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Case report

Human herpesvirus 6 meningoradiculitis treated with intravenous immunoglobulin and valganciclovir

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Human herpesvirus 6 (HHV-6) is being increasingly associated with multiple neurological conditions. The authors report the case of a 26-year-old man with subacute meningoradiculitis initially treated with intravenous immunoglobulin. The cerebrospinal fluid (CSF) showed pleocytosis and polymerase chain reaction (PCR) was positive for HHV-6 type B DNA in the CSF and peripheral blood. He was subsequently treated with valganciclovir with near resolution of his symptoms. *Journal of NeuroVirology* (2009) **15,** 108–109.

Keywords: HHV-6B; IVIG; meningoradiculitis; valganciclovir

Case presentation

A previously healthy 26-year-old man presented with acute weakness and numbness of his lower extremities, bilateral foot drop, and mild headache. He denied fever, chills, nuchal rigidity, or photophobia. There was no change in bowel habits or urination. He had 3/5 strength on dorsiflexion of both ankles and 4/5 strength in both extensor halluci longi. Pin-prick sensation was reduced in both feet. The rest of the exam, including tone and reflexes, was normal.

He was initially diagnosed with Guillain-Barré syndrome (GBS). A complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein, electrolytes, liver function tests, thyroid functions, vitamin B12 level, folate level, and protein electrophoresis were normal. Lyme and syphilis antibodies were negative. Herpes simplex virus type 1 and 2 immunoglobulin M (IgM) were negative. Serologies for human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) were negative. Cerebrospinal fluid (CSF) obtained by lumbar puncture (LP) showed normal protein and glucose, 158 red blood cells (RBCs)/mm^3, and 19 white blood cells (WBCs)/mm^3 (90% lymphocytes). Magnetic resonance imaging (MRI) of the brain and spine with and without contrast was normal. He completed 5 days of intravenous immunoglobulin (IVIG) and was discharged with partial improvement of symptoms. Two weeks later, he developed fever associated with chills, sweats, pharyngitis, diarrhea, desquamation of the fingertips, and mild transaminitis. He continued to complain of residual weakness and numbness in his lower extremities. Electromyography (EMG) showed reduced right peroneal compound muscle action potential response amplitudes. Needle EMG showed frequent fibrillations and positive sharp waves in the toe and ankle dorsiflexors, with reduced recruitment of normal motor units. A repeat LP revealed CSF with 3 lymphocytes/mm3 and 5 RBCs/mm3, no xanthochromia, a glucose of 49 mg/dl, and a protein of 74mg/dl. Polymerase chain reaction (PCR) was positive for Human herpesvirus 6 (HHV-6) type B DNA in the CSF and peripheral blood. CSF PCR for Borrelia burgdorferi, West Nile virus, adenovirus, herpes simplex viruses, cytomegalovirus, varicella-zoster virus, Epstein-Barr virus, Eastern equine encephalitis virus, Saint Louis encephalitis virus, enterovirus, and California group and Cache valley encephalitis viruses was negative.

The patient was then treated with valganciclovir 900 mg orally twice daily for 6 weeks, with complete recovery of motor strength but persistence of mild numbness in his feet. Electromyography and nerve conduction studies (EMG/NCS) confirmed

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the near-complete recovery with resolution of the denervation activity in the ankle dorsiflexors. Another LP was performed and all results were normal except for persistence of HHV-6B DNA.

Discussion

HHV-6 type B is usually contracted during the first 2 years of life and is one of the agents associated with roseola infantum. Since its discovery in 1986, the virus has been increasingly linked to multiple neurological conditions. It is responsible for 31% of febrile convulsions in children (Hall *et al,* 1994). Atypical febrile seizure with clustering seizures, long lasting seizures, partial seizures, and postictal paralysis are more likely to be secondary to a HHV-6 infection (Schvoerer *et al,* 2006). It has been associated with facial palsy, meningitis, GBS, and acute myelitis (Studahl *et al,* 2000). It is thought to play a role in temporal lobe epilepsy (Donati *et al,* 2003). Post-transplant acute limbic encephalitis (PALE) has been found to be secondary to HHV-6 infection (Seeley et al, 2007). HHV-6 infection is not necessarily more frequent in immunocompromised hosts (Hall et al, 1994; Schvoerer et al, 2006; Studahl et al, 2000; Donati et al, 2003). One study has shown that the prevalence of HHV-6 B DNA in the CSF is 1.3% (Ward et al, 2007).

It is unclear whether our patient suffered from acute infection, reinfection, or reactivation of latent infection. The initial clinical presentation suggested GBS, which led to therapy with IVIG. HHV-6 type B antibodies present in IVIG may enhance viral clearance and decrease inflammation.

HHV-6 infection of the central nervous system (CNS) can result in a specific syndrome, as in PALE syndrome. On the other hand, it can result in a wide array of nonspecific clinical manifestations, as prior studies reported (Studahl et al, 2000; Seeley et al, 2007).

The clinical course in our patient is consistent with a subacute lumbosacral polyradiculitis. It remains unclear whether the febrile illness that followed IVIG therapy was related to IVIG or the underlying viral illness. As we did not have access to a quantitative assay for HHV-6B DNA, we were not able to follow HHV-6B DNA viral load throughout the patient's illness, which may have been able to confirm response to treatment and resolution of viremia. Persistence of HHV-6 DNA in the CSF even after resolution of symptoms may be secondary to genomic integration of viral DNA (Ward et al, 2006, 2007).

Because our patient's CSF was abnormal, extensive investigation for other viral causes was negative, HHV-6 type B DNA was present in his CSF, and clinical symptoms resolved after antiviral therapy, we suspect our patient's syndrome was secondary to HHV-6B infection. HHV-6B infection should be included in the differential diagnosis when otherwise healthy adults present with lumbosacral polyradiculitis. Treatment of HHV-6–associated diseases with IVIG and/or valganciclovir merits further investigation.

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