

## Letter to the Editor

## A case of cerebellar ataxia associated with VZV infection



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## ABSTRACT

The varicella zoster virus (VZV) is a neurotropic virus that becomes latent in the sensory ganglia, but later causes various neurologic complications such as meningitis, encephalitis, myelitis, meningoencephalitis, cranial neuropathy, and peripheral neuropathy [1]. While acute cerebellitis is one of the most frequent acute cerebellar diseases associated with VZV in childhood, VZV rarely causes cerebellitis in adults, with or without skin manifestations, and only a few isolated cases of adult VZV cerebellitis have been reported. We report a case of acute cerebellitis associated with VZV infection after a herpetic rash in an 80-year-old male. Functional imaging of his cerebellum showed high blood perfusion during the acute stage of the disease, though perfusion decreased in the subacute stage.

## Dear Editor,

An 80-year-old man who complained of a rash in his left occipital area around the neck also had cervicodynia. He had a mild left deviation when walking beginning on June 1, 2011 (day 1). He visited a dermatology clinic on June 14 and was prescribed valacyclovir. The patient's rash was cured after taking valacyclovir for 7 days, but the deviation progressed. He visited our hospital on day 23 and was admitted on the same day due to neuralgic pain from the left side of the back of the head and neck. He had had an operation for rectal cancer (stage 2) in 1982 and had had chicken pox about 75 years before admission. Neurological examination upon admission revealed alert consciousness, no herpetic skin rash, no meningeal irritation signs, mild truncal ataxia, inability to walk with tandem gait, slight limb ataxia and nystagmus, and no slurred speech. Laboratory findings revealed normal cell blood counts and biochemical results, with the exception of renal dysfunction (creatinine, 1.42 mg/dl; blood urea nitrogen, 36.7 mg/dl) on day 26. The complement fixation titer of VZV (varicella zoster virus) immunoglobulin G (IgG) in the serum was 1:128 and that of serum VZV IgM was 1:0.80. On day 26, cerebrospinal fluid (CSF) examination revealed the presence of 528 cells/ $\mu$ l (97% lymphocytes), 285 mg/dl protein, and 68 mg/dl glucose (blood glucose, 109 mg/dl). The VZV IgG and IgM titers in the CSF were 1:128 and 1:0.80, respectively (normal titer in the CSF is  $\leq$ 1:0.80). VZV DNA, but not herpes simplex virus DNA, detected in CSF using polymerase chain reaction (PCR).

We suspected the patient of having cerebellar disease associated with VZV infection and began intravenous administration of acyclovir at a dosage of 3 mg/kg/day on day 26. Brain magnetic resonance imaging (MRI) revealed age-matched brain atrophy and no Gd enhancement of T1-weighted images on day 25. The patient's balance disorder and cervicodynia began improving three days after the first CSF tap (day 29). The second CSF tap on day 29 revealed reduced cell numbers (208/ $\mu$ l, 97% lymphocytes) and protein (174 mg/dl) and glucose levels (78 mg/dl) (blood glucose, 109 mg/dl). We therefore

concluded that acyclovir was effective and increased its dosage from 3 to 6 mg/kg/day. Acyclovir was continued until day 40, and then replaced with oral valacyclovir (3 g/day). There was gradual improvement of the truncal ataxia. The third CSF tap on day 40 revealed further reduced cell numbers (105/ $\mu$ l, 100% lymphocytes), and the VZV IgG and IgM titers in the CSF were 1:65.4 and 1:0.80, respectively. For brain single photon emission computed tomography (SPECT) on days 28 and 68, we used a domain of  $3 \times 3$  pixels for the cerebellum and thalamus, and compared the highest domains between the two regions. We calculated the ratio between the cerebellar and thalamic domains. The ratio was 1.1918 on day 28 and was reduced to 1.0645 on day 68 (Fig. 1). We believed that the hyperperfusion of the cerebellum may be correlated with cerebellar inflammatory changes. We diagnosed the patient with acute cerebellitis.

Here we report a case of adult acute cerebellitis alone as a complication post-VZV infection. Neurological examination revealed truncal ataxia after development of a skin rash at the left occipital area and neck. Though the herpetic exanthema healed, truncal ataxia developed without hearing loss. The patient was diagnosed with acute cerebellitis with the etiology determined based on VZV PCR in CSF cells. Metastasis of primary cancer may have caused the cerebellitis. However, CSF cell cytology performed twice did not support the above conclusion and the administration of intravenous acyclovir was very effective. There are only few reports of adult acute cerebellitis on functional imaging.

Cerebellar ataxia is generally viewed as a partial sign co-existing with encephalitis and brainstem encephalitis due to VZV infection [1]. However, there are few reports of proven cerebellitis alone associated with VZV in adults confirmed by CSF viral examinations [2–6], none of which have been accompanied by a rash. Other herpetic neurological complications such as encephalitis, meningitis, optic neuritis, cranial neuropathy, myelitis, and vasculopathy have been reported in several adult cases [7]. There are two types of adult acute cerebellitis associated with VZV infection: with and without skin rash. When the

**Abbreviations:** CSF, cerebrospinal fluid; IgG, immunoglobulin G; MRI, magnetic resonance imaging; PCR, polymerase chain reaction; SPECT, single photon emission computed tomography; VZV, varicella zoster virus

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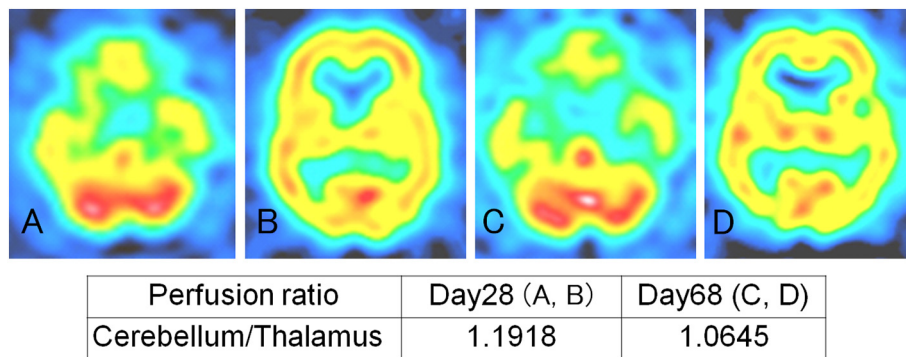


Fig. 1. Axial brain SPECT. The initial brain SPECT results are shown in panels A and B, and the follow-up brain SPECT results after 40 days are shown in panels C and D.

appearance of skin lesions due to VZV is inhibited by immunomodulation of the host in spite of reactivation of VZV, herpetic skin rash may not occur [8]. The patient in this case had a skin rash. The pathophysiology of VZV encephalitis or meningitis differs between patients with and without skin rash [1]. In patients with skin rash due to prior replication of the virus, large amounts of virus cause encephalitis with a short latency period through axonal transport or via the bloodstream. In patients without skin rash, it is thought that the virus is reactivated within spinal sensory ganglia and spreads to the central nervous system centrifugally through axonal transport. In such cases, the viral load should be low and there would be a long latency period. Although it was thought that large numbers of virus had replicated through axonal transport in our patient due to the presence of the skin lesion, we believe that selective inflammation in the central nervous system is extremely rare.

Acute cerebellitis as determined using neuroimaging in children and adults has been reported, although they are controversial. T2-weighted MRI and fluid-attenuated inversion recovery have revealed hyperintensity in the cerebellar gray matter [9], and hyperintensity as determined using T2-weighted sequences has been reported in the pons [10]. However, in the above studies, no functional imaging was performed. Our patient had hyperperfusion in the cerebellum, as determined using brain SPECT, which we believe was due to inflammation based on our CSF study results.

In conclusion, we report a case of acute cerebellitis associated with VZV infection in an adult confirmed using laboratory examination with high cerebellar perfusion at the acute stage. Adult patients with cerebellar ataxia purely due to VZV infection with rash are extremely rare.

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#### References

- [1] J.M. Echevarría, I. Casas, P. Martínez-Martín, Infections of the nervous system caused by varicella-zoster virus: a review, *Intervirology* 40 (1997) 72–84.
- [2] Y. Suzuki, A. Kanno, A.M. Minami, et al., Case of acute cerebellitis as a result of varicella zoster virus infection without skin manifestations, *Geriatr Gerontol Int* 4 (2012) 756–757.
- [3] P. Ratzka, J.C. Schlachetzki, M. Bähr, et al., Varicella zoster virus cerebellitis in a 66-year-old patient without herpes zoster, *Lancet* 367 (2006) 182.
- [4] H. Moses, M.A. Nagel, D.H. Gilden, Acute cerebellar ataxia in a 41 year old woman, *Lancet Neurol.* 5 (2006) 984–988.
- [5] S. Shilo, Y. Wiener-Well, I. Korn-Lubetzki, et al., Varicella zoster virus Cerebellitis without a rash in an immunocompetent 85-year-old patient, *Neurologist* (3) (2015) 44–45.
- [6] M. Lubomski, L. Brown, R. Markus, An unusual presentation of varicella zoster virus with acute cerebellitis and SIADH without a rash, *J. Clin. Neurosci.* 41 (2017) 90–91.
- [7] D. Gilden, R. Mahalingam, M.A. Nagel, et al., Review: the neurobiology of varicella zoster virusinfection, *Neuropathol. Appl. Neurobiol.* 37 (2011) 441–463.
- [8] D.H. Gilden, A.N. Dueland, M.E. Devlin, et al., Varicella-zoster virus reactivation without rash, *J. Infect. Dis.* 166 (1992) 30–34.
- [9] M.A. Montenegro, S.L. Santos, L.M. Li, et al., Neuroimaging of acute Cerebellitis, *J. Neuroimaging* 12 (2002) 72–74.
- [10] F. Calabria, F. Zappini, G. Vattemi, et al., Pearls & Oysters: an unusual case of varicella-zoster virus cerebellitis and vasculopathy, *Neurology* 82 (2014) e14–5.

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