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Clinical characteristics of headache or facial pain prior to the development of acute herpes zoster of the head



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ABSTRACT

Objectives: When physicians encounter patients with headache or facial pain (preeruptive pain) associated with acute herpes zoster of the head, especially before the appearance of characteristic skin eruptions (preeruptive phase), they typically find it difficult to make clinical impressions and apply appropriate diagnostic or therapeutic procedures. The objectives of this study were to describe the clinical characteristics of headache or facial pain associated with acute herpes zoster of the head and to elucidate the association between the manifestation of these symptoms in the preeruptive phase and incoming herpes zoster.

Methods: We retrospectively analyzed the clinical features of 152 patients with acute herpes zoster involving only the head who presented within 10 days of rash onset at Chungbuk National University Hospital, a tertiary hospital in Chungcheongbuk-do in South Korea, between January 2011 and December 2015. Results: The mean age of the patients was 54.3 ± 19.8 years. One hundred patients had herpes zoster in the trigeminal nerve, 34 in the nervus intermedius, and 18 in the upper cervical nerves. Preeruptive pain was present in 112 (73.7%) patients and had a mean duration of 3.0 ± 1.3 days (range, 1–6 days). Severity of pain was associated with the presence of preeruptive pain (p = 0.040). Headache or facial pain was limited to the ipsilateral side of the face and head in all patients, except for two who had with severe symptoms of meningitis, and was of moderate to severe intensity (90.1%). Pain of a stabbing nature was observed in 128 (84.2%) patients, and 146 (96.1%) reported experiencing this type of pain for the first time. Pain awakened 94 (61.8%) patients from sleep. Sixty-one (54.5%) of the 112 patients with preeruptive pain visited a hospital during the preeruptive phase; their preeruptive phase was significantly longer (p < 0.001) and more frequently awakened them from sleep (p = 0.008). Their presumptive diagnoses were as follows: tension-type headache (n = 20, 32.8%); no decision (n = 18, 29.5%); herpes zoster (n = 5, 49.5%); herp 8.2%); migraine (n = 3, 4.9%); pain associated with upper respiratory tract infection (n = 3, 4.9%); parotitis (n=2, 3.3%); dry eye (n=2, 3.3%); and other (n=1 each: trigeminal neuralgia, glaucoma, pharyngitis,vestibular neuronitis, tonsillitis, teeth problems, otitis media, and occipital neuralgia).

Conclusion: These results suggest that the typical pain of acute herpes zoster of the head has a stabbing quality, is felt unilaterally, is moderate to severe, often awakens patients from sleep, and has not been previously experienced by most patients. When encountering patients with these features accompanied by pain onset of less than one week, acute herpes zoster of the head should be considered, even without characteristic vesicles, after excluding other secondary causes by appropriate diagnostic workup.

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1. Introduction

In 70–80% of patients with herpes zoster, a prodrome of dermatomal pain begins several days before the appearance of the characteristic rash [1]. This pain has been described as sharp, stabbing, tender, shooting, throbbing, itching and hot. Herpes zoster with craniocervical involvement tends to be more severe and cause greater pain [2]. When physicians encounter patients with headache or facial pain (preeruptive pain) associated with acute

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herpes zoster of the head before the characteristic skin eruptions appear (preeruptive phase), they often find it difficult to make clinical impressions and proceed with appropriate diagnostic or therapeutic procedures. In this study, we describe the clinical characteristics of headache or facial pain associated with acute herpes zoster of the head, especially before the appearance of vesicular eruptions, and attempt to elucidate the association between the manifestation of these symptoms in the preeruptive phase and incoming herpes zoster.

2. Patients and methods

We retrospectively reviewed the records of patients with acute herpes zoster involving only the head who had presented within 10 days of rash onset at Chungbuk National University Hospital, a tertiary hospital in Chungcheongbuk-do in South Korea, between January 2011 and December 2015. Patients with other illnesses causing headache or facial pain, such as acute otitis media, cancer of the head, and systemic infection with fever, were excluded. Patients who could not describe their pain because of dementia, mental retardation, or a young age (less than 10 years old) were also excluded. Most patients with acute herpes zoster of the head visited the departments of dermatology, ophthalmology, otorhinolaryngology, neurology, and emergency medicine. Based on the liaison system at our hospital, physicians in the departments of dermatology, ophthalmology, otorhinolaryngology, and emergency medicine consult neurologists in cases of acute herpes zoster of the head, regardless of the severity of headache or facial pain, in order to exclude possible involvement of the nervous system, such as cranial neuropathy, meningitis, or encephalitis. Neurologists had previously interviewed the patients included in the present study about their pain and medical histories. Data were collected on demographics, medical history, clinical presentation, and pain characteristics. This study was approved by the Institutional Review Board of Chungbuk National University Hospital.

Herpetic eruption in the ear and/or oral mucosa in the territory of the nervus intermedius was ascribed to nervus intermedius zoster. When determining the specific type of herpes zoster and the site of headache or facial pain in trigeminal and upper cervical zoster, we arbitrarily use a line passing through the ear and the angle of the mandibular ramus as a reference. Herpetic eruptions without involvement of the ear in the head was ascribed to trigeminal or upper cervical zoster according to whether they are anterior or posterior to this line. The sensation of headache beyond this line represents ipsilateral spreading of headache or facial pain beyond the territory of the involved nerve. Similarly, in zoster of the nervus intermedius, the presence of frontal and/or occipital headache in addition to temporal (aural or periaural) headache represents ipsilateral spreading of headache beyond the territory of the involved nerve.

SPSS for Windows (version 23.0; IBM) was used for statistical analyses. All tests were two-tailed, and statistical significance was defined as p < 0.05. We conducted univariate analysis using Z-tests, Fisher's exact test, one-way analysis of variance, and chisquare tests for comparison where appropriate. Multinominal or binary logistic regression analysis was then conducted to identify independent factors associated with demographic and clinical characteristics between the specific type of herpes zoster, the presence of preeruptive pain, and the visit to a hospital. Variables with p < 0.1 on univariate analysis were included in the multivariate model.

3. Results

During the study period, 172 patients met the inclusion criteria, 17 of whom were subsequently excluded owing to a lack of

adequate information. Ten of the 17 excluded patients had not consulted a neurologist, and the medical records of the remaining seven patients did not contain adequate information for this study. Three of the remaining 155 patients were also excluded because they had not complained of headache or facial pain, even though they had characteristic vesicular eruptions of acute herpes zoster of the head (two in the territory of the trigeminal nerve and one in the ear).

Of the remaining 152 patients with acute painful herpes zoster of the head, 67 were men and 85 were women (mean age \pm standard deviation, 54.3 ± 19.8 years; age range, 10-93years). Multinominal logistic regression analysis using sex and presence of preeruptive pain as independent variables and trigeminal nerve group as a reference category showed the higher proportion of male sex in patients with superior cervical zoster (OR 3.49; 95% CI 1.15-10.64, p = 0.028) (Table 1). One hundred patients had herpes zoster in the trigeminal nerve (ophthalmic nerve, n = 77; maxillary nerve, n=9; mandibular nerve, n=6; ophthalmic and maxillary nerves, n = 6; and maxillary and mandibular nerves, n = 2), 34 in the nervus intermedius, and 18 in the upper cervical nerves (greater occipital nerve, n=7; lesser occipital nerve, n=7; greater and lesser occipital nerves, n = 2; lesser occipital and great auricular nerves, n = 1; and great auricular nerve, n = 1). Eighty-five patients had herpes zoster on the right side and 67 on the left side. Four patients were immunocompromised (acquired immunodeficiency syndrome, n = 1; taking immunosuppressants after receiving hepatic transplant, n = 1; and receiving chemotherapy for cancer with metastasis, n = 2).

Preeruptive pain prior to the appearance of typical vesicles was present in 112 of the 152 patients, with a mean duration of 3.0 ± 1.3 days (range, 1–6 days). Preeruptive pain was significantly more frequently observed in patients with nervus intermedius zoster by multinominal logistic regression analysis (OR 7.85; 95% CI 1.77-34.88, p=0.007). In the other 40 patients, pain started on the day of rash onset or thereafter. The details of the preeruptive phase of each type of herpes zoster are shown in Table 1. Pain in patients with the preeruptive phase was significantly more severe (p=0.040) (Table 2).

Sixty-one (54.5%) of the 112 patients with preeruptive pain visited a hospital (mostly primary care centers in the region) before the appearance of typical eruptions (Table 1). Their pain more frequently awakened them from sleep (OR 4.21; 95% CI 1.46-12.14, p = 0.008) and was associated with a longer preeruptive phase (OR 2.17; 95% CI 1.46–3.20, p < 0.001) compared with patients who did not visit a hospital (Table 3). The presumptive diagnoses were as follows: 20 (32.8%) patients were diagnosed as having tension-type headache; 11 (18.0%) received no clear diagnosis; seven (11.5%) were told that they might have a serious problem in the head and were advised to visit a hospital with advanced medical facilities and headache specialists; five (8.2%) were diagnosed as possible herpes zoster; three (4.9%) as having a migraine; three (4.9%) as having headache or pain associated with upper respiratory tract infection; two (3.3%) as having parotitis; two (3.3%) as having dry eye; and eight (13.1%) as other (trigeminal neuralgia, glaucoma, pharyngitis, vestibular neuronitis, tonsillitis, teeth problems, otitis media, and occipital neuralgia). In 24 (39.3%) of 61 patients, brain computed tomography (CT) or magnetic resonance imaging (MRI) was performed during the preeruptive phase. In two patients, cerebrospinal fluid was examined (one in ophthalmic and mandibular zoster and the other in nervus intermedius zoster) (Table 1).

The quality of pain from pain onset to examination by a neurologist could be grossly divided into the following three categories: 1) mainly stabbing (sharp, shooting, or electric shock-like) pain lasting less than a few seconds and recurring irregularly without other qualities or other negligible pain, $n=60;\ 2)$ coexistence of stabbing pain and pain of another quality, such as aching, tightening,

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