

# A case of acute aseptic meningitis associated with herpes zoster

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## = Abstract =

Herpes zoster is caused by the varicella-zoster virus (VZV), which affects nerve ganglions. VZV infection may be associated with neurologic complications, which are usually observed after vesicular exanthem. Acute aseptic meningitis is a rare complication of VZV reactivation. We report the case of a previously healthy 14-year-old boy who suffered from aseptic meningitis that was attributed to reactivated VZV infection with exanthem; the patient had undergone vaccination against varicella. This condition can be confirmed by the detection of VZV DNA in the cerebrospinal fluid. The patient was treated with acyclovir and recovered fully. (Korean J Pediatr 2009;52:705-709)

**Key Words :** Varicella-zoster virus, Aseptic meningitis

## Introduction

Varicella-zoster virus (VZV), one of the herpes viruses, causes chickenpox in children; the virus remains latent in the sensory ganglia and causes herpes zoster on reactivation. Herpes zoster is characterized by painful vesicular skin lesions along the dermatome and may lead to various neurological complications such as postherpetic neuralgia, motor paralysis, aseptic meningitis, encephalitis, and myelitis<sup>1)</sup>. Among these complications, aseptic meningitis is quite rare, and there are few reports in literature<sup>2)</sup>.

Here, we report the case of a 14-year-old boy who was diagnosed with aseptic meningitis after suffering from herpes zoster; the polymerase chain reaction (PCR) analysis revealed the presence of VZV DNA in the patient's cerebrospinal fluid.

## Case report

A 14-year-old boy visited our outpatient clinic with a

primary complaint of high fever, periorbital vesicles with swelling, and headache. The patient, who did not have any specific medical history, had noticed vesicles with pruritis and tenderness around his left forehead and the medial side of the left periorbital region 1 week before his visit; 4 days after noting these symptoms, he visited a local practitioner for the treatment of high fever, headache, and progressive swelling and pain around the skin lesion. The patient was treated with per oral medication; however, there was no improvement in his symptoms and after experiencing stiffness and pain in the neck for 1 day, he was referred to our outpatient clinic. He had suffered from chickenpox at the age of 5, despite being vaccinated at 15 months of age. Among his 3 siblings, a younger brother had suffered from chickenpox at 3 years of age, and the patient and his mother had a history of herpetic oral lesions.

At his first visit, the patient's weight and height were 51.1 kg (50-75<sup>th</sup> percentile) and 169.5 cm (75-90<sup>th</sup> percentile), respectively, and the examination of his vital signs revealed the following findings: pulse rate, 90/min; body temperature, 37.8°C; respiratory rate, 22/min; and blood pressure, 110/70 mmHg. He complained of severe headache and otalgia and showed left periorbital swelling, mild conjunctival injection of the left eye, and painful vesicular skin lesions around the left forehead and left medial periorbital area (Fig. 1, 2). Tonsillar injection, or enlargement, and eardrum injection were not observed; however, we could observe oral ulcers and

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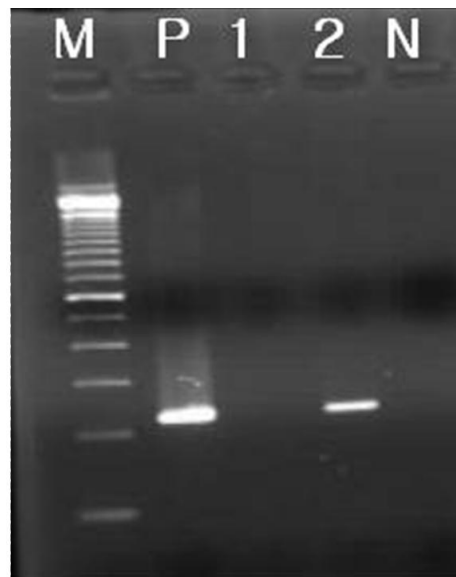


**Fig. 1.** Multiple vesicles are seen on the left medial periorbital area.



**Fig. 2.** Multiple vesicular eruptions are seen on the left forehead and the left medial periorbital area.

prominent left cervical lymph nodes. The results of the physical examinations of the chest and abdomen were normal, and the patient did not show any deformity or limitation in the motion range of the limbs. In the neurological examination, neck stiffness and Kernig sign were noted; however, we did not note Brudzinski sign, ataxia, and other focal ne-



**Fig. 3.** VZV DNA shown by polymerase chain reaction.

urological abnormalities.

The laboratory examinations provided the following results: WBC count,  $8,400/\text{mm}^3$ ; hemoglobin concentration,  $13.8 \text{ g/dL}$ ; hematocrit,  $41.6\%$ ; and platelet count,  $273,000/\text{mm}^3$ ; the values obtained from the electrolyte analysis and urinalysis were within normal limits, and C-reactive protein (CRP) was absent. In the cerebrospinal fluid (CSF) analysis, the opening pressure was  $250 \text{ mmH}_2\text{O}$ , and the cell counts were  $180 \text{ WBCs}/\text{mm}^3$  (100% mononuclear cells) and  $6 \text{ RBCs}/\text{mm}^3$ ; the protein and glucose levels were  $76.2 \text{ mg/dL}$  and  $52 \text{ mg/dL}$ , respectively. We did not observe any bacteria in the CSF gram stain and the CSF culture. The CSF was positive for anti-VZV IgG and VZV by PCR (Fig. 3), and the serum VZV antibody tests by ELISA (enzyme linked immunosorbent assay) gave positive results for anti-VZV IgG but negative results for anti-VZV IgM.

The patient did not exhibit any symptoms of hearing loss, and the results of the otoscopic examinations and the auditory-function test revealed a normal eardrum and normal pure tone, respectively; however, keratoconjunctivitis was noted during an eye check up. There were no indications of epileptogenic discharges in the EEG, which had normal background waves, and the MR images of the patient's brain did not show any abnormal features.

The CSF studies proved that the patient was suffering from aseptic meningitis, and the oral ulcers and the vesicular skin lesions around the patient's left forehead and left periorbital area indicated an infection by Herpes simplex virus

or VZV; therefore, we performed PCR for HSV and VZV in the blood and CSF, and treated the patient with acyclovir 10 mg/kg every 8 hours via intravenous (IV) route. The patient's symptoms showed an improvement after 4 days, and on the 5th day of admission, the results from the CSF PCR for VZV were found to be positive, confirming the initial impression. A follow-up CSF study was done after 8 days, and we obtained better results in this study: closing pressure, 130 mmH<sub>2</sub>O; WBC count, 57/mm<sup>3</sup> (100% mononuclear cells); RBC count, 0/mm<sup>3</sup>; protein content, 28 mg/L; and glucose content, 52 mg/L. There was no bacterial growth, and the results of the second round of CSF PCR for VZV were negative. The patient was discharged 10 days after he had been admitted; at discharge, his general condition had improved, and he is undergoing treatment for keratoconjunctivitis at the ophthalmology clinic.

## Discussion

Herpes zoster appears as a vesicular skin lesion that develops along the unilateral skin sensory dermatomes; it is caused by the reactivation of latent VZV in aged or immunocompromised patients. Most patients are easily treated without any sequelae; however, in some patients, herpes zoster may lead to ophthalmologic, dermatologic, and neurologic complications. The infection usually affects the dermatome of the thoracic and craniocervical ganglia, and it is usually limited to 1 or 2 ganglia on one side; the infection is rarely manifested in a bilateral or systemic form<sup>3-5</sup>.

The mechanism behind VZV reactivation has yet not been clarified. However, patients who have suffered from chickenpox harbor the virus in their neuronal system through their lifetime; in these patients, virus reactivation is suppressed by acquired immunity against the virus. However, lymphoma, hematologic tumors, immunosuppression, and malignancies, which usually suppress the immune system, are associated with a high rate of viral reactivation<sup>6</sup>, reactivation is especially high in pediatric patients who have suffered from chickenpox in the first year of life<sup>7</sup>.

VZV infection may appear in various forms such as asymptomatic herpes zoster, postherpetic neuralgia, and vasculitis; it may also manifest with stroke, meningitis, myelitis<sup>8</sup>, and rare GI problems such as intestinal pseudo-obstruction by VZV<sup>9</sup>.

The common neurological complications associated with herpes zoster are postherpetic neuralgia, myelitis, encephalitis,

ventriculitis, aseptic meningitis, white-matter disease, etc., and these complications are usually seen in aged or immunosuppressed patients. The infections that invade the cerebral and cervical ganglia or show disseminated skin lesions are associated with higher mortality<sup>3</sup>. These CNS complications are closely related to the multiplication of the virus in the neurons, as VZV may enter from the blood stream or directly from the sensory ganglia in which the latent viruses were harbored<sup>8</sup>. Patients with VZV meningitis may suffer from high fever, severe headache, cervical rigidity, seizure, ataxia, hemiplegia, and even coma; these symptoms may appear within days after the appearance of the skin lesion, but VZV meningitis may also develop without any of these symptoms<sup>10</sup>. In a previous study, 38% of herpes zoster patients showed cellular increment in the CSF without exhibiting any symptoms of meningeal irritation, except headache<sup>2</sup>, and some reports have stated that up to 30%-40% of asymptomatic herpes zoster patients show increased cell counts and elevated protein levels in the CSF<sup>11</sup>. VZV meningitis occurs in 0.5%-2.5% of the patients, and they usually show a full recovery without developing other complications<sup>12, 13</sup>.

Encephal meningitis due to herpes zoster can be diagnosed on the basis of characteristic clinical manifestations and laboratory findings<sup>14</sup>. The findings of CSF analysis in this condition are similar to those reported in case of viral encephal meningitis, including increased intracranial pressure, lymphocytosis, increased protein level, and normal glucose levels<sup>15</sup>. There are various methods of testing CSF for VZV. First, the virus can be isolated from either CSF or brain tissue, or CSF can be tested for the presence of VZV antibodies. Second, VZV particles can be directly visualized by electron microscopy. Third, the VZV antibody titer in serum or CSF can be quantified. Lastly, VZV DNA in CSF can be isolated by PCR<sup>14</sup>. PCR analysis of blood and CSF can be used to detect systemic and CNS VZV infections, and PCR is especially useful in diagnosing CNS infections and zoster sine the infection which requires early antiviral medication; PCR is being widely used because of its speed and accuracy<sup>3</sup>. Kang and his colleagues<sup>16</sup> has reported two immunocompetent children with zoster meningitis, diagnosed by PCR. In the present case, the VZV antibody titer in the patient's blood and CSF were positive for IgG, but negative for IgM. However, we were able to diagnose a herpes zoster meningitis by PCR of the CSF samples. Since the nature of the patient's pain was indicative of acute-phase disease, we presumed that the IgM-negative results

from the serum and CSF samples were either false-negative results or that the anti-VZV IgM level decreased rapidly before testing<sup>17)</sup>.

Since herpes zoster is a viral disease, conservative care or acyclovir administration is the routine treatment, and steroid therapy is employed as an optional addition<sup>6, 18)</sup>. The administration of acyclovir within 48-72 hours of the appearance of zoster effectively relieves acute pain and the vesicles, induces a higher rate of remission, and deters the virus from spreading throughout the patient's body<sup>19)</sup>. However, since herpes zoster in children with no underlying disease is not painful and critical enough to mandate the use of acyclovir, it is recommended to use this drug in children with complications or those with suppressed immune systems<sup>15, 20)</sup>. In patients with suspected VZV infection of the central nervous system, IV injection of acyclovir is necessary, since oral medication is not sufficient to provide the effective dosage<sup>2)</sup>. The concomitant use of steroids helps to repress the inflammation process and alleviates edema, thereby decreasing acute pain and preventing neuralgia after herpes zoster; however, the use of steroids in children suffering from comparatively lesser pain is not advisable<sup>21)</sup>.

Vaccination is the most important factor in the management of herpes zoster infections. When appropriately performed, chickenpox vaccination not only reduces the possibility of acquiring the virus but also decreases mortality, morbidity, and the costs associated with an infection, if it does happen<sup>22)</sup>. There are reports of herpes zoster infections in vaccinated patients, e.g., the patient in this case, who had undergone vaccination at 15 months of age<sup>22, 23)</sup>. Various types of chickenpox vaccinations are available to prevent such infections, but there are few reports on the immune reaction or efficacy of these vaccination procedures; therefore, further in-depth studies on this aspect are called for.

## 한글 요약

### 대상포진에 의한 무균성 수막염 1예

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대상포진은 흔한 질환으로 여러 가지 합병증을 동반 할 수 있으나 대상포진에 동반되어 수막염이 생긴 경우는 보고는 많지 않다. 저자들은 15개월에 수두 예방접종을 시행 받았고, 5세 때 수두를 앓은 과거력이 있던 건강한 14세 남자 환자에서 대상포진

에 동반되어 급성 무균성 수막염이 발생한 증례에서 뇌척수액에서 중합효소연쇄반응을 통해 VZV DNA를 검출한 1예를 경험하였기에 문헌 고찰과 함께 보고하는 바이다.

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