Acta Med. Okayama, 2020
Vol. 74, No. 3, pp. 257–260

Acta Medica Okayama
http://escholarship.lib.okayama-u.ac.jp/amo/

Case Report

Intravenous Vitamin C as Ancillary Treatment for Cranial Polyneuritis and Meningitis due to Varicella Zoster Virus Reactivation

Takashi Hongo[a], Fusao Ikeda[b]*, Shinichi Fujioka[b], Riku Akatsuka[b], Tosifumi Fujiwara[a], and Kazuhide Yamamoto[b]

Departments of [a]Emergency Medicine,
[b]Internal Medicine, Okayama Saiseikai General Hospital, Okayama 700-8511, Japan

A 65-year-old Japanese woman developed vesicular eruptions on her right ear due to varicella zoster virus (VZV) reactivation, followed by cranial polyneuritis and meningitis affecting her right cranial nerves V, VII, VIII, IX, and X. After acyclovir administration, her facial paralysis worsened. Intravenous methylprednisolone and vitamin C were administered on Day 4 post-admission. Her symptoms steadily improved, and by Day 45 she had fully recovered. Cranial polyneuritis is a rare complication of VZV reactivation, and there is no established method of treatment. This is the first report of full recovery from cranial polyneuritis using intravenous vitamin C as ancillary treatment.

Key words: varicella zoster virus, polyneuritis, vitamin C, meningitis, facial nerve palsy

A reactivation of varicella zoster virus (VZV) may result in severe dermatomal, ophthalmic, splanchnic, cerebral, and motor complications. Because VZV is a neurotropic virus in the Herpesviridae family, the most common and troubling symptom of VZV reactivation is prolonged neuralgia. Serious neural and cerebral complications such as cranial polyneuritis and meningitis are rare [1]. There are no established methods for treating cranial polyneuritis and meningitis caused by VZV, and there are few published reports on the treatment and outcomes of patients with cranial polyneuritis and meningitis due to VZV reactivation [1-5]. Early diagnosis and treatment with acyclovir and corticosteroids is important, but only ～30% of patients experience a full recovery [4].

A multicenter prospective cohort study revealed that restoring the physiological vitamin C plasma concentration by administering intravenous vitamin C may promote recovery from VZV-associated shingles, and that doing so may relieve VZV-associated pain [6,7]. Vitamin C might thus have a beneficial effect on recovery from VZV-associated neuritis. We report the case of our patient with cranial polyneuritis and meningitis due to VZV; the patient achieved a full recovery in response to the concomitant use of intravenous vitamin C, acyclovir, and corticosteroids.

Case Report

A 65-year-old Japanese woman visited an otologist because of vesicular eruptions and pustules in her right auricle and external auditory canal (Fig. 1A). She was a hepatitis B virus (HBV) carrier but did not have a history of viral hepatitis. She had no chronic medical conditions or medical disease history of note. She was diagnosed as having VZV reactivation and was treated with oral valaciclovir hydrochloride (1,500 mg daily). Her physical condition deteriorated, and she visited the

Received September 9, 2019; accepted January 16, 2020.
*Corresponding author. Phone: +81-86-252-2211; Fax: +81-86-252-7375
E-mail: fikeda@md.okayama-u.ac.jp (F. Ikeda)

Conflict of Interest Disclosures: No potential conflict of interest relevant to this article was reported.

emergency department of our hospital with severe headache and a 2-day history of dysphagia.

On presentation, the patient was alert and, except for an axillary temperature of 37.6°C, her vital signs were normal. On neurological examination, she was found to have a hoarse voice, right-sided peripheral facial asymmetry, hypoesthesia on the right side of her face (Fig. 1B), hearing loss in her right ear, and an absent gag reflex. Her uvular was deviated to the left (Fig. 1C) but her tongue movement was normal. Her eye movement and light reflection was normal. She did not have signs of neck or limb stiffness, or paralysis of her extremities. She was clinically diagnosed as having neuritis of her right cranial nerves (V, VII, VIII, IX, and X) and was admitted to our hospital.

Her cerebrospinal fluid contained 46 lymphocytes/μL, with normal pressure and total protein levels. VZV-DNA was detected by the real-time polymerase chain reaction (PCR) method [8]. Her blood tests revealed no obvious signs of infection. She had a normal neutrophil count, and no atypical lymphocytes were detected. She was seropositive for VZV immunoglobulins G (IgG) and M (IgM) (Table 1). Her results of IgG anti-GM1, and IgG anti-GQ1b were negative, ruling out a diagnosis of Guillain-Barré syndrome or Fisher syndrome.

T2-weighted magnetic resonance imaging revealed high signal intensity in the basal neural canal and the right inner auditory canal (Fig. 2). No abnormalities associated with sarcoidosis, malignant lymphoma, or

Table 1 The patient's laboratory test on admission

Hematology			
White blood cells	4,800 cells/μL	Red blood cells	480 × 10^4/μL
Neutrophils	52.5%	Hemoglobin	14.3 g/dL
Eosinophils	1.0%	Platelet count	18.4 × 10^4/μL
Monocytes	6.5%	Prothrombin time	12.1 sec
Lymphocytes	38.0%	APTT	29.3 sec
Atypical lymphocytes	0%	D-dimer	0.5 μg/mL
Blood biochemistry			
Total protein	7.7 g/dL	BUN	21.0 mg/dL
Albumin	4.6 g/dL	Creatinine	0.55 mg/dL
Total bilirubin	1.0 mg/dL	Sodium	138 mEq/L
AST	27 IU/L	Potassium	4.1 mEq/L
ALT	19 IU/L	CRP	0.06 mg/dL
ALP	261 IU/L	Glucose	76 mg/dL
Serum viral, autoimmune, tumor markers			
HBs antigen	566 IU/mL	Anti-GM1 IgG	negative
HBV-DNA	1.8 Log IU/mL	Anti-GQ1b IgG	negative
VZV IgM	1.26 COI		
VZV IgG	128 COI	ACE	14 IU/L
VZV-DNA	negative	sIL-2R	233.9 U/mL
HSV-DNA	negative		
CMV-DNA	negative		
Cerebrospinal fluid findings			
Neutrophils	0 μ/mL	VZV-DNA	positive
Monocytes	46 μ/mL	HSV-DNA	negative
Protein	36 mg/dL	CMV-DNA	negative

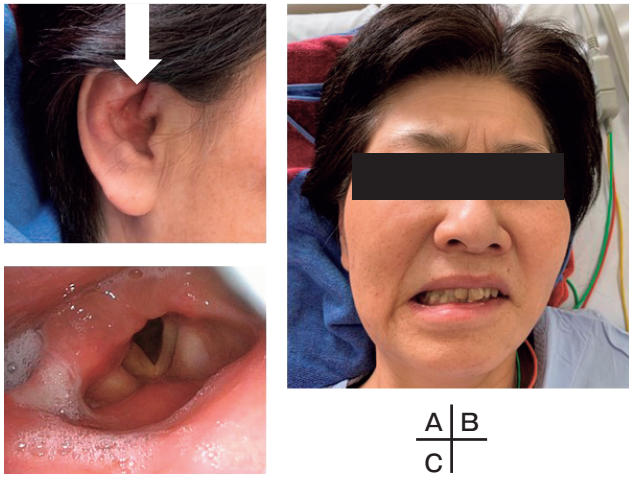

Fig. 1 The patient's physical signs. **A**, Vesicular eruptions and pustules in the right ear auricle; **B**, Facial nerve palsy on the right side of the face; **C**, Right vocal cord paralysis and deviated uvula saliva retention by laryngoscopy.

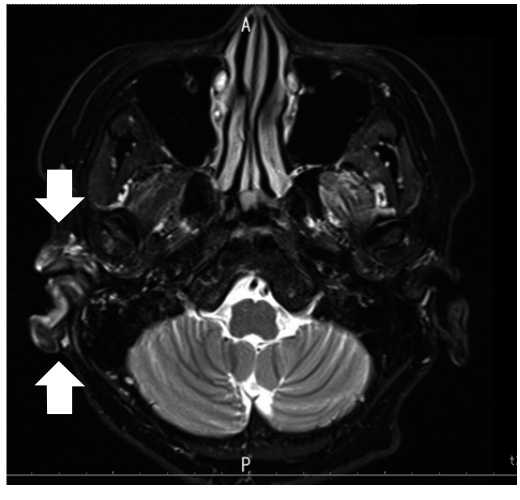

Fig. 2 MRI of the patient's head. High signal intensity at the right inner auditory canal and the basal neural canal on T2-weighted imaging.

other malignancies were detected on the CT scan of her whole body, endoscopic examination of her gastrointestinal tract, or laboratory findings. She was diagnosed with cranial polyneuritis and meningitis due to VZV reactivation.

We started treatment with intravenous acyclovir at 10 mg/kg of body weight every 8 h. Her facial paralysis and headache became more severe after admission. By Day 3 she had developed an obvious gait disorder with pain in her legs and buttocks, associated with meningitis. On Day 4, we concomitantly administered 1g of methylprednisolone and 2 g of vitamin C intravenously, with 0.5 mg of oral entecavir to prevent HBV reactivation. After 3 days of the intravenous methylprednisolone, the patient was started on oral prednisolone, which was gradually tapered from 40 mg/day to 5 mg/day over a period of 7 weeks. Her dysphagia and hoarse voice had resolved by Day 13 of her hospitalization.

The patient's neurological disorders resolved, and she was able to eat jelly on Day 15 and a normal meal on Day 26. Her clinical course is shown in Fig. 3. She was discharged on Day 45, having fully recovered from her polyneuritis. Since her discharge from hospital approx. She has not experienced a recurrence of neuritis.

Discussion

Our patient had cranial polyneuritis and meningitis due to VZV reactivation. A VZV reactivation can be triggered by emotional stress, physical trauma, smoking, recent viral infection, and decreased cell-mediated immunity, as a feature of advancing age or an immunocompromised state [9]. The neurological disorders that have been associated with VZV reactivation include neuralgia, meningitis, meningoencephalitis, cerebellitis, vasculopathy, myelopathy, Ramsay-Hunt syndrome, and cranial polyneuritis [9]; there are few published reports of cranial polyneuritis as a rare complication.

There are no established methods for treating cranial polyneuritis and meningitis caused by VZV. It has been reported that the neurological outcome is better if acyclovir and corticosteroids are administered soon after the onset [10], but that only approx. 30% of patients experience a full recovery [4]. We administered high doses of corticosteroids and vitamin C intravenously on Day 4 of the patient's hospitalization, and by Day 45 her paralysis had fully resolved. This is the first report of cranial polyneuritis and meningitis due to VZV reactivation in which the patient fully recovered from the neurological symptoms. This case suggests that use of vitamin C in addition to acyclovir and corticosteroids may result in a better outcome.

Vitamin C is a water-soluble micronutrient that acts as a potent antioxidant, cofactor of enzymes, and neuromodulator [6, 7]. Vitamin C acts as an antioxidant by scavenging reactive oxygen species to protect cells and tissues from oxidative damage. The cofactor of enzymes

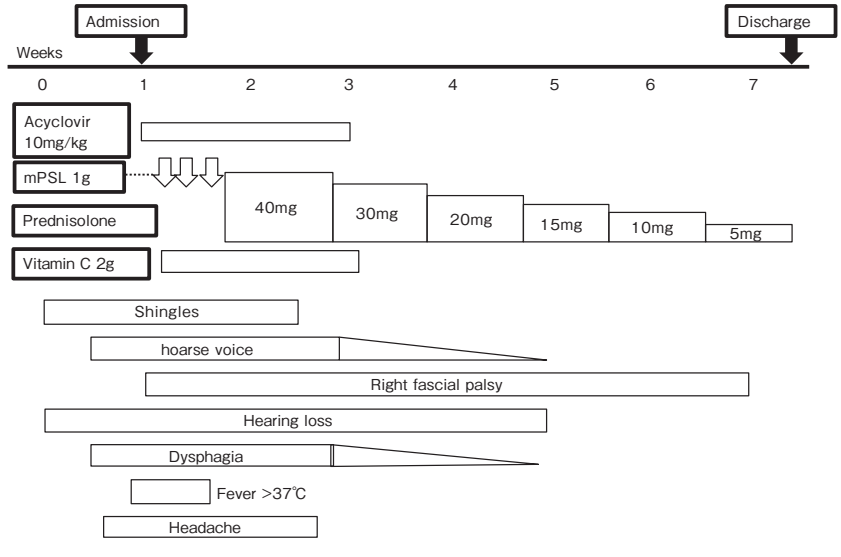

Fig. 3 The clinical course of the patient's varicella zoster virus reactivation. mPSL: methyl-prednisolone.

in Vitamin C is used for dopamine β-hydroxylase, which converts dopamine into norepinephrine. The highest vitamin C levels are found in cells of the immune system and nerve cells, reflecting the pivotal role of vitamin C in the function of these tissues. Vitamin C also plays a critical role in cellular immunity.

In cases of the reactivation of a VZV infection, neuronal tissues are vulnerable to oxidative stress, and the utilization of vitamin C is increased due to the increased oxidation caused by VZV reactivation [6,7]. We did a PubMed search on the treatment of cranial polyneuritis and meningitis, and the search did not identify any studies evaluating the effectiveness of vitamin C as ancillary treatment for cranial polyneuritis or meningitis.

The dose and duration of intravenous vitamin C treatment administered to prevent herpes zoster-associated pain has varied from 2 to 15 g daily for 5-14 days [11]. It is recommended that the daily dose of intravenous vitamin C should not exceed 10 g because high doses cause increased oxalate excretion and metabolic alkalosis [12]. We decided to administer the maximum recommended dose of intravenous vitamin C for the maximum recommended duration because our patient was depleted of vitamin C due to stress. The dose and duration were also the maximum amounts that could be claimed from insurance coverage.

The full recovery of our patient with cranial polyneuritis and meningitis due to VZV reactivation suggests that intravenous vitamin C might be an effective ancillary treatment for cranial polyneuritis and meningitis. A prospective cohort study is needed to evaluate the effectiveness intravenous vitamin C as ancillary treatment for cranial polyneuritis due to VZV reactivation.

Acknowledgements All authors made substantial contributions to the acquisition, analysis, or interpretation of data for this report: drafting the manuscript, revising it critically for important intellectual content, and final approval of the version to be published. The patient provided informed consent for her case details to be published.

References

1. Tecellioglu M, Kamisli S, Erbay MF, Kamisli O and Ozcan C : A rare presentation of cranial polyneuropathy without rash caused by Varicella Zoster Virus. Med Arch (2017) 71: 293–295.
2. Tanaka S and Mizukami S: Vagal communicating branches between the facial and glossopharyngeal nerves, with references to their occurrence from the embryological point of view. Acta Anat (1991) 142: 25–32.
3. Bharadwaj S, Moffat AC, Wood B and Bharadwaj A: Herpetic cranial polyneuritis mimicking brain stem infarction-an atypical presentation of Ramsay Hunt syndrome. BMJ Case Rep(2016) 2016: bcr2016215182.
4. Shim HJ, Jung H, Park DC, Lee JH and Yeo SG: Ramsay Hunt syndrome with multicranial nerve involvement. Acta Otolaryngol (2011) 131: 210–215.
5. Mueller NH, Gilden DH, Cohrs RJ, Mahalingam R and Nagel MA: Varicella zoster virus infection: clinical features, molecular pathogenesis of disease, and latency. Neurol Clin (2008) 26: 675–697.
6. Chen JY, Chang CY, Feng PH, Chu CC, So EC and Hu ML: Plasma vitamin C is lower in postherpetic neuralgia patients and administration of vitamin C reduces spontaneous pain but not brush-evoked pain. Clin J Pain(2009) 25: 562–569.
7. Schencking M, Vollbracht C, Weiss G, Lebert J, Biller A, Goyvaerts B and Kraft K: Intravenous Vitamin C in the treatment of shingles: Results of a multicenter prospective cohort study. Med Sci Monit (2012) 18: CR215–CR224.
8. Kimura H, Wang Y, Pesnicak L, Cohen JI, Hooks JJ, Straus SE and Williams RK: Recombinant varicella-zoster virus glycoproteins E and I: immunologic responses and clearance of virus in a guinea pig model of chronic uveitis. J Infect Dis (1998) 178: 310–317.
9. Nagel MA and Gilden D: Neurological Complications of VZV Reactivation. Curr Opin Neurol (2014) 27: 356–360.
10. Anitra C, Car and Cate McCall: The role of vitamin C in the treatment of pain: new insights. J Transl Med (2017) 15: 77.
11. Kinishi M, Amatsu M, Mohri M, Saito M, Hasegawa T and Hasegawa S: Acyclovir improves recovery rate of facial nerve palsy in Ramsay Hunt syndrome. Auris Nasus Larynx (2001) 28: 223–226.
12. De Grooth HJ, Manubulu-Choo WP, Zandvliet AS, Spoelstra-de Man AME, Girbes AR, Swart EL and Oudemans-van Straaten HM: Vitamin C pharmacokinetics in critically ill patients: A randomized trial of four IV regimens. Chest (2018) 153: 1368–1377.