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Acute Retinal Necrosis Following Contralateral Herpes Zoster Ophthalmicus

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Background: A case report of contralateral acute retinal necrosis (ARN) following herpes zoster ophthalmicus.

Case: A 61-year-old male patient developed iridocyclitis and well-demarcated creamy-white retinal lesions at the nasal periphery in the right eye 1 month after herpes zoster ophthalmicus in the left eye. The patient had undergone surgery for primary lung cancer, and had subsequent intracranial metastasis of the tumor.

Observations: The clinical diagnosis of ARN was supported by polymerase chain reaction investigation of the aqueous humor resulting in positive for varicella-zoster virus. Retinal lesions disappeared after systemic treatment with acyclovir, corticosteroids, and acetylsalicylate. No retinal detachment developed.

Conclusions: We propose a careful ophthalmic follow-up for herpes zoster ophthalmicus patients because of the possibility of acute retinal necrosis developing in the contralateral eye.
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Key Words: Acute retinal necrosis, contralateral eye, herpes zoster ophthalmicus, polymerase chain reaction, varicella-zoster virus.

Introduction

Acute retinal necrosis (ARN) syndrome is an established clinical entity that is characterized by unilateral or bilateral circumferential dense creamy-white retinal patches at the periphery, occlusive retinal vasculitis with hemorrhage, dense vitreous reaction, anterior uveitis, and frequent retinal detachment. The pathogenesis of ARN is attributed to a herpes virus group infection: herpes simplex virus (HSV) or varicella-zoster virus (VZV).

Association of ARN with herpetic skin lesions is uncommon,[1,2] although an association has been found in immunocompromised patients. Ipsilateral association of dermal and ocular infection is usual, and ARN contralateral to dermal lesions is extremely rare.[1–3]

We report a patient who developed mild ARN in the contralateral eye after herpes zoster ophthalmicus of the left dermatome of the first branch of the trigeminal nerve.

Case Report

The patient was a 61-year-old man whose complaint was conjunctival infection of the left eye of 3 days duration. In his first ophthalmic examination on April 8, 1997, the corrected visual acuity was 1.2 OU. The bulbar and palpebral conjunctiva in the left eye were hyperemic with discharge, but otherwise the left eye was normal. No pathology was found in the right eye. Antibiotics and corticosteroid eyedrops were prescribed.

The patient's history revealed that he had had central serous chorioretinopathy in the right eye about 10 years before. He had been diagnosed as having adenocarcinoma in the left lung and underwent lobectomy and regional lymphectomy in January 1995. In February 1997, 2 months before his first

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visit to our department, the intracranial metastasis was found, and 43.6 Gy radiation was given. No further chemotherapy was planned.

The conjunctival injection in his left eye disappeared after 2 days, but a vesicular rash developed in the left dermatome of the first branch of the trigeminal nerve. The vesicular skin lesion was painful. The lesion was diagnosed as herpes zoster ophthalmicus by dermatologists, and acyclovir ointment was given. The serum anti-VZV IgG antibody titer was 16× and increased to 128× after 2 weeks.

On May 6, one month after his first examination, the herpes zoster ophthalmicus in the left eye had been cured. Slit-lamp examination of the right eye, however, revealed iritis with anterior chamber cells and mutton fat keratic precipitates. The right fundus disclosed creamy-white retinal patches at the nasal periphery, while the left eye was normal. The patient was diagnosed as having ARN in the right eye.

The corrected visual acuity on admission was 1.2 OU. Measurement of anterior flare intensity was 14.7 OD and 4.7 OS in photon counts per millisecond by a laser flare meter (FM-500; Kowa, Tokyo). Intraocular pressure was normal in both eyes. The creamy-white retinal patch was well-demarcated and located at the nasal periphery. Small satellite retinal lesions were observed at the lower nasal periphery (Figure 1). Retinal vessels traversing the patch appeared occlusive with hemorrhage. Fluorescein angiography demonstrated moderate leakage from the retinal patches, occlusion of the vessels traversing the patch, and leaking vessels at the nasal periphery.

Intravenous acyclovir at1,500 mg per day and prednisolone at100 mg per day were administered in combination with acetylsalicylate, 330 mg per os, and local corticosteroid eyedrops (Figure 2). Results of polymerase chain reaction (PCR) investigation of aqueous humor from the right eye were positive for varicella-zoster virus, but negative for HSV and cytomegalovirus. Serum antibody titer for herpes virus showed no significant further rise.

The ocular lesions responded well to systemic treatment. The creamy-white retinal patch disappeared, and sheathing of the retinal vessels was observed. Fluorescein angiography showed decreased leakage. Apparent ocular lesions had disappeared by 24 days after admission. We performed prophylactic laser photocoagulation at the border of the pre-existing patch to prevent retinal detachment.

Routine systemic data did not suggest an immunocompromised status; the total serum protein at 6.0 g/dL (normal: 6.7–8.5 g/dL) was low, and creatinine phosphokinase at 26 IU/L (normal: 35–200 IU/L) was also low, but other laboratory data remained within normal limits. Serum IgG was 1060 mg/dL (normal: 800–1900 mg/dL) and IgM was 172 mg/dL (normal: 70 - 300 mg/dL). No further examinations were conducted for the study of immunocompromised status. The patient was followed thereafter as an outpatient. In July 1997, three months after the first examination, he noticed chest discomfort. He was admitted to the Department of Internal Medicine of our hospital and died from carcinomatous ascites in September 1997.

Discussion

The ocular lesions in the right eye of the patient were compatible with those in ARN: creamy-white retinal patches at the periphery, occlusive vasculitis, and anterior segment inflammation. No noticeable vitreitis was found, and the intensity of anterior segment inflammation, as quantitatively shown by laser flare measurement, was slight. The lesions responded to systemic anti-herpes virus treatment combined with corticosteroids and acetylsalicylate. The pathogenesis of retinitis was considered to be a varicella-zoster infection because of the preceding herpes zoster ophthalmicus in the contralateral eye and the evidence of varicella-zoster gene obtained by PCR of the aspirated aqueous humor from the right eye.

The ARN syndrome includes a range of disease severities. The fulminant form is characterized by severe granulomatous iridocyclitis, dense vitreitis, and yellow-white retinal patches circumscribing the peripheral ocular fundus, and it frequently results in secondary rhegmatogenous retinal detachment. Milder forms respond to systemic antiviral treatment with acyclovir, and progression of retinal patches to the posterior segment is limited; some patients do not show retinal detachment. The early disappearance of the retinal lesions, the mild anterior uveitis, and the responsiveness of the disease to treatment in the present case indicate that the lesions were a mild form of ARN.

The association of ARN with herpetic periocular or dermal lesions is rare. Acute retinal necrosis, when it develops in immunocompromised individuals, is sometimes associated with an antecedent cutaneous herpes virus infection, and herpes zoster ophthalmicus or herpetic keratitis is associated with ARN. The site of ARN is usually ipsilateral, and

Figure 1. Fundus color photograph of right eye on admission. Creamy-white retinal patches are shown at nasal periphery.

ARN contralateral to herpes zoster ophthalmicus is extremely rare.[1,2]

Suzuki et al[3] reported an association of herpes zoster ophthalmicus and keratitis with acute retinal necrosis in the contralateral eye in an immunocompetent patient. They speculated that the retrograde invasion of the virus through the ipsilateral oculomotor nerve carried the virus to the Edinger-Westphal nucleus and then to the contralateral optic nerve and retina.[4]

An experimental model for HSV infection demonstrated that the virus, injected into the anterior chamber of one eye, caused anterior segment inflammation but no retinitis in the injected eye, and it induced no anterior segment inflammation but retinitis in the noninjected fellow eye.[5] The mild anterior uveitis and retinitis in the present case seem compatible with the above description.

The most likely mechanism for contralateral ARN following herpes zoster ophthalmicus in the present case is neural and trans-synaptic spread of the virus via the trigeminal nerve. The herpes virus in the ophthalmic division of the trigeminal nerve may pass to the eye through the long ciliary nerve.[2] The virus may then spread through the oculomotor nerve to the Edinger-Westphal nucleus and infect the contralateral eye via the optic nerve and the retina.[4]

The present case was considered to be a mild form of ARN. Acute retinal necrosis following contralat-

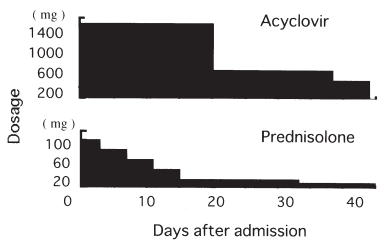

Figure 2. Treatment with acyclovir and prednisolone. Acetylsalicylate was also given.

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eral herpes zoster ophthalmicus is extremely rare in immunocompetent individuals. The patient might have been immunocompromised despite the normal routine laboratory data: he had had lung cancer, intracranial metastasis, and died 5 months after the first visit. Herpes zoster ophthalmicus must be carefully followed, and ophthalmic examination must include both eyes because of the possible association of the disease with ARN in the contralateral eye.

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