Persistent Hiccups and Vomiting with Multiple Cranial Nerve Palsy in a Case of Zoster Sine Herpete

Takeshi Yoshida¹, Natsumi Fujisaki¹, Ryo Nakachi¹, Takeshi Sueyoshi², Shugo Suwazono¹ and Masahito Suehara¹

Abstract

A 76-year-old man came to our hospital complaining of hiccups and vomiting lasting for five days. A neurological examination showed dysfunction of cranial nerves V, VII, VIII, IX and X on the left side. Cerebrospinal fluid polymerase chain reaction for varicella zoster virus-DNA was positive. The patient responded well to treatment with intravenous acyclovir and steroids. To the best of our knowledge, this is the first case report of zoster sine herpete presenting with persistent hiccups and vomiting. It is important to keep in mind that herpes zoster can present with symptoms that closely resemble those of intractable hiccups and nausea of neuromyelitis optica. Early detection of the virus is critical for making appropriate treatment decisions.

Key words: varicella zoster virus, zoster sine herpetica, hiccups, intractable hiccups and nausea

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Introduction

Varicella zoster virus (VZV) infection causes a wide variety of neurological symptoms, including cranial neuropathy; these neurological symptoms may present without associated herpetic skin eruptions (zoster sine herpete) (1). There have also been a few case reports of herpes zoster accompanied by the neurological complication of persistent hiccups (2-6). To the best of our knowledge, this is the first case report of zoster sine herpete presenting with persistent hiccups and vomiting. However, intractable hiccups and nausea (IHN) has been recognized to be an early sign of neuromyelitis optica (NMO) (7). We herein present this case and discuss the importance of herpes zoster as a differential diagnosis of persistent hiccups.

Case Report

A 76-year-old man came to our hospital complaining of a low-grade fever, left-sided facial pain, hiccups and vomiting lasting for five days, followed by the development of hoarseness and difficulty in walking. His medical history included type II diabetes mellitus and, in the remote past, pulmonary tuberculosis. On a physical examination, he was found to be afebrile, and his other vital signs were within the normal limits. Frequent hiccups were noticed throughout the examination. A meticulous search for herpetic eruptions on his face, ear, mouth and pharynx did not reveal any lesions. A neurological examination showed mild left facial weakness, a delayed vestibulo-ocular reflex upon leftward head rotation, hoarseness and a decreased gag reflex. No nuchal rigidity was detected. The patient was unable to walk more than a few steps, as his gait was wide-based and ataxic. He was therefore admitted to our hospital for a further evaluation. A few days after admission, he developed left-sided hearing loss and dysphagia (Fig. 1). A follow-up examination showed a positive curtain sign on the left side. On laryngeal fiberoscopy performed on day 15, his left vocal cord was fixed at the near-midline position. The results of a blood test conducted on day 5 were within the normal ranges: white blood cells, 8,310/μL; red blood cells, 6.03×10⁶/μL; hemoglobin, 16.3 g/dL; platelets, 13.2×10⁴/μL; and C-reactive protein, 0.27 mg/dL. The patient was negative for all tested autoantibodies, including antinuclear antibodies, SS-A, SS-B, myeloperoxidase anti-neutrophil cytoplasmic protein.
antibody (MPO-ANCA) and PR-3 ANCA. A cerebrospinal fluid (CSF) analysis performed on day 5 demonstrated marked pleocytosis (total cells, 227/μL; mononuclear cells, 220/μL; polymorphonuclear cells, 7/μL). There were also a mild increase in the CSF protein level (68.0 mg/dL) and IgG index (0.74). The VZV antibody index was significantly elevated (9.82), and a CSF polymerase chain reaction (PCR) test for VZV-DNA was positive. The CSF adenosine deaminase (ADA) level was 4.5 U/L, and a CSF culture for Mycobacterium tuberculosis was negative. A nerve conduction test of the left facial nerve showed a decreased combined muscle action potential and an abnormal blink reflex with a diminished R1/R2 recorded at the left orbicularis oculi, both consistent with left facial nerve palsy. Brain magnetic resonance imaging (MRI) revealed enlarged cranial nerves with contrast enhancement in the area adjacent to the entrance to the auditory canal. There were no lesions in the brain parenchyma, including the medulla oblongata (Fig. 2). We immediately initiated treatment with intravenous ampicillin (6 g/day to cover Listeria infection) and intravenous acyclovir (1,500 mg/day). However, the patient’s facial weakness and ataxia worsened, and the dysphagia progressed, necessitating tube feeding. A follow-up MRI scan obtained on day 16 showed no changes from the previous image. Beginning on day 17 and upon confirmation of VZV-DNA PCR positivity, a three-day course of pulsed methylprednisolone was added to the current treatment regimen, followed by oral prednisolone (50 mg/day) with gradual tapering. After receiving the steroid therapy, the patient’s symptoms began to gradually improve. A follow-up CSF analysis performed on day 37 showed dramatic improvements in the pleocytosis, CSF protein level and VZV antibody index, as well as a negative VZV-DNA PCR test result. Two months after admission, the patient achieved an almost complete recovery, with the exception of left-sided hearing loss. Follow-up laryngeal fiberscopy performed on day 45 revealed normalized left vocal cord movement, without any herpetic eruptions. A follow-up blink reflex test
conducted on day 72 also showed a significant improvement in the facial nerve function.

**Discussion**

In this report, we presented the case of a patient with zoster sine herpete presenting with persistent hiccups and vomiting. CSF VZV-DNA PCR and serological tests were effective in making an early diagnosis. The most important lesson in this case is that herpes zoster can present with persistent hiccups and vomiting, thus mimicking IHN. The early detection of the virus not only enabled the prompt initiation of antiviral treatment, but also prevented the administration of a possibly unnecessary large dose of steroids for NMO.

Although persistent hiccups are caused by many other pathologic conditions (8) (Table 1), the presence of nausea/vomiting may help to limit the differential diagnosis. As shown in Table 2, among the five previous case reports, the patient reported by Morinaka et al. presented with hiccups associated with nausea and vomiting and was later found to have laryngeal zoster. Although our patient did not display any herpetic eruptions on either the larynx or pharynx, vagus nerve dysfunction was undoubtedly present based on the findings of our neurological examination and the results of laryngeal fiberscopy. The remaining four patients presented with zosteric skin lesions on the neck, trunk or leg and did not have accompanying nausea or vomiting. Taken together, it is likely that vagus nerve involvement in patients with herpes zoster results in persistent hiccups associated with nausea and/or vomiting.

As Misu et al. previously reported, the dorsal medulla, including the area postrema and solitary tract nucleus, is thought to be responsible for IHN in patients with NMO (9). The area postrema directly receives sensory input from the vagus nerve and is a key component in the emetic response (10). Based on this anatomic connection, we speculate that herpes zoster of the pharynx and/or larynx may present with symptoms indistinguishable to the IHN of NMO.

We herein presented a case of zoster sine herpete presenting with persistent hiccups, vomiting and unilateral multiple cranial nerve palsy. It is important to keep in mind that herpes zoster can present with symptoms that closely resemble the IHN of NMO. Early detection of the virus is critical for making appropriate treatment decisions.

**The authors state that they have no Conflict of Interest (COI).**

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**Table 1. Causes of Persistent Hiccups**

<table>
<thead>
<tr>
<th>Central nervous system</th>
<th>Cranio cerebrospinal injury</th>
<th>Neoplastic diseases</th>
<th>Cerebrovascular diseases</th>
<th>Infectious diseases</th>
<th>Spinal cord processes</th>
<th>Psychiatric</th>
<th>Metabolic, toxic and infectious</th>
<th>Renal failure, hyponatremia, herpes zoster</th>
<th>Ear, nose, and throat diseases</th>
<th>Thoracic</th>
<th>Pneumonia</th>
<th>Pleuritis</th>
<th>Mediastinitis</th>
<th>Myocardial infarction</th>
<th>Esophageal diseases</th>
<th>Diaphragm abnormalities</th>
<th>Abdomen</th>
<th>Gastric disorders</th>
<th>Pancreatic disorders</th>
<th>Hepatobiliary disorders</th>
<th>Subphrenic abscess</th>
<th>Abdominal aortic aneurysm</th>
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</thead>
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**Table 2. Comparison of Clinical Data of the Present Case and Previous Literature of Intractable Hiccups Associated with Herpes Zoster**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Our case</th>
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<th>4</th>
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<th>6</th>
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<td>73 M</td>
<td>29 M</td>
<td>73 M</td>
<td>70 M</td>
<td>44 M</td>
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<td>DM</td>
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<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>Cranial nerve palsy</td>
<td>V, VII, VIII, IX, X</td>
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<td>-</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>Herpetic eruption</td>
<td>-</td>
<td>larynx, pharynx, external ear</td>
<td>C 3-5</td>
<td>C 2-3</td>
<td>L 2-3 zoster and varicella</td>
<td>Th 3-5</td>
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<td>-</td>
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<tr>
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NE: Not Examined
References


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