Lounes R, Legeai C, Clemencón S, Perez J, Auvert B (2007) The HIV/AIDS epidemic in Cuba: description and tentative explanation of its low HIV prevalence. *BMC Infect Dis* 7:130.
8. McLinden JH, Stapleton JT, Chang Q, Xiang J (2008) Expression of the dengue virus type 2 NS5 protein in a CD4(+) T cell line inhibits HIV replication. *J Infect Dis* 198:860-863.
9. Goyal S, Kannangai R, Abraham AM, Ebenezer DL, Sridharan G (2007) Lack of increased frequency of human immunodeficiency virus infection in individuals with dengue-like illness in South India. *Indian J Med Microbiol* 25:300-301.

Informed Consent

Informed consent was obtained from patient B and the next of kin of patient A for publication of this case report.

Corresponding Author

Prof. Maria G. Guzman
 Head of Virology Department, Pedro Kouri Tropical Medicine Institute (IPK), and Head of PAHO/WHO Collaborating Center for the Study of Dengue and its Vector
 P.O. Box 601, Marianao 13, Havana, Cuba
 Tel. 537-2020450, Fax: 537-2046051,
 Email: lupe@ipk.sld.cu

Conflict of interest: No conflict of interest is declared.