Symptomatic Primary Infection with Human Herpesvirus 6 Variant A

The first isolation of human herpesvirus 6 (HHV-6) was reported in 1986, although the infection is common in humans. The clinical manifestation of primary HHV-6 infection is exanthem subitum, a benign febrile disease that typically occurs in childhood [1]. HHV-6 has been variously associated with chronic fatigue syndrome, multiple sclerosis, a mononucleosis-like lymphoproliferation, afebrile lymphadenopathy, hepatitis, meningitis, meningoencephalitis, myalgic encephalomyelitis, and the hemophagocytic syndrome [2].

Recently, two major subspecies of HHV-6 have been identified; they have been designated as variant A (HHV-6A) and variant B (HHV-6B) on the basis of their genetic, biological, and immunologic features [3-5]. Reactivation of HHV-6 is common among immunosuppressed patients; both variants have been isolated from such patients [6, 7]. Although HHV-6A and HHV-6B are prevalent in humans, only HHV-6B has been isolated from patients with a symptomatic primary infection [8]. To our knowledge, we report the first case of symptomatic primary infection with HHV-6A.

A male Japanese infant had an uncomplicated perinatal period and was well until he was 50 days old, when he developed a fever (temperature of 38.2 °C) and a generalized rash. Because he was <2 months old, he was admitted to the hospital on day 2 of his illness. His general condition was good despite his high fever. He had a generalized, small maculopapular, pinkish rash. He did not have any neurological abnormalities.

Laboratory findings on admission were as follows: WBC count, 5,100/µL with 31% segmented neutrophils, 11% band forms, 36% lymphocytes, 20% monocytes, and 2% other cells; hemoglobin, 9.5 g/dL; and platelet count, 217,000/µL. Serum concentrations of C-reactive protein, aspartate aminotransferase, and alanine aminotransferase are shown in table 1. Examination of CSF revealed 2 cells/µL, a protein level of 24 mg/dL, and a glucose level of 54 mg/dL. Culture of blood and CSF was negative for bacteria. The patient’s fever persisted for 3 days, and the rash diminished gradually. The serum levels of AST and ALT remained elevated on day 5 of the illness but had decreased by day 9.

Viral studies for HHV-6 and HHV-7 were done with use of nested PCR in peripheral blood mononuclear cells and CSF specimens. The PCR primers were described by Yalcin et al. [9]. Samples of peripheral blood mononuclear cells were digested with protease K and then boiled; CSF samples were boiled only. HHV-6A DNA (195 kb) was detected in peripheral blood mononuclear cells and CSF obtained from the patient on day 2 of the illness. HHV-6B and HHV-7 DNA was not detected. Serological tests showed the same level of HHV-6 antibody on day 2 and on day 50 of illness. In comparison, the level of measles antibody from those paired sera decreased over 50 days, as is typical of maternal immunoglobulin.

To our knowledge, we report the first case of symptomatic primary infection in a patient with HHV-6A. Furthermore, this Japanese case indicates that HHV-6A can be isolated in Japan, although HHV-6A has been thought to be rare in Japan.

Since HHV-6A and HHV-6B are common in adult patients, why is symptomatic primary infection with HHV-6A rare? It may be that infection with HHV-6A occurs later in life than infection with HHV-6B and that HHV-6A infection is usually mild because of immunity to HHV-6B. The findings in the present case showed that HHV-6A can cause symptomatic disease if such infection occurs before exposure to HHV-6B.

HHV-6 is commonly detected in the CSF of patients with exanthem subitum, which is caused by HHV-6B [10]. HHV-6A DNA was detected in our patient’s CSF, which suggests that HHV-6A is neurotropic, as is HHV-6B. In addition, HHV-6 sometimes causes liver dysfunction. Our patient also had mild liver dysfunction that resolved without complications.

In the present case, HHV-6A DNA was identified in our patient’s peripheral blood mononuclear cells and in his CSF by
Resolution of Intractable Molluscum Contagiosum in a Human Immunodeficiency Virus–Infected Patient After Institution of Antiretroviral Therapy with Ritonavir

Molluscum contagiosum (MC) is a viral infection of the skin caused by a member of the family Poxviridae [1]. The HIV epidemic has greatly expanded the clinical manifestations of this infection [2, 3]. Although local therapies are highly effective in immunocompetent patients, HIV-infected patients often do not respond completely to these treatments.

HIV-infected patients who experience the more disfiguring manifestations of MC usually have relatively advanced HIV infection [2]. This observation suggests that improving immune function in patients with severe MC may be beneficial. Most investigators, however, have found that antiretroviral therapy does not have a significant effect on MC, perhaps because the impact of antiretroviral therapy on HIV infection has until recently been relatively modest [2].

The introduction of HIV protease inhibitors into clinical practice has significantly enhanced the management of HIV-infected patients [4–7]. The effect of improved antiretroviral therapy on the more difficult-to-treat complications of HIV infection (including MC) may be substantial. We report the case of a patient with severely refractory MC whose lesions healed following the initiation of ritonavir therapy.

HIV infection was first diagnosed in a 35-year-old man in September 1990. He was treated with zidovudine, didanosine, and dideoxycytidine at various times, but all drugs were discontinued because of side effects. By July 1995 his CD4 cell count had declined to 15/mm$^3$ (2% of total lymphocytes), and he enrolled in an investigational protocol in which patients were randomized to receive either ritonavir or an identical-appearing placebo. He was randomized to twice daily ritonavir therapy in January 1996, his CD4 cell count was 23/mm$^3$.

Informed consent was obtained from the patient enrolled in this study, and the guidelines for human experimentation of the U.S. Department of Health and Human Services and Duke University Medical Center were followed in the conduct of this clinical research. Financial support: The patient enrolled in an investigational drug study (M94-247) sponsored by Abbott Laboratories (Abbott Park, IL).

References


Clinical Infectious Diseases 1997; 24:1023–5
© 1997 by The University of Chicago. All rights reserved.
1058-4838/97/2405-0057$02.00