An unusual presentation of human immunodeficiency virus and dengue coinfection

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ABSTRACT

The global incidence of dengue has grown dramatically in recent decades, with around half of the world's population currently at risk. Despite an overlapping epidemiology, limited data are available on human immunodeficiency virus (HIV) and dengue coinfection. Some reported evidence suggests that the patients with HIV infection are more at risk of a severe dengue outcome, while other reports suggest a transitory inhibition of the HIV-1 viral load, as well as a benign clinical progression of dengue. Our case is of a 44-year-old HIV-infected obese gentleman with typical features of dengue infection. He was closely monitored and his clinical profile was thoroughly studied during in-hospital stay and post-discharge. However, further research is required to comprehend the pathology, as well as the clinical course of these coinfections.

Key words: *Coinfection, Dengue, Human immunodeficiency virus*

Dengue, caused by four closely related dengue virus strains 1-4 (DENV 1-4), is endemic in the tropical and subtropical areas of the world, where human immunodeficiency virus (HIV), a human retrovirus of the family Retroviridae that causes the acquired immunodeficiency syndrome pandemic, is also likely to be prevalent. Transmission of dengue virus is by female mosquitoes mainly of the species *Aedes aegypti* and, to a lesser extent, *Aedes albopictus*. Recovery from dengue infection imparts lifelong immunity against that particular serotype. However, cross-immunity to the other serotypes after recovery is only partial and temporary. Subsequent infections by other serotypes increase the risk of developing severe dengue [1].

The current era of combination antiretroviral therapy (ART) has improved the longevity and quality of life of HIV-infected individuals. Such patients residing in tropical regions are exposed to a range of infections, such as malaria, dengue, or chikungunya, having a severe clinical progression and are difficult to diagnose [2]. Theoretically, coinfection of HIV-1 with other tropical agents can worsen the clinical progression of HIV-1 infection [3]. However, when it comes to coinfections of certain flaviviruses, such as the GB virus C, hepatitis C virus, or dengue virus (DENV), a reduction of the HIV-1 viral load has been observed [4]. Despite the fact that HIV infection has worldwide distribution and that extensive regions are endemic for HIV/DENV coinfection, this association is not well studied. Here, we present a less commonly encountered case of dengue coinfection in a known case of HIV seropositive individual.

CASE REPORT

This 44-year-old obese gentleman with known medication for hypothyroidism (Tab. Levothyroxine 75 mcg) presented to the OPD with complaints of low-grade fever of 1 week duration. The fever was occasionally associated with chills and subsided with medication (Tab. Paracetamol 1 g SOS). He also complained of multiple episodes of vomiting, abdominal pain, and loose stools for the past 2 days. However, he had no history of recent travel or consumption of unhygienic food and water. Furthermore, there was no history of burning micturition, shortness of breath, chest pain, palpitation, retro-orbital pain, headache or yellowish discoloration of eyes, urine, or skin. He also mentioned that he was incidentally diagnosed HIV serology positive 5 years ago, during a routine health check, following which he was started on highly active ART (HAART), in which he has discontinued of his own will, around 6 months ago. However, the source of the HIV infection could not be found even after a detailed query – he denied a history of unprotected sexual intercourse, intravenous (IV) drug abuse, or any history of blood transfusion in the past.

On examination, his pulse rate was 98/min, blood pressure 110/80 mm of Hg, respiratory rate 20/min, and temperature was 99.8°F. Per abdomen was soft with generalized tenderness and mild splenomegaly. On auscultation, there were no murmurs or additional breath sounds. He was admitted with a provisional diagnosis of dengue infection, keeping in mind gastroenteritis, enteric fever, malaria, and urinary tract infection as differential diagnosis. Routine investigations revealed that

he was HIV seropositive and also positive for dengue serology – both IgM and IgG were reactive. He was also found to have bicytopenia, transaminitis, elevated pancreatic enzymes, signs of hemoconcentration and splenomegaly, fatty changes in liver, and sludge in the gall bladder on ultrasonography. Chest X-ray PA view done on the day of admission showed clear bilateral costophrenic angle and increased cardiothoracic ratio (Fig. 1). As per the WHO classification and grading of severity of dengue infection, our final diagnosis was dengue fever (DF) with transaminitis in a known case of HIV coinfection [5].

The opinion of a gastroenterologist was sought and he was managed conservatively (adequate oral and IV fluids, IV paracetamol 1 g SOS, tepid sponging SOS, and Tab. Ursodeoxycholic acid 300 mg twice daily for a total of 15 days, IV antiemetics SOS, and Tab. Levothyroxine 75 mcg was continued. He was also started on oral antibiotics (Sulfamethoxazole 800 mg + Trimethoprim 160 mg, twice daily) considering his immunocompromised state. He gradually improved, both clinically and symptomatically. He and his spouse were adequately counseled about the source, progress, and probable consequences of the HIV infection, besides the precautionary measures that have to be taken. He was started on ART–oral combination of Lamivudine 150 mg + Zidovudine 300 mg + Nevirapine 200 mg, twice daily. After 5 days of in-patient care, he was discharged on oral ART, oral antibiotic (Sulfamethoxazole 800 mg + Trimethoprim 160 mg, one tablet twice daily for 2 weeks), Tab. Ursodeoxycholic acid (300 mg twice daily), Tab. Levothyroxine 75 mcg, oral multivitamin, and zinc supplements. Postdischarge, he was followed up after 15 days, 2 months, and 10 months. Table 1 summarizes the investigations carried out to monitor HIV during the follow-up period.

DISCUSSION

DF and its severe forms – dengue hemorrhagic fever (DHF) and dengue shock syndrome – have become major public health concerns. About 3.9 billion people in 128 countries are at risk of infection with dengue viruses. Dengue and DHF are endemic in more than 100 countries in the WHO regions of Africa, the Americas, Eastern Mediterranean, South-East Asia, and Western Pacific. South-East Asia and Western Pacific regions are most seriously affected [5]. ART can control HIV replication indefinitely in most HIV-infected individuals who are compliant [6]. Both Dengue and HIV have a high prevalence in the Asian population, contributing to a substantial public health burden [7].

The first thing to strike us was the fact that it is uncommon to find obese HIV infected patients. The body mass index (BMI) of our patient was 39 kg/m^2 (Grade I obesity) at presentation. A longitudinal cohort study conducted among HIV-infected Chinese patients has concluded that higher baseline BMI could predict better immune reconstitution in HIV-infected patients after HAART initiation. In their study, 17.6% were overweight/obese before HAART, while, 10.7% were underweight and the remaining were normal weight [8]. In fact, despite appropriate counseling, at the 2-month follow up, our patient had gained weight by another 5 kg.

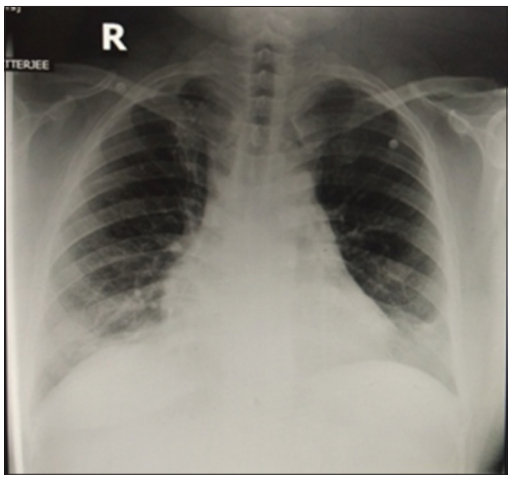

Figure 1: Chest X-ray PA view showing increased cardiothoracic ratio but a clear costophrenic angle

Table 1: Monitoring of HIV status through CD4 and CD8 count

CD4 and CD8	Reference	Day 0	After 2 months	After 10 months
CD3 (cells/μL)	600–2500	621	1444	1229
CD4 (cells/μL)	400–1500	187	411	355
CD8 (cells/μL)	200–1100	346	841	759
CD4/CD8	0.7–3.5	0.54	0.49	0.47
HIV viral load (copies/ml)			<40 HIV-1 detected	<20

At first presentation, there were no significant differences in the clinical symptoms and signs elicited between our index case and other DENV patients – nausea/vomiting, aches and pains, leucopenia, thrombocytopenia, and tachycardia. A matched case–control study conducted in Singapore in 2015 noted that over the course of hospitalization, DENV-HIV patients were less likely to have hemorrhagic manifestation and rash, compared to HIV-uninfected DENV patients. The study had also noted the association of clinical fluid accumulation, hepatomegaly, and severe organ involvement in the DENV-HIV patients, though the differences were not statistically significant. Hence, close monitoring of these coinfected patients for organ involvement is critical to reduce morbidity [9]. During hospitalization, a significant association of certain parameters, namely, higher eosinophils proportion, lower hematocrit level, and hypokalemia were noted in the study; similarly, our patient was found to have lower serum hematocrit levels.

In a cross-sectional study published in 2017, the seroprevalence of dengue virus IgG antibodies (using ELISA kits) among febrile HIV-infected patients attending the particular hospital was determined to be 44.4%. While IgM accounts only for the current exposures to dengue infections, IgG accounts for both previous and present exposure to dengue virus and appears from day5 to day7 of infection [10]. Our patient was found to be both IgM and IgG reactive for the dengue virus antibodies.

There have been various reports of false-positive reactivity of rapid HIV antibody tests in patients with acute DF; however, the opposite has not been observed [11]. As observed in various

studies, pulmonary manifestations such as acute respiratory distress syndrome, pneumonia, and pleural effusion are more common in severe cases of dengue as compared to DF [12]. Similarly, chest X-ray of our patient done during admission did not show any evidence of pulmonary manifestation. Not much has been reported about the clinical characteristics and outcome among dengue patients with HIV infection. There is a lack of a large cohort study to validate the observations of the handful case reports and cohort studies available till date. Our observation was limited by the lack of data on the HIV viral load of the gentleman before the coinfection.

CONCLUSION

HIV infection is known to alter the natural history of other infections, often leading to more severe presentations and worse outcomes. However, the dengue infection in our patient ran a mild course. No severe complication was observed during hospital stay and on follow-up. Hence, close monitoring and a thorough follow-up cannot be stressed enough, as part of dengue clinical care and management. With the increasing trend of DENV-HIV coinfection in Asia, a better understanding of the pathophysiology through a systemic meta-analysis is the need of the hour. In addition, a prospective evaluation on the HIV and DENV viral load may help us analyze the impact of viral load and ART on the disease outcome among DENV-HIV and DENV patients.

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