The Journal of dermatology (2017.10) 44(10):e268-e269.

Herpes zoster-related aseptic meningitis and encephalomeningitis: A single faculty retrospective case study.

Mizue Fujii, Masaru Honma, Akemi Ishida-Yamamoto

Letter to the Editor **JDE-2017-0138**

Herpes zoster-related aseptic meningitis and encephalomeningitis: a single faculty retrospective case study

Mizue Fujii, Masaru Honma, and Akemi Ishida-Yamamoto

Department of Dermatology, Asahikawa Medical University, Asahikawa, JAPAN

Correspondence: Mizue Fujii MD PhD

Department of Dermatology, Asahikawa Medical University, 2-1-1-1 Midorigaoka-Higashi, Asahikawa, 078-8510, JAPAN

TEL: +81-166-68-2523 FAX: +81-166-68-2529

Email: ma0dj@asahikawa-med.ac.jp

Word count: 497/500words

Tables and figures: 1 table

Running head: zoster-related encephalomeningitis (33/50 characters)

Key words: herpes zoster, aseptic meningitis, encephalomeningitis, skin score, fever up, headache

Dear Editor

In contrast to zoster-related pain, involvements of central nervous system (CNS), such as myelitis and encephalomeningitis, are relatively rare complication of herpes zoster (HZ), but an essential factor determining prognosis and impaired quality of life (1). In this study, details of HZ-related aseptic meningitis and encephalomeningitis were verified focusing on the clinical features.

The information was retrospectively collected from medical records at the Department of Dermatology, Asahikawa Medical University from January 2006 to December 2016. There were seven cases of HZ-related CNS involvements (Table). In all cases, the symptoms of CNS involvements followed skin lesions of HZ, and varicella-zoster virus (VZV)-DNA was detected in cerebrospinal fluid by polymerase chain reaction. While no case presented dissemination of HZ eruption, the skin lesions were widespread and the severity was rated as score 2 or more than score 2 in most of the cases. Fever higher than 37.5°C and headache expanded on entire scalp were observed in all cases and five cases (71.4%), respectively. Three cases including two encephalomeningitis cases showed signs of meningeal irritation, such as neck stiffness and Kernig's sign. Laboratory findings reflecting systemic inflammation, such as leukocytosis and elevation of C-reactive protein level in peripheral blood, were within

minimal change. While none of the meningitis case died, all encephalomeningitis cases died of sepsis or circulation/respiratory failure caused by encephalitis.

Except a 58-year-old immunocompetent individual, four cases were elder than 70 years old, and two cases in her thirties or forties were treated with long term systemic prednisolone. It is noteworthy that HZ lesions emerged even on extracranial nerve area in three of seven cases (42.9%) as previously described (2). In all cases with CNS involvement, severity scores of skin rashes were relatively high, which can be correlated with development of post-herpetic neuralgia (PHN) (3). Although a relationship between severe skin lesions and CNS involvements has not been clearly described, severe widespread HZ skin lesion might be associated not only with PHN but also with CNS involvements.

Regarding symptoms related with meningitis and encephalomeningitis, fever and headache expanding on entire scalp were most frequently observed at first visit, and these symptoms may be key signs for diagnosis of zoster-related meningitis in early period as previously described (2). A persistent febrile symptom higher than 37.5°C with unknown sources even against anti-viral treatment for two or three days requires examination of CSF collected by lumbar puncture to determine CNS infection. Moreover, focal symptoms, such as acutely altered consciousness, personality change, or epileptic

seizures, suggest complication of encephalomeningitis and the poor prognosis compared with aseptic meningitis (4). Duration until initiation of treatment was not significantly related to the zoster-associated CNS complication. While patient of herpes simplex encephalitis treated with acyclovir can present better outcome compared with vidarabine (5), any difference cannot be shown in this study.

Zoster-related CNS involvement can be a life-threatening complication requiring proper diagnosis in the early period. Clinicians should pay attention to the higher risk of VZV-related CNS infection especially in elderly or immunocompromised patient.

Conflict of interest: None declared

Reference

1. Gilden DH, *et al.* Neurologic complications of the reactivation of varicella-zoster virus. *N Engl J Med* **342**:635-45, 2000..

2. Becerra JC, *et al.* Infection of the central nervous system caused by varicella zoster virus reactivation: a retrospective case series study. International journal of infectious diseases. *Int J Infect Dis* **17**:e529-34, 2013.

3. Nagasako EM, *et al.* Rash severity in herpes zoster: correlates and relationship to postherpetic neuralgia. *J Am Acad Dermatol* **46**:834-9, 2002.

4. Cunha BA, Strollo S, Durie N, Ibrahim MS. Facial herpes zoster complicated by varicella zoster virus (VZV) encephalitis: The diagnostic significance of atypical lymphocytes in cerebrospinal fluid (CSF). *Heart Lung* **40**:164-7, 2011.

5. Whitley RJ, *et al.* Vidarabine versus acyclovir therapy in herpes simplex encephalitis. *N Engl J Med* **314**:144-9,1986.

Table1 Summary of HZ cases with aseptic meningitis and encephalomeningitis

Case 1-5: aseptic meningitis, case 6-7 encephalomeningitis

M: male, F: female, lt: left, rt: right

SLE: Systemic lupus erythematosus, APS: anti-phospholipid syndrome, HT: hypertension, DM: diabetes mellitus, PAF: parenchymal atrial fibrillation

PSL: prednisolone, CyA: ciclosporine A, ACV: acyclovir, N.A: not available

*Period: Period from the onset of zoster to the start of antiviral treatment

Duration of fever: duration of fever over 37.5°C after initiation of anti-viral treatment

Encephalomeningitis was diagnosed if the patients presented signs of cerebral parenchymal involvement such as acutely altered consciousness, personality change, epileptic seizures or focal neurologic signs and either an elevated CSF white blood cell (WBC) count ($>5\times10^6$/l) or protein level >40 mg/l, or electroencephalogram findings consistent with encephalomeningitis. Aseptic meningitis did not show signs of cerebral parenchymal involvement.

Skin index (the severity of skin lesion) was scored depending on lesional area of involved dermatome: Score 1 for <30%, score 2 for 30-70%, score 3 for >70% area of an involved dermatome.

Table: Summary of HZ cases with aseptic meningitis and encephalomeningitis

case	age/sex	complication	immuno-suppressant	skin lesion of HZ		treatment for HZ (period*)	symptoms other than skin lesions					outcome
				dermatome	severity		duration of fever	headache	vomiting	parenchymal involvement	meningeal irritation	
1	72/F	bronchial asthma	-	lt. V1	2	ACV (3 days)	2 days	+	-	-	-	PHN
2	49/F	SLE	PSL15mg/day	rt. S2-5	N.A.	vidarabine (N.A.)	1day	+	+	-	-	voiding dysfunction
3	37/F	SLE, APS	PSL10mg/day, CyA 160mg/day	rt. Th3-4	2	ACV (1 day)	1 day	+	-	-	+	PHN
4	89/M	neurogenic bladder	-	rt. V1	3	ACV (4 days)	3 days	-	-	-	-	-
5	58/F	-	-	rt. C2-3	3	ACV (11 days)	1 day	+	-	-	-	PHN
6	77/M	HT, DM	-	lt. V1	3	ACV (2 days)	5 days	-	+	+	+	deceased by sepsis
7	84/M	HT, PAF	-	lt. V3	2	vidarabine (2 days)	4 days	-	-	+	+	deceased by encephalitis