Meningoencephalitis Associated with Human Herpesvirus-6 in an Adult

Key words: human herpesvirus-6, meningoencephalitis, adult, virus-associated hemophagocytic syndrome

A 74-year-old woman without a remarkable medical history developed a generalized maculo-papular rash on July 6, 1995, 17 days after ticlopidine was started for vertebrobasilar insufficiency. Ticlopidine was stopped at once and the rash subsided. She was then placed on aspirin on July 10, but developed a fever on July 17, followed by generalized wheals with petechiae in the lower limbs. Although aspirin was discontinued immediately, she became progressively unresponsive, and was admitted to our hospital on July 23. Physical examination revealed a febrile, stuporous woman with a stiff neck and marked generalized lymphadenopathy.

Complete blood count revealed leukopenia, followed by progressive anemia and thrombocytopenia. Serum IgG and IgA were increased, but no monoclonal component was noted. Direct and indirect Coombs' tests were negative, and anti-platelet antibodies were not detected. Bone marrow aspiration revealed a slight increase of matured plasma cell counts. Lumbar puncture yielded 57 white cells/mm³ (98% lymphocytes) with a protein of 171 mg/dl. Blood, urine and cerebrospinal-fluid (CSF) cultures were negative for bacteria and fungi. Imaging studies showed bilateral pleural effusions, hepatosplenomegaly and enlarged para-aortic lymph nodes. Head CT and MRI were unremarkable, but electroencephalogram showed diffuse slowing. On serological tests by an indirect immunofluorescence assay, the titer of anti-IgG human herpesvirus-6 (HHV-6) antibody was 40 (sample from July 26), which increased to 640 (August 31), and then decreased to 80 (November 18), and that of IgM was less than 10 in the first measurement. A polymerase chain reaction (PCR) on CSF (obtained on July 29) using HHV-6 primers was negative. No evidence of recent infections with other viruses was found by reciprocal antibody titers, which included Epstein-Barr virus, herpes simplex virus, cytomegalovirus, varicella-zoster virus, mumps, measles and adenovirus.

Since her condition continued to deteriorate despite the intravenous administration of broad-spectrum antibiotics and acyclovir, one gram of intravenous methylprednisolone was tried for three days followed by oral prednisolone (40 mg daily) in conjunction with intravenous heparin and replacement of blood products. Within a few days of initiating the therapy, all the enlarged lymph nodes decreased in size, followed by marked improvements of hematological data and clinical conditions. She was discharged 2 months later without

sequelae.

While HHV-6 is responsible for exanthema subitum occasionally complicated with meningoencephalitis in children (1, 2), the pathogenesis of the reactivation of latent infection of HHV-6 is elusive in adults, most of whom harbor the virus. As with the case of other herpes viruses, however, it seems reasonable to assume that the reactivation of HHV-6 could also be hazardous. The considerable increase of IgG antibodies to HHV-6 in the absence of IgM antibodies indicates reactivation of the virus in this patient. It is noteworthy that except for the absence of hemophagocytosis in the bone marrow aspiration, she had most of the clinical features seen in virus-associated hemophagocytic syndrome (VAHS), a reported complication by HHV-6 (3, 4), and her condition was dramatically improved with large doses of corticosteroids. Hence we suspect that reactivated HHV-6 might have been associated with meningoencephalitis with a VAHS-like condition in this elderly woman.

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