Post varicella zoster virus myelitis in immunocompetent patients

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ABSTRACT

Varicella-zoster virus (VZV) leads to numerous disorders of the central and peripheral nervous systems. It usually affects immunocompromised individuals, particularly those with cancer or acquired immunodeficiency syndrome (AIDS). Those complications occur rarely in immunocompetent patients. The CNS involvement has been reported as 0.1–0.75% in several studies. The frequency of transverse myelitis during or following the varicella infection is reported as 0.3%. Those associated with herpes zoster are even less common (occurring in less than one per 1000 cases). Clinical features are paraparesis with a sensory level and sphincter impairment. We describe 2 cases of virologically confirmed myelopathy caused by VZV to highlight the possibility of its occurrence in immunocompetent subjects.

We report 2 immunocompetent patients with myelitis. The first was a 55-year-old man who developed myelitis after intercostal herpes zoster. The second was a 19-year-old boy who presented with myelopathy after varicella infection. Varicella-zoster virus (VZV) myelitis was diagnosed based on the close temporal relationship between rash and onset of clinical symptoms, and by the elevated rate of anti-VZV IgG in the CSF without oligoclonal bands in the first case, and presence of VZV DNA in the second. The course was favorable after a 3-day course of corticosteroids and 3 weeks of acyclovir. Varicella-zoster virus myelitis is uncommon; it affects essentially immunodepressed patients. We highlight the importance of considering the possibility of VZV myelitis, even in immunocompetent patients. The combination of corticoids and acyclovir must be instituted, quickly, to improve functional outcome.

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The (CSF) contained one white blood cell/mm³, 500 red blood cells/mm³, 3.8 mmol/l glucose, and 1.4 g/l protein (normal range, 0.2-0.35 g/l). Polymerase chain reaction (PCR) and antibodies of Epstein-Barr virus, herpes simplex virus, and cytomegalovirus in the CSF were negative. Elevated rates of anti-VZV IgG and anti-VZV IgM in the serum were found. The CSF anti-VZV antibody IgG was detected using the anticomplement immunofixation method. The serum/CSF ratio of anti-VZV IgG was reduced compared to ratios for total IgG and albumin, consistent with intrathecal synthesis of anti-VZV IgG antibody. An HIV screen was negative. Neoplastic markers (CEA, Ca 19.9, Ca 125, Ca 15.3, alfa-fetoprotein, beta2-microglobulin) were within normal limits. No other causes of immunological impairment were found. Intravenous (i.v.) acyclovir 10 mg/kg/8 hours for 3 weeks, and i.v. steroids (methylprednisolone 500 mg/day) for 3 days were started. He initially required urinary bladder catheterization. His gait improved slightly with physical therapy. Two years after presentation, he was asymptomatic; his neurologic examination was normal, with no recurrences or other episodes.

**Patient 2.** The second case was an immunocompetent young adult. There was no known exposure to VZV. At the age of 19 years, he developed fever and a diffuse papulovesicular rash consistent with varicella infection. Ten days later, he experienced sharp cervicalgia followed by bilateral leg paresthesia, weakness, and urinary retention after 2 days. On examination, he presented with various lesions some of which are crusty, others are infected, and a fever of 38.5°C. The neurological examination showed tetraparesis, bilateral pyramidal syndrome, cervical sensory level, disturbance of proprioceptive sensibility, and full bladder. The rest of the examination was normal. Routine hematococical tests were normal. A spinal cord MRI showed swelling of the spinal cord at the level of C4-C5, C6-C7 with 2 areas of hyper T2 signal without enhancement after Gadolinium injection (Figures 1 & 2). A cerebral MRI was normal. The CSF showed lymphocytic pleocytosis (50 cells/mm³) and elevated proteins (0.75 g/l). The search for intrathecal IgG was negative. Viral serology in blood and CSF of Epstein-Barr virus, herpes simplex virus, cytomegalovirus, and Lyme disease were normal. The VZV serology was positive with IgG, and IgM positive in blood and negative in CSF. The PCR in CSF was positive; $2 \times 10^6$ copies/ml of VZV-DNA were found. Visual and auditory evoked potentials were normal. He was treated with i.v. acyclovir 10 mg/kg for 14 days followed by oral valacyclovir 500 mg for one week, and i.v. steroids (methylprednisolone 500 mg/day) for 3 days. After 3 months, he could walk and had normal neurological examination. He has not had any recurrences or other episodes of demyelination in the 3 years since his presentation.

**Discussion.** Transverse myelitis is known to occur on a background of viral diseases, vaccinations, systemic lupus erythematosus, vasculitis, multiple sclerosis, heroin abuse, and trauma. Varicella zoster virus infection is not a common cause of transverse myelitis in immunologically normal patients. After primary infection, VZV usually remains within the ganglia. Sometimes, after reactivation in either immunocompetents or, especially, immunocompromised patients, VZV infects the spinal cord.
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cord from levels contiguous with affected dorsal root ganglia and nerves. The pathogenesis of VZV myelitis has been thought as a direct viral invasion, because the virus was isolated from the spinal cord of patients. Some researchers suggest allergic and vascular mechanisms after both primary varicella infection and herpes zoster. Post VZV myelitis typically causes bilateral sensory deficit at a certain level, paraparesis, quadriparesis, abnormal rectal and bladder function. Symptoms may appear from days to weeks after the appearance of a rash, but myelitis can develop in the absence of a rash. The lumbar CSF analysis usually reveals a mild mononuclear pleocytosis with a normal or elevated protein. Magnetic resonance imaging of the spine may produce normal results, or may demonstrate T2 hyperintense lesions in the spinal cord with occasional swelling and enhancement.

Early diagnosis of VZV-related myelitis is based on its temporal relationship to the rash and detection of VZV DNA or VZV-specific antibodies or both in the CSF. There are no established treatment regimens for transverse myelitis as a complication of VZV infection. Some researchers recommend high doses of acyclovir and steroids. Although clinical recovery is variable, many immunocompetent patients improve significantly, though fatal cases have been reported. Varicella zoster virus associated myelitis rarely recurs, particularly in immunocompetent patients. Despite the development of a vaccine to prevent zoster, even if every healthy adult in the United States over the age of 60 years is voluntarily vaccinated, there would still be 500,000 zoster cases annually, around 200,000 of whom will experience post-herpetic neuralgia, as well as stroke, blindness, and myelopathy caused by VZV reactivation.

In both of our cases, transverse myelitis related to VZV infection was diagnosed on the development of motor weakness, paraparesis, and bladder dysfunction following appearance of a rash, and on the basis of the MRI and the results of the CSF analysis. In the first case, the CSF analysis revealed elevated protein as the CSF was hemorrhagic (500 red blood cells/mm³). In VZV myelitis, the virus cannot usually be isolated from the CSF, and diagnosis relies on virologic confirmation that detects VZV DNA, anti-VZV IgG antibody, or both in the CSF. In the 2 cases, demyelinating, other infectious, inflammatory, vascular, neoplastic, and paraneoplastic etiologies of myelitis were excluded. Negative HIV serology, no evidence of solid or hematological neoplasms, and a normal immunological profile led us to consider those patients as immunocompetent.

In conclusion, based on our patients and on previous reports, we would like to bring attention to the occurrence of myelitis after VZV infection even in immunocompetent persons. Cerebrospinal fluid PCR testing has played a critical role in establishing the diagnosis of VZV infection of the CNS. Early treatment including acyclovir and steroids should improve the outcome.

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References


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