Herpes Zoster Ophthalmicus Masquerading as Cluster Headache, Complicated by Delayed Eruption

Hidenori Sanayama 1, Michito Namekawa 2, Yoshio Sakiyama 3, Hitoshi Sugawara 1

1. Department of Comprehensive Medicine 1/Division of General Medicine, Saitama Medical Center, Jichi Medical University, Saitama, JPN
2. Health Administration Center, Saitama Prefectural University, Saitama, JPN
3. Department of Comprehensive Medicine 1/Division of Neurology, Saitama Medical Center, Jichi Medical University, Saitama, JPN

Corresponding author: Hidenori Sanayama, sanayama@jichi.ac.jp

Abstract

We present a 61-year-old Japanese man afflicted with Herpes zoster ophthalmicus masquerading as cluster headache, complicated by delayed eruption.

His initial clinical presentation featured intractable left-sided cephalic pain, persistent nausea, ipsilateral ophthalmalgia, accompanied by periorbital edema and conjunctival injection. An initial diagnosis of “cluster headache” was rendered, and transient relief was achieved through the administration of pure oxygen inhalation and subcutaneous sumatriptan. However, the emergence of periocular vesicles on the left side more than a week following symptom onset necessitated a reevaluation, leading to a revised diagnosis of “painful trigeminal neuropathy attributed to acute Herpes zoster.”

Analysis of cerebrospinal fluid revealed pleocytosis and an elevated protein concentration, despite the absence of meningeal signs, and a high titer of antibodies specific to the varicella-zoster virus. The prompt administration of intravenous acyclovir and oral prednisolone successfully alleviated his cephalic pain. Regrettably, a delay in the initiation of appropriate therapeutic measures resulted in the development of secondary glaucoma. However, a favorable outcome was achieved as his visual acuity was restored following intensive ophthalmological intervention.

It is imperative to emphasize the importance of distinguishing herpes zoster from cluster headache, especially in cases involving elderly patients or characterized by persistent cephalo-ophthalmalgia without typical fluctuation of symptoms.

Introduction

Herpes zoster ophthalmicus (HZO), constituting approximately 10 to 20 percent of all herpes zoster (HZ) cases, arises from the reactivation of the varicella-zoster virus (VZV) and primarily affects the ophthalmic division of the trigeminal nerve [1]. Typically, acute painful trigeminal neuropathy and cutaneous eruptions manifest concurrently, albeit with instances of pain preceding rashes by several days. Notably, an extended temporal interval of more than a week between these occurrences is feasible, and in some cases, the characteristic rash may never materialize, denoted as ‘zoster sine herpete.’ The diagnosis of such cases can be challenging, and in these circumstances, a polymerase chain reaction (PCR) assay for VZV in cerebrospinal fluid (CSF) serves as a valuable diagnostic tool [2].

The ophthalmic division of the trigeminal nerve further anatomically segregates into the nasociliary, frontal, and lacrimal branches. The nasociliary branch encompasses innervation of both the ipsilateral nasal region and the anterior segment of the eyeball, encompassing critical ocular structures such as the cornea, iris, sclera, and choroid. Therefore, the presence of herpetic eruptions in the lateral aspect of the nose assumes particular significance as a harbinger of ophthalmic complications in HZO, a phenomenon known as “Hutchinson’s sign” [1].

In this report, we detail a case of HZO that was initially misdiagnosed as cluster headache due to the delayed onset of characteristic eruptions.

Case Presentation
FIGURE 1: Ocular lesions, and facial skin eruption thought to be Hutchinson’s sign

The visage of the patient under scrutiny. A conspicuous discrepancy is evident when comparing the left and right sides of the face. The left side is distinguished by marked conjunctival injection and edematous eyelid. As shown in the arrow part, the presence of scabbed pigmented blisters is discerned along the left forehead, eyelid, and the lateral aspect of the nose. The patient has given written consent for this image to be published.

A 61-year-old Japanese man, bearing a medical history marked by diabetes mellitus (Hemoglobin A1c 7.1%) and hypertension, experienced the sudden onset of left-sided cephalalgia, accompanied by nausea. He had a prior diagnosis of pearl tumor tympanitis, and surgical interventions had conferred upon him sensorineural hearing impairment, without any accompanying facial sensory disturbances or palsy. The unrelenting headache progressively worsened. Brain computed tomography (CT) scans yielded no remarkable findings, and the administration of both loxoprofen and carbamazepine proved ineffectual.

Two days following the onset of symptoms, the patient sought evaluation at an ophthalmological clinic due to pronounced periorbital edema and ophthalmalgia in his left eye. He received a diagnosis of conjunctivitis, and intraocular pressure was noted to be within the normal range. Importantly, corneal herpes was excluded as a contributing factor. Three days later, as his cephalalgia became more severe, his agitation escalated. Subsequently, a diagnosis of cluster headache was established. A treatment composed of inhaling pure oxygen and receiving subcutaneous sumatriptan injection provided temporary relief. However, oral
© 2023 Cureus

verapamil and amitriptyline failed to produce any beneficial effects.

Two days later, vesicular eruptions emerged on his left forehead and the dorsum of his nose. About three
days later, at a follow-up visit, he was diagnosed with shingles, even though the rashes had scabs. His ability
to move the left eye was partially constrained in all directions. An oral prednisolone regimen at a dose of 40
mg per day was initiated, resulting in a rapid improvement in his headache. However, his visual acuity
deteriorated, necessitating admission to our hospital for further management.

He presented alert and normothermic. The headache was markedly relieved. At the same time, there were
obvious signs of hyperesthesia, hyperalgesia and dysesthesia localised to the left frontal region, with discrete
scabby herpetic eruptions (Figure 1). Importantly, meningeal signs were absent.

On detailed ophthalmologic examination, the patient’s right eye was unremarkable, while his left eye
showed a significant reduction in visual acuity to the point of only recognizing hand movements. In
particular, the left eye was characterized by marked bulbar conjunctivitis, corneal opacity with associated
edema, sluggish pupililar light reflex, and elevated intraocular pressure, measured at 36 mmHg. The range
of motion of the left eye was significantly reduced, presumably due to intraorbital edema. The patient was
diagnosed with secondary glaucoma secondary to HZO.

Laboratory studies revealed leukocytosis (11,390/μL), possibly due to prednisolone administration, and an
unremarkable C-reactive protein (CRP) level (0.11 mg/dL). A lumbar puncture was performed, and CSF
analysis revealed pleocytosis (91/μL) and a mildly elevated protein level (70 mg/dL). Of clinical significance,
immunoglobulin G (IgG) and immunoglobulin M (IgM) levels directed against VZV were elevated in both
serum (IgG > 128, IgM 4.29) and CSF (IgG > 12.8, IgM 0.49). Based on these findings, the patient was
diagnosed with VZV meningitis.

A therapeutic regimen of intravenous acyclovir and methylprednisolone (1000 mg per day for 3 days) was
initiated, followed by a gradual taper of oral prednisolone, starting at 60 mg/day and decreasing weekly.
After a three-day hospital stay, our ophthalmology team performed phacoemulsification and aspiration,
culminating in the implantation of an intraocular lens in the left eye. Gratitude to the careful and intensive
ophthalmologic intervention, the patient’s left eye achieved a progressive recovery of visual acuity,
eventually reaching a level of 1.0. The visual field also returned to normal. The patient was discharged after
a 15-day hospital stay marked by complete resolution of cephalalgia.

Discussion
This patient was initially diagnosed with an inaugural manifestation of cluster headache, characterized by
profundely severe left-sided cephalalgia, ophthalmalgia, ipsilateral conjunctival injection, and eyelid
edema. It is noteworthy to mention that a transient alleviation of symptoms, precipitated by the
management of cluster headache, potentially contributed to the diagnostic misstep. A course correction was
not initiated until the emergence of cutaneous vesicles on the left upper face, an occurrence transpiring
more than a week subsequent to the onset of the headache.

In retrospect, two salient observations challenged the veracity of the initial cluster headache diagnosis.
Firstly, the age at onset of majority of the patients with cluster headache is thought to be under fourth
decades [3]. Nevertheless, approximately 10% of cluster headache presentations unfold in individuals aged
over 50 years [4], thereby mitigating the significance of age as a critical diagnostic determinant. Secondly,
the prototypical cluster headache symptomatology entails the spontaneous remission of both cephalalgia
and ocular manifestations within a three-hour time frame (coded as 3.1 in ICHD-3) [5]. In stark contrast, the
patient under scrutiny endured persistent symptoms. Hence, an appreciation of this discrepancy becomes
imperative in guiding a prompt and accurate diagnosis, culminating in appropriate therapeutic measures.

Manifestations typified by persistent cephalalgia and ipsilateral autonomic symptoms, confined unilaterally,
necessitate differentiation from hemicrania continua (HC), as delineated in ICHD-3 under code 3.4 [6]. Given
that many conditions can simulate HC symptoms, a comprehensive and meticulous diagnostic exclusion
procedure is imperative. [6]. It is pertinent to note that the diagnosis of HC hinges on a favorable response to
indomethacin. However, it is incumbent upon clinicians to remain cognizant that an indomethacin response
does not foreclose the possibility of secondary etiologies underpinning HC [7]. In this particular case, the
patient presented with VZV meningitis devoid of meningeal sign. In atypical clinical scenarios, the prudent
recourse to a cerebrospinal fluid examination becomes compelling.

Conclusions
This report elucidates a case of painful trigeminal neuropathy attributed to acute Herpes zoster, initially
erroneously diagnosed as cluster headache, primarily due to the delayed cutaneous eruption. It is paramount
to consider this disorder as a pivotal candidate in the differential diagnosis of cluster headache, particularly
when confronted with persistent cephalalgia and ocular sequelae devoid of fluctuations. In the presence of
clinical suspicion, an expeditious lumbar puncture should be prioritized for the evaluation of
immunoglobulin titers (both IgG and IgM) and VZV PCR in CSF, with the overarching goal of expediting the
correct diagnosis.

**Additional Information**

**Disclosures**

**Human subjects:** Consent was obtained or waived by all participants in this study. Institutional Review Board of Jichi Medical University, Saitama Medical Center. issued approval No number was approved. Ethical approval for this study was waived by the Institutional Review Board of the authors’ institution (Jichi Medical University, Saitama Medical Center) because of a case report with written patient consent. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

**References**