Pearls & Oysters: Trigeminal neuropathy associated with herpes labialis

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PEARLS

- Herpes labialis is a common disease, but there are very few reports on herpes labialis-related trigeminal neuropathy.
- Trigeminal neuropathy can be associated with frequently recurring herpes labialis, and abnormal lesions may appear concurrently in the spinal trigeminal nucleus and tract (STNT) on MRI.

CASE REPORT A previously healthy 41-year-old woman with recurrent herpes labialis since her 20s noticed a herpes labialis lesion on the left side of the lower lip. After 2 days, she experienced the acute onset of tingling and a swollen sensation of the left side of the face, beginning at the V3 division of the trigeminal nerve and progressing to involve the V1 and V2 divisions over the course of 2 days. A dermatologist diagnosed herpes labialis and prescribed acyclovir 1,000 mg in 2 divided doses for 5 days. However, the symptoms did not improve after the lesion disappeared. The left side of the tongue perceived a bitter taste 8 days after the onset of symptoms. Examinations on the following day revealed decreased pinprick, temperature, and light touch sensations in the 3 divisions of the left trigeminal nerve, as well as tingling and a swollen sensation in the affected region. A swollen sensation was also present in her inner cheek. Corneal reflexes and trigeminal motor function were normal. The results of other neurologic examinations were normal. T2-weighted MRI revealed a hyperintense lesion, corresponding to the left STNT (figure, A and B). The lesion was surrounded by edema and showed slight contrast enhancement with gadolinium (figure, C). Examination of the CSF showed 0.7 cells/ μ L and a protein content of 22 mg/dL; herpes simplex virus (HSV) DNA was negative on PCR.

After the diagnosis of trigeminal neuropathy associated with herpes labialis and treatment with IV methylprednisolone (1,000 mg) for 3 days, the lack

of facial sensation improved rapidly, but slight tingling (especially in the V3 division) and dysgeusia remained. After that, the patient's symptoms gradually resolved spontaneously and disappeared about 3 weeks after onset. T2-weighted images after resolution of all symptoms showed that the edematous lesion had disappeared, whereas the hyperintense lesion corresponding to the STNT partially remained (figure, D).

Three months later, the patient had recurrence of a herpetic lesion on the opposite side of the lower lip, but did not experience trigeminal sensory disturbance at that time.

DISCUSSION In our patient, the viral reactivation at the trigeminal ganglion led to widespread facial symptoms and abnormal signal intensity on MRI, corresponding to the STNT. The STNT receives primary afferent fibers from the trigeminal, facial, glossopharyngeal, and vagus nerves. Therefore, the dysgeusia in our patient might have been caused by retrograde impulses from the inflamed STNT to the facial and glossopharyngeal nerve.

Four patients with herpes labialis-related sensory disturbances have been documented previously.^{1,2} Only 2 of these patients had extensive sensory disturbances involving 3 divisions of the trigeminal nerve, including 1 patient with dysgeusia, similar to our case. Three of the 4 patients were female. Two patients had episodes without or preceding a herpes labialis lesion. In 3 patients, symptoms resolved spontaneously without therapy 2 to 4 weeks after onset. A common feature of their herpes labialis was frequent recurrence.

We could not determine whether our patient's herpes labialis was caused by HSV type 1 on examinations of serum or CSF. The patient's lip lesion was diagnosed as herpes labialis by a dermatologist. However, our patient had already received acyclovir. Transaxonal spread of virus along the trigeminal nerve to the STNT was therefore considered possible, without viral transmission via the CSF. These

Figure Abnormal lesions corresponding to the spinal trigeminal nucleus and tract on MRI

T2-weighted image shows hyperintense lesions corresponding to the left spinal trigeminal nucleus and tract (STNT) from the middle pons (A) to the upper medulla (B). Postgadolinium T1-weighted images show partial enhancement of the STNT (C). T2-weighted image after improvement of all symptoms shows partial persistence of abnormal lesions (D).

factors may have led to the negative test results for HSV DNA in the CSF on PCR.

Previously, among the Herpesviridae, only varicella-zoster virus,^{3–5} which causes both trigeminal herpes zoster and Ramsay Hunt syndrome, was shown to be associated with abnormal lesions involving the STNT on MRI. However, previous reports did not discuss expected pathologic changes in abnormal lesions. One report⁶ documented a patient with AIDS and a recent history of herpes zoster involving the mandibular division of the right trigeminal nerve. On autopsy, a predominantly demyelinating lesion involving the ipsilateral spinal trigeminal tract and nucleus was found. As for HSV type 1, experiments in animals⁷ have demonstrated that HSV type 1 inoculated into the cornea spreads transaxonally to the CNS through the first branch of the trigeminal nerve and induces selective demyelination of the intramed-

ullary trigeminal nerve root. The hyperintense lesion remaining in the STNT after resolution of all symptoms (figure, D) was therefore attributed to demyelination caused by HSV type 1 infection and associated inflammation.

HSV type 1 is a double-stranded DNA virus and belongs to alpha herpesvirus subfamily. The virion consists of a capsid into which the DNA is packaged, a tegument, and an external envelope in which virus-encoded glycoproteins are present.

Conversely, innate and adaptive immune responses to HSV type 1 inhibit viral transaxonal spread and transmission.^{8,9} Especially, the innate antiviral response is considered to play a pivotal role in determining the outcome of HSV infection through the production of type I interferon (IFN). Natural killer cells play important roles for cytokine production, recognition, and killing of virally infected cells, and plasmacytoid dendritic cells also play an important role for type I IFN production. The type I IFN signaling pathway begins with the recognition of viral antigens, such as viral proteins and nucleic acids. Adaptive immune response also plays a functional role, albeit controversial, for antibody-mediated protection against viral transmission.

A previous study¹⁰ showed there is a strong correlation between the frequency of HSV type 1 reactivation and the number of latently infected neurons in the ganglia. This study suggested that the amount of HSV latency increases in individuals with frequently recurring herpes labialis. However, it is unclear what enabled HSV type 1 to escape the host immune response and reach the STNT after transaxonal spread from the trigeminal ganglion.

AUTHOR CONTRIBUTIONS

Tadashi Umehara: drafting/revising the manuscript for content, including medical writing for content, study concept or design, analysis or interpretation of data, acquisition of data. Hisayoshi Oka: study concept or design, analysis or interpretation of data, acquisition of data. Chizuko Toyoda: study concept or design, analysis or interpretation of data. Soichiro Mochio: study concept or design, analysis or interpretation of data.

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DISCLOSURE

The authors report no disclosures relevant to the manuscript. **Go to Neurology.org for full disclosures.**

REFERENCES

1. Gominak S, Cros D, Paydarfar D. Herpes simplex labialis and trigeminal neuropathy. *Neurology* 1990;40:151–152.
2. Suzuki N, Mizuno H, Nakashima I, Itoyama Y. Herpes labialis in multiple sclerosis with a trigeminal lesion. *Intern Med* 2011;50:259.

3. Nagane Y, Utsugisawa K, Yonezawa H, Tohgi H. A case with trigeminal herpes zoster manifesting a long lesion of the spinal trigeminal nucleus and tract on MR T2-weighted image. *Rinsho Shinkeigaku* 2001;41:56–59.
4. Nogueira RG, Seeley WW. Ramsay Hunt syndrome associated with spinal trigeminal nucleus and tract involvement on MRI. *Neurology* 2003;61:1306–1307.
5. Chia-Wei Hung, Shuu-Jiun Wang, Shih-Pin Chen, Jiing-Feng Lin, Jong-Ling Fuh. Trigeminal herpes zoster and Ramsay Hunt Syndrome with a lesion in the spinal trigeminal nucleus and tract. *J Neurol* 2010;257:1045–1046.
6. Rosenblum MK. Bulbar encephalitis complicating trigeminal zoster in the acquired immune deficiency syndrome. *Hum Pathol* 1989;20:292–295.
7. Itoyama Y, Sekizawa T, Openshaw H, Kogure K, Goto I. Early loss of astrocytes in herpes simplex virus-induced central nervous system demyelination. *Ann Neurol* 1991; 29:285–292.
8. Chew T, Taylor KE, Mossman KL. Innate and adaptive immune responses to herpes simplex virus. *Viruses* 2009;1: 979–1002.
9. Mikloska Z, Sanna PP, Cunningham AL. Neutralizing antibodies inhibit axonal spread of herpes simplex virus type 1 to epidermal cells in vitro. *J Virol* 1999;73:5934–5944.
10. Sawtell NM. The probability of in vivo reactivation of herpes simplex virus type 1 increases with the number of latently infected neurons in the ganglia. *J Virol* 1998;72: 6888–6892.

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