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ORIGINAL ARTICLE

Epidemiology of human herpesvirus type 8 and parvovirus B19 infections and their association with HIV-1 among men who have sex with men and injection drug users in Taiwan



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Background/Purpose: Human herpesvirus 8 (HHV-8), the causal agent of Kaposi's sarcoma (KS), is transmitted sexually among men who have sex with men (MSM), but little is known of its transmission among injection drug users (IDUs). By contrast, human parvovirus B19 (B19), a causative agent for anemia, is most frequently detected in IDUs. The aim of this study was to investigate the associations between HHV-8 infection and human immunodeficiency virus type 1 (HIV-1), and between B-19 and HIV-1 among MSM and IDUs patients.

Methods: Serum samples from 553 IDUs and 231 MSM were analyzed for anti-HHV-8 lytic and anti-B19 viral structural capsid protein 2 (VP-2) antibodies using enzyme immunoassay, indirect immunofluorescence, and immunoblot assays. Odds ratios (ORs) and 95% confidence intervals (CIs) were used to evaluate the associations between different viral infections.

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Results: HIV-1-seropositive MSM had significantly higher rates of HHV-8 infection than seronegative MSM (32.3% and 15.4%, respectively; OR = 2.62, 95% CI = 1.37–5.02). Among HIV-1/AIDS patient groups, MSM had significantly higher HHV-8 seropositive rates (32.3% vs. 6.6%, $p < 0.0001$) and lower B19 infection rates (35.4% vs. 78.8%, $p < 0.001$) than IDUs. In addition, HIV-1-infected MSM were 5.95 times (95% CI = 3.38–10.46) more likely to be infected with HHV-8 than male HIV-1-infected IDUs. By contrast, male IDUs were 6.74 times odds (95% CI = 4.28–10.61) more likely to contract B19 infection than MSM.

Conclusion: In Taiwan, MSM have a significantly higher prevalence for HHV-8 than IDUs. The contrasting risks of HHV-8 and B19 infections between different HIV-1/AIDS groups suggest that the efficiency of viral infection is affected by their distinct transmission routes.

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Introduction

Kaposi's sarcoma-associated herpesvirus (KSHV), also known as human herpesvirus 8 (HHV-8), was discovered in 1994 and is the causative agent of Kaposi's sarcoma (KS), primary effusion lymphoma (PEL), and multicentric Castlemann's disease.¹ Among HIV-1 exposure categories at risk of AIDS KS in North America and Europe, the prevalence of HHV-8 shows a distinct spread. Within a defined geographical area, this prevalence is highest among HIV-1-infected men who have sex with men (MSM), lower among HIV-1-infected injection drug users (IDUs) or HIV-1-infected non-IDU heterosexual individuals, and lowest among children.^{2,3} Interestingly, in one US region, the HHV-8 prevalence rates among young MSM (15–22 years old) were comparable with the rates among young heterosexual men, and both were noticeably lower than rates among older MSM in that region.⁴ Moreover, HHV-8 acquisition has been associated with multiple sex partners among both MSM and heterosexuals, and practices involving saliva are thought to increase transmission, which may account for differences in incidence of HHV-8 and HIV.^{5,6} International studies have provided some evidence that HHV-8 can be transmitted by blood or blood products.^{7,8} Atkinson et al also showed that longer duration of injection drug use is associated with an increase in the risk of HHV-8 infection that is not explained by sexual behavior or demographic differences.⁷ Among IDUs, while syringe sharing is a common means of transmitting HIV-1, hepatitis B virus (HBV), and hepatitis C virus, it may also result in the spread of HHV-8.⁹

Human parvovirus B19 (B19) can cause a common childhood disease with symptoms of exanthema and fever known as erythema infectiosum.¹⁰ B19 has a strong tissue tropism for erythroid progenitor cells and can cause anemia. Study of occult B19 infection is recommended in patients with hematological disease.¹¹ In common with other latent viruses such as herpesviruses, infections with parvovirus B19, HBV, and hepatitis GB virus C (HGBV-C) are contained successfully by the immune response and persist in the host. When immune control breaks down, reactivation of both latent and persistent viruses occurs.^{12,13} The background seroprevalence in blood donors is high for B19 ($\geq 64\%$), HBV ($\geq 70\%$), CMV, and EBV ($\geq 90\%$), and is significantly increased in individuals infected with HIV, HBV, cytomegalovirus (CMV), varicella-zoster virus (VZV);

symptomatic HIV), and HHV-8 (asymptomatic and symptomatic HIV).^{14,15} Persistent parvovirus B19 infection has been reported in patients both with and without underlying immunodeficiencies.^{16–18} Antibody prevalence provided an estimate of viral exposure and allowed adjustment for the prevalence of potential reactivation to be calculated as well as the odds ratios (ORs) for reactivation in susceptible individuals. Levels of exposure among susceptible HIV-infected patients to parvovirus B19 are comparable to those for HIV-negative controls, because this infection is transmitted via the respiratory route.¹⁹ Previous studies also demonstrated that prolonged parvovirus infection with anemia in HIV-infected patients was typically associated with the absence of an antibody response to B19.²⁰ In this study, we compared the seroprevalence of HHV-8 and B19 infection between MSM and IDU groups among HIV-1/AIDS patients in Taiwan.

Materials and methods

Subjects

This cross-sectional study was conducted among subjects from the following three populations: 553 inmates who had history of using injection drugs were recruited from detention centers and prisons in Taiwan^{21,22}; 127 HIV-1-infected MSM were selected randomly from 879 patients attending the outpatient clinics of Taipei City Hospital from 2004 to 2006, and 104 HIV-1 seronegative MSM were randomly selected from 1093 patrons from gay saunas in Taiwan.²³ Their HIV status and demographic data were recorded by reviewing their medical history or assessed through a self-administered questionnaire. Informed consent was obtained from all participants and this study was approved by the Institutional Review Board of the National Yang-Ming University. Plasma samples were obtained from the subjects for serological testing. The samples were processed and stored at -80°C .

Serological testing

Sera were tested for HHV-8 antibodies by HHV-8 whole virus lytic immunoglobulin G (IgG) enzyme-linked immunosorbent assay (ELISA; Advanced Biotechnologies Inc., Columbia, MD, USA)^{24,25} and indirect fluorescent assay (IFA; Advanced Biotechnologies Inc., Columbia, MD, USA),^{26,27} which

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