A case of herpes zoster ophthalmicus with optic neuritis of the total length of the optic nerve in the orbital space and ischemic optic neuropathy

Takashi Kudo *, Kodai Yamauchi, Yukihiko Suzuki, Mitsuru Nakazawa, Shinji Ueno

Department of Ophthalmology, Hirosaki University Graduate School of Medicine, 5 Zaifu, Hirosaki, 036-8562, Japan

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ABSTRACT

Purpose: We herein report a case of optic neuritis and ischemic optic neuropathy associated with herpes zoster ophthalmicus and decreased visual acuity.

Observations: A 65-year-old man with no special medical history had a headache on the right side in December 2019, and a few days later, a facial rash appeared on the same side. A dermatologist diagnosed him with herpes zoster ophthalmicus and started antiviral drug therapy. On the same day, he was referred to a local ophthalmologist and was found to have inflammatory signs in his right cornea and conjunctiva. The next day, when he visited the ophthalmologist again, he had decreased visual acuity, optic disc swelling, and fundus hemorrhaging in his right eye, so he was referred to our department. At the first visit to our department, his best-corrected visual acuity was light sense OD, 1.0 OS. His right fundus showed optic disc swelling, spotted fundus hemorrhaging, and dilation/tortuosity of the retinal vein. Fluorescein angiography showed the near absence of optic disc filling as well as delayed retinal vein perfusion in his right eye, and magnetic resonance imaging confirmed high signals in the total length of the right optic nerve in the orbital space using the short inversion-time inversion recovery method. Based on these findings, we diagnosed him with optic neuritis and ischemic optic neuropathy associated with inflammation of the orbital part caused by herpes zoster ophthalmicus. We started systemic administration of antiviral drugs (acyclovir) and oral steroid. However, after treatment, his visual acuity improved only to hand motion OD, and the fundus appearance was ultimately optic atrophy OD.

Conclusion and Importance: Various complications can occur with herpes zoster ophthalmicus, however, few reports have described cases of herpes zoster ophthalmicus associated with optic neuritis and ischemic optic neuropathy. Therefore, there is no consensus concerning the ideal treatment for these conditions. By referencing cases involving issues such as orbital apex syndrome and optic neuritis caused by herpes zoster ophthalmicus, antiviral drugs and oral steroids were administered, but the prognosis of the visual acuity was poor.

1. Introduction

Herpes zoster ophthalmicus caused by the varicella-zoster virus (VZV) is latent in the trigeminal ganglion after initial infection with VZV reactivates when the T-cell immunity weakens, spreads transaxially, and affects the first trigeminal nerve of the face. This disease induces the development of characteristic painful eczema of the first branch of the trigeminal area and is accompanied by a strong inflammatory reaction.

The rate of certain ocular complications caused by herpes zoster ophthalmicus is reportedly about 50%, and among them, the rate of optic neuropathy is <0.5%. Ischemic optic neuropathy is even rarer, and in our investigation, we found several reports of anterior ischemic optic neuropathy and posterior ischemic optic neuropathy shortly after the onset of herpes zoster ophthalmicus, however, there have been no such reports from Japan.

We herein report a case of severe visual loss due to inflammation of the optic nerve over the entire length of the optic nerve in the orbit and ischemic optic neuropathy in a patient suffering from herpes zoster ophthalmicus.

2. Case report

A 65-year-old man with no special medical history had a rash on his right face a few days after becoming aware of a headache on the right side and visited a local dermatologist in December 2019. He was diagnosed with herpes zoster in the first branch of the right trigeminal nerve.
and started taking an antiviral drug (Amenamevir). On the same day, he was referred to a local ophthalmologist and found to have inflammatory signs in his right cornea and conjunctiva, so he was prescribed acyclovir eye ointment and pranoprofen eye drops. His visual acuity was 0.7 OD with his glasses. The next day, when he visited the ophthalmologist again, he had decreased visual acuity, optic disc swelling, and fundus hemorrhaging in his right eye. He was therefore referred to our department for a further ophthalmic examination and treatment.

At the first visit to our department, his best-corrected visual acuity (BCVA) was light sense OD, 1.0 OS, and his intraocular pressure was 21 mmHg OD, 13 mmHg OS. The right relative afferent pupillary defect was positive, and no ocular motility disorder was observed. Shingles were observed around the right eye lid, conjunctival hyperemia (+) was seen, and the cornea, anterior chamber and lens were almost clear, while the anterior vitreous to vitreous cavity was slightly cloudy (+). His right fundus showed optic disc swelling, spotty retinal hemorrhaging and dilation/tortuosity of the retinal vein (Fig. 1). No notable abnormalities were found in the left eye.

Systemic laboratory data showed that the erythrocyte sedimentation rate was 4 mm (1 h)/12 mm (2 h), white blood cell count was 7980/µl, C-reactive protein level was 0.24 mg/dl, aspartate aminotransferase level was 22 U/l, alanine aminotransferase level was 17 U/l, serum creatinine level was 0.78 mg/dl, blood urea nitrogen level was 14 mg/dl, and anti-nuclear antibody, lupus anticoagulant, anti-cardiolipin antibody, PR3-ANCA and MP3-ANCA were negative.

Fluorescein angiography (FA) showed remarkable optic disc filling defect and mild hyperfluorescence in the later stage as well as delayed retinal vein perfusion in his right eye. The arm to retina time (ART) of the right eye was within the normal range at 20 sec (Fig. 2). Magnetic resonance imaging (MRI) confirmed optic nerve swelling and high signals in the total length of right optic nerve in the orbital space, and high signals in the overall orbit space were confirmed using the short inversion-time inversion recovery (STIR) method. No abnormality was found in his left eye or optic nerve (Fig. 3). Optical coherent tomography (OCT) findings were not suggestive of photoreceptor damage in the posterior pole of the right eye (Fig. 4). Based on these findings, we diagnosed him with optic neuritis and ischemic optic neuropathy associated with inflammation of the orbital part caused by herpes zoster ophthalmicus.

After hospitalization, we started systemic administration of acyclovir 375 mg (5mg/kg) 3 times per day for 7 days (standard dosage approved in Japan) and steroid orally. Although corticosteroid administration was initially started with prednisolone 30 mg/day for 3 days, there was no visual recovery effect, on the other hand, the herpes zoster did not worsen, so the dose was thus increased to 40 mg and continued for another 4 days. Because there was no significant change in visual acuity after the treatment, he was discharged with BCVA of light sense OD. In January 2020, one month later, his BCVA slightly recovered to hand motion OD, but no further improvement has been noted. Although the optic disc swelling was resolved, he ultimately showed optic atrophy OD.

3. Discussion

Given the pathophysiology of this case, FA showed that ischemic optic neuropathy and central retinal vein occlusion coexisted, and MRI showed a high signal via the STIR method in the entire right optic nerve and right orbital space (especially around the optic nerve behind the eyeball). Since no ocular motility abnormality was observed, orbital apex syndrome was ruled out. At the time of consultation at our department, the findings of keratoconjunctivitis and uveitis were not severe. Given the above, the pathologic conditions capable of causing such a severe decrease in visual acuity were speculated to be severe inflammation due to herpes zoster ophthalmicus in the orbital part, especially in the posterior part of the eyeball, rather than the apex of the orbit, including the superior orbital fissure or the eyeball itself, and the presence of an occlusive vasculitis-like pathology was also considered; alternatively, since FA showed central retinal vein occlusion, swelling due to inflammation near the optic nerve-eyeball junction might have caused ischemic optic neuropathy by strangling the surrounding blood vessels. In addition, the therapeutic process in which the recovery of the visual function was not obtained even by systemic administration of antiviral drugs and steroid drugs supports the prognosis of irreversible visual dysfunction due to ischemic changes considered to be caused by the above pathological condition.

In terms of treatment, we believed that early anti-inflammatory treatment should be performed, and after consulting with our dermatologist, we chose systemic administration of antiviral drugs and oral...
corticosteroid administration after hospitalization. Strong anti-inflammatory treatment, such as steroid pulse treatment, is only ideal for calming inflammation of the optic nerve and its surroundings, and concern remains regarding encephalitis and systemic dissemination due to exacerbation of the underlying disease; for this reason, we selected the above treatment. As mentioned above, since case reports of herpes zoster ophthalmicus combined with ischemic optic neuropathy are extremely rare, and no similar cases have been reported in Japan, it was difficult to determine what strength corticosteroid treatment was needed. In previous reports of optic neuritis and orbital apex syndrome associated with herpes zoster ophthalmicus, which is considered to have a similar pathological condition, the systemic administration of antiviral drugs was the basis, and systemic administration of steroids was performed at various intensities. However, the prognosis of treatment varied, regardless of the strength of steroid treatment. (Table 1)

Another factor that had to be kept in mind was the differences in doses and types of antiviral and steroid drugs due to differences in body size and drug responsiveness between Asians and other ethnic groups. Kaufman et al. have already reported on herpes zoster optic neuropathy in Americans, but in this study, we ventured to investigate previous

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**Fig. 2.** Fluorescein angiographic findings. The ART of the right eye was within the normal range (20 sec), with the near absence of optic disc vascular filling (1 and 2.5 min), and mild hyperfluorescence occurred in the later stage (6 min), along with delayed retinal vein perfusion in his right eye (1 min).

**Fig. 3.** MRI findings (STIR method). (a) Sagittal section (b) Coronal section. Optic nerve swelling and high signals along the total length of the right optic nerve in the orbital space, as well as high signals in the overall right orbit.

**Fig. 4.** OCT findings. There was no signs suggestive of photoreceptor damage in the posterior pole of the right eye.
There have been a few reports concerning ischemic optic neuropathy after the onset of herpes zoster ophthalmicus. Some of these reports have speculated that these conditions are part of VZV vasculopathy, and VZV antigens were reportedly found in a temporal artery biopsy specimen. In our case, the presence of temporal arteritis could not be confirmed, and the presence of other obstructive vasculitis was unable to be objectively determined. However, we suspect that some inflammatory or ischemic lesions over the entire length of the orbital optic nerve may have developed based on the MRI, FA and fundus findings, and the background may have been similar to that of VZV vasculopathy.

Regarding treatment, in previous studies, treatment was often performed using prednisolone 1 mg/kg, which was slightly higher than the dose administered in this case. However, in those previous cases, ischemic optic neuropathy did not develop almost at the same time of skin lesion of herpes zoster ophthalmicus, as experienced in our case, instead usually developing a little later, after the manifestation of herpes zoster ophthalmicus. The difference of our case and previous reported cases is that there was less concern about systemic dissemination of herpes zoster due to immunosuppressive treatment. Nevertheless, we avoided methods such as increasing the dose of steroids (for example, pulse therapy) because we thought there was a high risk of causing systemic dissemination of the virus.

T. Kado et al. reported a case of encephalitis-induced disturbance of consciousness after systemic steroid administration, and Nakamoto et al. reported that care concerning the risk of inducing and exacerbating retinal lesions needs to be practiced when performing systemic steroid administration for optic nerve lesions. The treatment policy needs to consider the pathological condition, including the general condition of each case, the degree of severity of ophthalmic findings and the understanding concerning complications on the patient’s side. If ischemic changes outweigh inflammatory changes in the etiology of visual impairment, intense steroid therapy increases the risk of systemic complications, making it difficult to consider the most appropriate treatment in this case. In conclusion, in our case, the ischemic changes were so severe that antiviral and anti-inflammatory drugs were not sufficiently effective, and the final visual prognosis was poor.

4. Conclusion

We experienced a case of optic neuritis over the entire length of the optic nerve and ischemic optic neuropathy during the course of herpes zoster ophthalmicus. The patient was treated with systemic acyclovir and oral steroids but showed a poor prognosis.

Statement of ethics

All clinical procedures were conducted according to the principles of the Declaration of Helsinki. Written informed consent was obtained from the patient prior to the procedure, and possible complications were explained. The Ethics Committee of the Hirosaki University Graduate School of Medicine does not require approval for retrospective case reports.

Data availability statement

All data generated or analysed during this study are included in this article and its supplementary material files. Further enquiries can be directed to the corresponding author.

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Author contributions

T.K. and M.N. participated in drafting the manuscript. T. K., Y. K., Y. S., M. N. and S. U. made substantial contributions to diagnosis and treatment of the patient, acquisition of data, or analysis and interpretation of data, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Declaration of competing interest

The authors report no conflicts of interest.

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