Acute Encephalitis Due to Human Herpesvirus 6

Human herpesvirus 6 (HHV-6) has been identified as one of the causes of exanthema subitum [1]. An increase in the titer of antibody in CSF may also be evidence that HHV-6 is responsible for CNS complications [2]. PCR analysis has revealed the viral genome in the CSF of patients with encephalitis and/or encephalopathy [3] and in the CSF of patients with focal encephalitis of unknown etiology [4]. However, this finding is not necessarily associated with the presence of a cerebral infection, since active viral replication in brain tissue has not been demonstrated.

Two cases of fatal HHV-6 encephalitis have recently been described: the first case occurred in an adult bone marrow transplant recipient [5], and the second occurred in an HIV-infected infant [6]. In both cases, immunohistochemical staining of CNS tissue demonstrated active infection of CNS cell types. We recently observed an infant with acute CNS involvement with HHV-6; the virus was isolated from both the blood and CSF.

An 8-month-old girl presented to our institution because she had had four short generalized seizures during the previous 2 weeks. She was given phenobarbital. After 2 weeks, during which time she appeared well, she was found to have a cutaneous temperature of 38°C and a pruritic maculopapular rash. Her temperature rose to 39.5°C, and the rash diffused over her whole body. Administration of phenobarbital was discontinued. The patient became somnolent and irritable, with a poor response to stimuli. She had an increase in the titer of antibodies to HHV-6; the diagnosis to HHV-6 was documented. IgM and IgG antibodies to HHV-6 were not detected in the blood and CSF. These results were obtained from slides with HSB-2 cells infected with GS strain [7] and fixed with a mixture of acetone plus methanol 1 + 1; the slides were examined by means of indirect immunofluorescence.

Because we believed that the encephalitic symptoms could be related to HHV-6 infection, analysis with PCR was performed. Four primers from the region ORF 2L of the HHV-6 genome, with no homology to known herpesvirus sequences [8], were selected: DM1-5'TAACCATTCTTGGTAGGTCGA3' and DM2-5'TTC-GATGTGACGTGGTTGCA3' as external primers and A-5'ATGC-GATCCGGACGTATACGGA3' (9) and E-5'GATCGATGCT-GAACAGGC3' as primers for nested PCR. With use of these primers, the HHV-6 genome was detected in blood and CSF mononuclear cells. The virus was subsequently isolated from both blood and CSF by cocultivation with noninfected peripheral blood mononuclear cells. Presence of the virus was confirmed by indirect immunofluorescence, which was performed with use of the monoclonal antibody p41/38 (Virotech International, Rockville, MD).

This is the first time, to the best of our knowledge, that active HHV-6 replication has been extensively demonstrated in the blood

References
and CSF of an immunocompetent patient with an acute encephalitic syndrome.

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References

Prevalence of Bartonella henselae Antibodies Among Human Immunodeficiency Virus–Infected Patients from Bahrain

Bartonella (formerly Rochalimaea) henselae is the most frequent etiologic agent of cat-scratch disease. In the HIV-infected or otherwise immunocompromised host, B. henselae may cause bacillary angiomatosis, parenchymal bacillary peliosis, bacteremia, weight loss, and prolonged fever [1, 2].

Since it is difficult for many clinical laboratories to perform PCR and culture for B. henselae, serological techniques are being evaluated for use in seroepidemiologic and clinical studies [3, 4].

Despite the proliferating literature about B. henselae, little is known about the seroprevalence of this infection in different geographical areas. This study aims to determine the frequency of B. henselae antibodies in the serum of HIV-infected patients in Bahrain, a small island nation located in the Arabian (Persian) Gulf.

The B. henselae reference strain was provided by Jean Creek from the Office of the San Diego County Veterinarian. The strain was recultured on tryptic soy agar with 5% sheep blood and harvested on the 10th day in sterile PBS (pH, 7.4); autoagglutination was not observed. This suspension was fixed in 3.7% formalin for 1 hour and washed 3 times in PBS. After the final wash, the pellet was resuspended in coating buffer (0.05 M carbonate; pH, 9.6) and adjusted to 1.2 × 10^7 bacteria/mL with use of the McFarland opacity standard.

The views expressed in this article are those of the authors and do not reflect the official policy or position of the U. S. Department of the Navy, the U.S. Department of Defense, or the U.S. Government. Reprints or correspondence: Commander Mark R. Wallace, Medical Corps, U. S. Navy, c/o Clinical Investigation Department, Naval Medical Center, 34800 Bob Wilson Drive, San Diego, California 92134-5000.

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During performance of the indirect fluorescent antibody assay, we compared the antigen prepared in our laboratory with the killed antigen provided by the Division of Viral and Rickettsial Diseases at the Centers for Disease Control and Prevention (CDC) in Atlanta using the basic method described by Slater et al. [4]. Convalescent human sera (provided by the CDC) of patients with cat-scratch disease were used as positive controls; titers of ≥1:32 were considered positive. All the immunofluorescent antibody assays were done in parallel, once with the antigen prepared in our laboratory and another time with the antigen provided by the CDC. The HIV-infected patient sera were obtained from HIV-infected patients identified in Bahrain by blood donations. The control sera were from age-matched HIV-seronegative blood donors in Bahrain.

Nine (16%) of 56 HIV-seropositive patients had antibodies to B. henselae, although only two (3.5%) of 56 HIV-seronegative individuals had detectable titers (estimated relative risk, 4.5; P = .026 by Mantel-Haenszel). Both patients who were not infected with HIV who had detectable antibodies had titers of 1:32. In the HIV-seropositive group, two (22%) of nine had a titer of 1:32, one (11%) of nine had a titer of 1:64, and the others (six of nine [66%]) had high titers (≥1:128). When the B. henselae antigen prepared in our laboratory was used, the results were the same as those obtained when the antigen provided by the CDC was used.

Given the broad array of illnesses caused by B. henselae in patients who are infected with HIV, it is surprising how little is known about the geographic epidemiology of bartonella infections. Within the United States, regional differences in the incidence of cat-scratch disease have been documented, with lower rates in the western states [5]. In the current study, we found that 16% of HIV-infected subjects in Bahrain were seropositive for B. henselae as compared with only 3% of healthy blood donor controls. The 3% seropositivity among the HIV-negative subjects is similar to published seropositivity rates for healthy controls from the United States [3].

It is unclear why HIV-infected subjects were more frequently seropositive for B. henselae. Perhaps HIV-infected patients have more persistent B. henselae infections than the HIV-negative controls, who would most likely have had self-limited cat-scratch disease as their only B. henselae illness. Another plausible explanation is that there is a higher rate of cat ownership among HIV-