Optic Neuropathy and Central Retinal Vascular Obstruction as Initial Manifestations of Acute Retinal Necrosis

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Background: The purpose of this brief communication is to alert ophthalmologists that optic neuropathy may herald acute retinal necrosis (ARN).

Case: A previously healthy 54-year-old man exhibited optic neuropathy as an initial presentation of ARN, 8 weeks after varicella-zoster dermatitis.

Observations: Central retinal vascular obstruction developed subsequently in his left eye. Later, the classic presentation of ARN appeared in his contralateral eye. Systemic acyclovir therapy stopped the progression of retinitis and resulted in healing of retinal lesions in his right eye.

Conclusions: This case suggests that optic neuropathy, especially with preceding herpetic dermatitis, should be suspected as the prodrome of ARN.

Key Words: Acute retinal necrosis, central retinal vascular obstruction, optic neuropathy.

Introduction

Acute retinal necrosis (ARN) is a distinct ocular inflammatory syndrome with a constellation of clinical features. It was initially reported just 30 years ago. The prominent findings in ARN syndrome include severe occlusive vasculitis that primarily involves the arterioles of the retina as well as the choroid, a full thickness, diffuse necrotizing retinitis that preferentially affects the peripheral retina, and a moderate to severe vitreous cellular reaction.

Other posterior segment findings with ARN include optic disc swelling that can be either hyperemic or pallid. Optic neuropathy usually develops concurrently or during the course of ARN. Rarely, optic neuropathy may precede ARN syndrome, as was the case in an individual infected with human immunodeficiency virus.1

We describe a case of bilateral ARN that developed in an otherwise healthy patient, in whom the initial presentation was unilateral optic neuropathy.

Case Report

A 54-year-old man complaining of upper field defect that developed suddenly in his left eye visited a community ophthalmologic clinic on January 13, 2000. Varicella-zoster dermatitis on the left forehead had developed 8 weeks earlier and was treated with oral acyclovir for 1 week. He had no remarkable systemic disease.

His visual acuity at that time was 20/20 OD, 20/80 OS. There was a relative afferent pupillary defect in the left eye. Ophthalmoscopic examination of the left eye revealed optic disc swelling and parapapillary splinter hemorrhages. Macular edema, especially at the inferior side, was also noted when he visited the clinic 3 days later (Figure 1). However, no abnormality of the peripheral fundus was detected at that time.

The patient was referred to our hospital when further visual deterioration in his left eye developed on
January 25, 2000. His visual acuity was 20/20 OD, and light perception OS. Slit-lamp examination of the left eye revealed mild cellular reaction in the vitreous. Severe retinal hemorrhage and edema were noted throughout the entire fundus of his left eye, mimicking the fundus appearance of central retinal vein occlusion. Fluorescein angiography revealed obstruction of both the central retinal artery and vein, with mild vascular leakage at the late phase of angiography. No abnormality was found in his right eye on ocular examination and fluorescein angiography. The systemic cause for his ocular condition was investigated. The results of chest x-ray, electrocardiogram, blood cell count with erythrocyte sedimentation rate, and C-reactive protein and liver function tests were all within normal range, except for mild leukocytosis (12,100 cells/mm$^3$). Because the disease process had been progressive and predominantly hemorrhagic, antibody titers against cytomegalovirus and human immunodeficiency virus were checked but results were negative. Supportive medication was prescribed and his ocular condition was followed up weekly.

When the patient revisited our hospital on February 16, 2000, he complained of foggy vision in his right eye. Visual acuity at that time was 0.8 OD, and no light perception OS. There was 2+ cellular reaction in the anterior chamber bilaterally. Compared with the earlier visit, fundus appearance in the left eye was stationary except for slightly increased haziness in the vitreous cavity. At this time, mild vitreous haziness and parapapillary retinal edema were noted in the right eye. There were three spots of whitish necrotic lesions, which were wedge-shaped and scattered in the peripheral retina of the right eye. Retinal vascular sheathing posterior to the necrotic lesion was conspicuous.

The diagnosis of ARN was established and the patient was hospitalized for treatment and further evaluation. Serum antibody study was done for several viruses known to be associated with ARN. Immunoglobulin G (IgG) titers against herpes simplex, herpes zoster, and Epstein Barr virus were all positive. However, immunoglobulin M (IgM) titers against those three viruses were all negative. IgG titer against varicella-zoster virus (VZV) was 43.8 IU on March 9, 2000, and 14.9 IU 3 months later. The treatment consisted of intravenous acyclovir (3,150 mg/day), oral prednisone (45 mg/day) and aspirin (1,000 mg/day), topical atropine, and steroid. On the second day after admission, one new peripheral necrotic retinal lesion and a slight enlargement of a previous lesion were noted in the right eye. However, no further progression was detected thereafter. Prophylactic laser photocoagulation was applied posterior to the areas of retinitis in the right eye on the eighth day after admission. There appeared a grayish white zone of retinal necrosis after resolution of the dense retinal hemorrhage that had been precluding visualization of retinal details in the left eye (Figure 2). Subsequently, total retinal detachment with numerous atrophic retinal holes developed in the left eye. However, surgery was not attempted because there was little hope for restoration of vision.

Acyclovir administration in oral form was started after 2 weeks of hospitalization and maintained for 2 months thereafter. Oral and topical steroids were tapered. Inflammatory reaction subsided and the retina remained attached in the right eye at 12 months after the initial visit. Visual acuity at the final visit was 20/20 OD and no light perception, OS.

**Discussion**

Acute retinal necrosis is a syndrome, the diagnosis of which usually depends on clinical observation. The classic presentation of ARN is peripheral retinal necrosis with progressive circumferential extension and with vitreous cellular reaction. Obliterative vasculitis, especially at the arterial side, is usually evident on
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Fluorescein angiography. The incidence of optic neuropathy occurring concurrently or during the course of retinal necrosis is reported to be 57%.\(^2\) When the optic nerve is involved in the ARN patient, optic disc swelling is found in acute presentation and late optic atrophy ensues. Intraneural inflammation and necrosis, presumably by direct viral infection, loculated exudate within the optic nerve sheath and ischemic necrosis due to intraneural vasculitis are known to be involved in the pathogenic mechanisms of optic neuropathy associated with ARN.

Recently, cases of optic neuropathy preceding ARN have been reported among immunocompromised patients with acquired immunodeficiency syndrome or rheumatoid arthritis. As far as we are aware, there has been no reported case of ARN when the initial presentation was optic neuropathy in a previously healthy immunocompetent person. Although optic neuropathy is observed at some point in the disease course in a significant proportion of patients with ARN, optic neuropathy as an initial manifestation of ARN imposes a diagnostic challenge because early institution of antiviral therapy has prognostic importance.

Diagnosis of the left eye condition was difficult until the classic presentation of ARN developed in the right eye. Aside from initial presentation as optic neuropathy, vascular obstruction occurred predominantly at the posterior pole of the left eye. Retinal hemorrhage and edema associated with central retinal vascular obstruction were so extensive that they masked necrotic whitening of the retina in the early stages of the disease. In contrast to ARN occurring in the immunosuppressed person, initial posterior pole involvement is an unusual finding in the manifestation of ARN occurring in an immunocompetent person.

Although the presentation in the left eye was atypical, we consider this case as bilateral ARN for the following reasons. First, vascular obstruction and vitreous cellular reaction as well as the appearance of well-demarcated necrotic whitening of retina in both eyes constitute the clinical hallmarks of ARN. Second, from the chronological standpoint, herpes zoster skin eruption with ensuing unilateral ARN followed by contralateral eye involvement is not an uncommon manifestation of this disease.\(^3\) Third, development of numerous atrophic retinal holes and retinal detachment is also supportive evidence of ARN in the left eye.

Serologic study to identify a causative agent was somewhat helpful in our case. Elevated IgM titer, which reflects recent infection, was not found in any viruses studied. Because the serologic test for viral antibody was done at 3 months after the onset of active dermatitis, serum IgM level might have already dropped. Anti-viral IgM is known to rise at 1 week and disappear 1 to 3 months after acute infection.\(^4\) That IgG titer against VZV dropped to about one third at 3 months after acute ARN in the right eye is regarded as indirect evidence of this viral etiology. In addition, the preceding dermatitis on the forehead strongly suggests ARN due to VZV. The interval between herpes zoster dermatitis and onset of ARN is reported to be 5 days to 3 months.\(^1\) According to one recent study by polymerase chain reaction (PCR)-based assays, VZV is the most common pathogen of ARN.\(^5\)

Initiation of high-dose intravenous acyclovir seemed to protect against progression of retinal lesion in the right eye of our case. In this regard, antiviral therapy for an extended period after dermatitis or early initiation of antiviral therapy even after the onset of disease in the left eye might have saved the left eye and prevented the development of bilateral ARN.

In retrospective review of our case, the preceding varicella-zoster dermatitis and vitreous cellular reaction would be alarming signs for suspecting the onset of ARN in the left eye. Recently, viral identification with vitreous sample by PCR is emerging as a useful tool to diagnose ARN. It is uncertain whether the evaluation by PCR will be a helpful means to establish early diagnosis in a clinical situation like our case. Further study regarding this issue is warranted.

Our case indicates that optic neuropathy and central retinal vascular obstruction may herald ARN.
Physicians should be alert to this possibility, especially when there is a recent history of herpetic dermatitis, because the prognosis of ARN usually depends on early diagnosis and intensive care including vigorous antiviral therapy.

References


