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ORIGINAL ARTICLE

Seroepidemiology of novel influenza A (H1N1) infection among HIV-infected patients in the era of highly active antiretroviral therapy

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Background: The seroprevalence and seroincidence of novel influenza A infection among HIV-infected patients, who were believed to have more severe outcomes than healthy individuals, are rarely investigated in the era of highly active antiretroviral therapy (HAART). Our aim was to determine the seroprevalence and seroincidence of novel influenza A infection among HIV-infected patients in Taiwan.
Methods: Between September and November 2009, before the implementation of a nationwide vaccination for novel influenza A in Taiwan, 931 HIV-infected patients and 566 persons seeking voluntary counseling and testing (VCT) for HIV infection at our university hospital were enrolled in this study. Antibody responses to novel influenza A were determined using a hemagglutination-inhibition (HI) assay.
Results: HIV-infected patients had a significantly lower seroprevalence of novel influenza A infection than VCT clients (14.7% vs. 33.9%, $p < 0.001$). The seroincidence of novel influenza A infection among HIV-infected patients was 9.4% (95% confidence interval [CI]: 7.6—11.4). On the multivariate analysis, heterosexual (odds ratio [OR]: 1.89; 95% CI: 1.105—3.227) and baseline HI titer (OR: 1.02; 95% CI: 1.001—1.038) were significantly associated with seroconversion to novel influenza A virus.

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Conclusion: HIV-infected patients demonstrated a lower seroprevalence of novel influenza A infection than HIV-uninfected patients in Taiwan in the HAART era. Among HIV-infected patients, seroconversion to novel influenza A virus, which was infrequent during the 2009 influenza epidemic, was associated with heterosexual behavior and baseline HI titer.

Introduction

In April 2009, the World Health Organization (WHO) reported that a swine-origin influenza A (H1N1) virus (novel influenza A virus) was spreading via human-to-human transmission and had raised serious public concerns around the world.[1] Between April 2009 and March 2010, an estimated 43—88 million cases were infected in the United States during this H1N1 pandemic.[2] By the end of May 2010, 18,114 deaths from causes related to H1N1 infection had been reported worldwide; pneumonia was reported as a contributing cause of death in 7.9% of all deaths reported in the 122 Cities Mortality Reporting System.[2]

Although it remains controversial whether novel influenza A is more virulent than seasonal influenza, several risk factors associated with adverse outcome following novel influenza A infection have been identified.[3—5] In addition, among individuals who were hospitalized for influenza and related complications, HIV-infected patients who had a lower CD4 count were reported to develop more severe complications to novel influenza A infection, and these patients often developed secondary bacterial infections including pneumonia.[6] Nevertheless, two recent publications reported that the clinical presentation and clinical outcomes of HIV-infected patients who were also infected with novel influenza A were similar to those of the general population.[7,8]

After the identification of the first case of novel influenza A infection in Taiwan in late May 2009, the novel influenza A epidemic started in June 2009.[9] From June 2009 through April 2010, a total of 13,931 specimens, mainly from patients with symptoms of influenza-like illness who sought healthcare at the hospitals or clinics around Taiwan, were screened for novel influenza A, and 3274 (23.5%) of these specimens were confirmed as novel influenza A infection.[9] A nationwide free-of-charge vaccination program for novel influenza A was implemented in November of 2009 for individuals at high risk of developing influenza A-related complications and, in December of 2009 this program was implemented in healthy adults. As of April 2010, the Taiwan Centers for Disease Control estimated that 24.5% (5,667,703/23,133,074) of the people living in Taiwan had received the novel influenza A vaccine.[10]

In this study, our aim is to compare the seroprevalence of novel influenza A virus infection between HIV-infected patients and persons seeking voluntary counseling and testing (VCT) for HIV and to examine the seroincidence of novel influenza A virus infection among HIV-infected patients who received HIV care, including highly active antiretroviral therapy (HAART), in Taiwan, where the novel influenza A epidemic started in June 2009, peaked in late August and November, and subsided in December 2009.[9]

Methods

Study setting and population

In Taiwan, HIV-related care, including HAART and the laboratory tests that monitor virological and immunologic status before or after the initiation of HAART, was introduced in Taiwan in 1997 and is provided free-of-charge to patients at designated hospitals. As a public health response to the HIV epidemic, a program that provides anonymous voluntary counseling and testing (VCT) for HIV has been in use since 1990.

Between September and November 2009, residual blood samples were collected from HIV-infected patients who visited the hospital for the determination of CD4 and plasma HIV-RNA load (PVL) and from HIV-negative persons who sought VCT services. The study period spanned 3 months, which is the interval the vast majority of HIV-infected patients who seek regular HIV care go before needing to refill their antiretroviral therapy. We included blood samples from all of the patients who returned to the hospital to monitor their CD4 count and plasma HIV-RNA load, which was performed every 3—6 months according to the DHHS guidelines.[11] In this study, we estimated that the blood samples included in this study were from 60% of all of the HIV-infected patients who sought HIV care during the 3-month study period.

VCT clients were chosen as a comparator group for this seroprevalence study because more than 70% of HIV-infected patients and VCT clients are homosexual males and they might share similar socioeconomic backgrounds in the metropolitan area around Taipei. Patients were excluded from the present study if they had received a novel influenza A vaccine at the time of enrollment. A standardized case collection form was used to retrospectively record data on demographics, clinical characteristics, and laboratory results of the HIV-infected patients. This study was approved by the institutional review board of the hospital and all patients gave written informed consent.

Laboratory investigations

The antibody response of the serum samples to a novel influenza A strain, A/California/07/2009, was determined using a hemagglutination-inhibition (HI) assay, according to the standard protocols of the World Health Organization Collaborating Centre for Reference and Research on Influenza, Melbourne, Australia.[12] The receptor-destroying enzyme (RDE [III], Deka Seiken Co. Ltd, Tokyo, Japan) was used to treat serum samples that were titrated in a 2-fold dilution from 1:10 to 1:1280 in order to examine its