Journal of HIV/AIDS Research

Research Article

Aids and non-Aids people who have a cerebral infection caused by the human viral disease herpes

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Received : August 03, 2023
Accepted: August 04, 2023
Published : Septmber 04, 2023

ABSTRACT

Infection of the central nervous system (CNS) by the human herpes virus (HHV) is a widespread issue throughout the world. At Rajavithi Hospital in Bangkok, Thailand, researchers have examined the prevalence of HHV-CNS infection in both HIV/AIDS patients and non-HIV patients. To determine the frequency and incidence of HHV1 (HSV), HHV3 (VZV), HHV4 (EBV), HHV5 (CMV), HHV6A,B, and HHV 7-CNS infection in patients at Rajavithi Hospital in Bangkok, Thailand, as well as to distinguish between HSV-encephalitis and non-HSV/HHV-CNS infection based on clinical manifestations and laboratory results. Patients with a clinically suspected CNS infection were included in an 18-month prospective trial. Examination and culture of the cerebrospinal fluid (CSF) were carried out, as well as real-time polymerase chain reaction (RT-PCR) testing for Mycobacterium tuberculosis, HSV-1, HHV3, HHV4, HHV5, HHV6, and HHV7.

The presence of fever, headache, seizures, altered consciousness, neurological localising symptoms, and/or stiff neck were necessary for the diagnosis of HHV-CNS infection. Between July 2008 and December 2009, 94 patients (mean + SD = 42.3 + 14.5 years) with 52 male and 42 female participants were enrolled. The patients ranged in age from 16 to 77 years. It was determined that 44 patients tested positive for HIV/AIDS. Twenty-seven percent of them received highly active antiretroviral therapy (HAART). Age and gender differences were statistically significant ($p < 0.026$) between the HIV/AIDS and non-HIV subgroups. 11.3% of cases of HHV encephalitis occurred annually. The annual incidence of latent infection caused by HHV5 (CMV), HHV4 (EBV) encephalitis, and HHV1 (HSV) viral encephalitis was 5.67, 4.2, and 0.6%, respectively. No signs of HHV6A, B, or HHV7-related CNS infections were found. HIV/AIDS patients had a significantly increased prevalence of HHV encephalitis ($p = 0.002$). Compared to patients without HSV/HHV-CNS infection, those with HSV1 encephalitis had a higher CSF/blood sugar ratio ($p = 0.06$). It has been discovered that human herpes virus, particularly HSV-CNS infection, is prevalent in both HIV/AIDS and non-HIV patients. VZV, EBV, HHV6, and HHV7-related CNS infections were uncommon. In contrast to the CSF/blood sugar ratio and CSF pleocytosis, clinical signs might not be useful in distinguishing between non-HSV/HHV-CNS infection and HSV encephalitis.

Keywords : *Human herpes virus (HHV), central nervous system (CNS) infection, human immunodeficiency virus (HIV), viral encephalitis, herpes simplex virus (HSV), varicella zoster virus (VZV), Ebstein barr virus (EBV).*

INTRODUCTION

Central nervous system (CNS) infection by the human herpes virus (HHV) is a widespread issue that can have serious consequences if therapy is not received (Boriskin et al., 2004). Thus far, there have been few reports of HHV-CNS infection in HIV/AIDS and non-HIV patients in Thailand (Subsai et al., 2004, 2006; Windy et al., 2008). HHV1 (Herpes simplex virus, or HSV) and HHV3-CNS infection were reported to be 15.3 and 5.8%, respectively, in a study conducted in the USA (New York). CMV, EBV, and HHV-6 infections are more common causes of encephalitis in immunocompromised hosts. In 2001 and 2002, the incidence rate of HHV5-CNS infection in AIDS cases with documentation was reported to be 7 per 100 person-years at Chiang Mai University Hospital in Thailand.

The following symptoms can be used to make a clinical diagnosis of HHV-CNS infection:

1) fever, headache, seizure, altered consciousness, neurological localising sign, and/or stiff neck;

2) lumbar puncture performing CSF lymphocytic pleocytosis, with the possible exception of HHV5 (CMV) - CNS infection, which may have neutrophilic pleocytosis;
3) increased CSF protein6; and
4) Polymerase chain reaction positivity for HHV DNA (Table 5).
The purpose of this study was to determine the prevalence and incidence of HHV1 (HSV), HHV3 (VZV), HHV4 (EBV), HHV5 (CMV), HHV6A, B, and HHV 7-CNS infection at Rajavithi Hospital in Bangkok, Thailand. Additionally, the study aimed to distinguish between HSV-encephalitis and non-HSV/HHV-CNS infection based on laboratory findings and clinical manifestations.

Patients and methods

Patients with a clinically suspected CNS infection were included in an 18-month prospective trial. Examination and culture of cerebrospinal fluid (CSF) were carried out, as well as polymerase chain reaction (PCR) testing for Mycobacterium tuberculosis, HSV-1, HHV3, HHV4, HHV5, HHV6, and HHV7. Fever, headache, seizures, altered awareness, and neurological localising signals +/- stiff neck were required for the diagnosis of HHV-CNS infection. Enrolled were patients over the age of 15, suspected of having a CNS infection without a lumbar puncture contraindication, capable of giving informed consent on their own or through a family member, and able to undergo the procedure. Individuals who were deemed to have a severe pathogenic viral infection, such as SARS or bird flu (H5N1), were not allowed to participate in this study.
Complete blood count (CBC), anti-HIV test results, and CD4 counts were documented in clinical laboratory data. Primers specific sequences for HSV-1, HHV3, HHV4, HHV5, HHV6, and HHV7 were used in the Sybergreen ®-Roche® real-time polymerase chain reaction (RT-PCR) in 20 µl. These sequences were designed to target specific viral strains based on a comprehensive search of the GenBank database (www.ncbi.nlm.nih.gov) (Boriskin et al., 2004) (Table 1), with sensitivity of 93 and specificity of 100. There was a 100% positive predictive value and an 83% negative predictive value. There was also use of Mycobacterium tuberculosis. 200 µl of CSF total, taken from patients suspected of having a CNS infection, was subjected to automated DNA extraction using the Roche MagNa pure Compact Nucleic and Isolation Kit.

RESULTS

Between July 2008 and December 2009, a total of 94 patients—52 men and 42 women—between the ages of 16 and 77 (Mean + SD = 42.3 + 14.5) were included. Of the 44 individuals whose HIV status was confirmed, 27 percent received highly active antiretroviral therapy (HAART). Age and gender differences were statistically significant ($p < 0.026$) between the HIV/AIDS and non-HIV subgroups. Table 2 provides specific demographic information. 141 CSF samples in all were taken during the enrollment phase 29 individuals were diagnosed with non-CNS infections, while 65 patients had a conclusive CNS infection. Clinical features of individuals who may have a central nervous system infection. Meningitis caused by tuberculous meningitis is a non-HHV CNS infection.
11.3% of cases of HHV encephalitis occurred annually. HHV1 viral encephalitis, HHV5 (CMV) latent infection, and HHV4 encephalitis had annual incidence rates of 5.67, 4.2, and 0.6%, respectively. The group that was enrolled did not exhibit any CNS infections caused by HHV6A, B, or HHV7. The frequency of HHV 16 patients had HHV-CNS infection, 8 had HSV-1 infection, 6 had latent CMV infection, 1 had VZV infection, and 1 had EBV encephalitis.

DISCUSSION

According to this study, HSV was the most frequent source of HHV-CNS infection (11.3%), particularly in those who were HIV positive (62.5%) as opposed to those who were not (37.5%). Rajavithi Hospital's HHV-related CNS infection prevalence was the same as that reported in other parts of the world (Laser et al., 2003). (Ali et al., 2005; Behnam et al., 2007; Mendoza et al., 2007). Comparing this prospective study to the USA (New York) study revealed a somewhat reduced prevalence of HHV-CNS infection.
Additionally, HHV-related CNS infection was shown to be significantly more common in HIV-positive patients ($p = 0.002$), according to this study. In contrast, HHV6 and HHV7 CNS infection was not found in our enrolled adult group in a prior publication of encephalitis in Thai children. Furthermore, HHV-related CNS infection was much more common in HIV-positive patients, according to our research ($p = 0.002$).
When compared to non-HSV/HHV - CNS infection, we did not discover seizure to be a predictive hint for HSV encephalitis, which is in contrast to a German encephalitis study (Ali et al.,

2005). In environments with limited resources and infrequent access to RT-PCR, the CSF/blood sugar ratio in cases with HSV encephalitis appeared to be greater than that of non-HSV/HHV CNS infection (p = 0.06). It's possible that a non-HSV/HHV CNS infection is the cause of the CSF pleocytosis (> 200 cells/mm 3) (p=0.19) (Table 7). But in environments with limited resources, it is necessary to screen out other prevalent CNS infections before making the diagnosis of HHV-related CNS infection.

For up to two thirds of HIV-positive patients, routine intravenous Acyclovir treatment may be helpful when encephalitis is suspected. In contrast, intravenous Acyclovir treatment may not be beneficial for HIV-positive individuals with low CSF/blood sugar ratios (20%) and CSF pleocytosis more than 200 cells/mm3, as the most likely cause was determined to be a CNS infection rather than HSV/HHV. It was discovered that CMV encephalitis was uncommon and that retinitis was the most frequent sign of CMV infection in HIV patients (Chokephaibulkit et al., 2001). We only discovered CMV latent infection in this investigation. The diagnosis of individuals with neurological immune restoration syndrome may also benefit from CSF study, which includes culture, RT-PCR for HHV DNA detection, and RT-PCR TB.

The small sample size, lack of CSF positive controls for HHV2, and lack of testing for CNS ribonucleic acid (RNA) viral infections were the limitations of our investigation. Future research should focus on developing multiplex RT-PCR with hybridization probes, as this will provide higher sensitivity and diagnosis confirmation.

Conclusions

At Rajavithi Hospital in Thailand, human herpes virus infections, particularly HSV-CNS infection, were prevalent in both HIV-positive and non-HIV patients. Although CSF/blood sugar ratio (p=0.06) and CSF pleocytosis (p=0.19) were helpful in this study in differentiating between HSV-encephalitis and non-HSV/HHV - CNS infection, they may not be as useful in other contexts where HSV/HHV - CNS infection may be a factor.

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