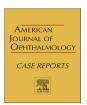


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#### Case report

# Poor prognosis of elderly individuals >80 years of age with acute retinal necrosis



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#### ABSTRACT

*Purpose*: To report the clinical features and prognosis of acute retinal necrosis (ARN) in elderly (>80 years of age) individuals.

Methods: Six consecutive patients with unilateral ARN who attended the Department of Ophthalmology at Yamaguchi University Hospital between 2014 and 2015 were retrospectively reviewed. Clinical characteristics, causative virus, time from symptom onset to physician visit, visual acuity at presentation and final visit, and treatment were evaluated and compared between the three elderly and three middle-aged (<80 years) patients.

Results: Varicella zoster virus (VZV) DNA was detected in aqueous humor by the polymerase chain reaction in all six cases. The mean  $\pm$  SD time between symptom onset and medical attention was  $18.0 \pm 8.7$  and  $8.3 \pm 1.5$  days in the elderly and middle-aged groups, respectively. All patients were treated with intravenous aciclovir, oral prednisolone, and a nonsteroidal anti-inflammatory drug, and five of the six patients also received oral <u>valaciclovir</u> and underwent vitrectomy. The final best corrected visual acuity of the affected eye was worse for the elderly patients (20/400, hand motion, and light perception negative) than for the middle-aged patients (20/15, 20/50, and 20/25).

Conclusions and importance: ARN in the elderly individuals of the present study was caused by VZV infection and associated with a poorer visual prognosis compared with that of middle-aged patients. A delay in the onset of antiviral treatment might contribute to the poor prognosis of elderly patients with ARN.

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#### 1. Introduction

Acute retinal necrosis (ARN) is a rare and aggressive form of retinal infection that was first described in 1971 and is characterized by confluent peripheral necrotizing retinitis, peripheral occlusive retinal arteritis, and moderate-to-severe vitritis. ARN is diagnosed predominantly on the basis of clinical findings, <sup>2–4</sup> with the success rate for isolation of DNA of the causative virus from aqueous or vitreous humor samples being variable. Both varicella zoster virus (VZV) and herpes simplex virus (HSV) have been implicated as causes of ARN. <sup>5–7</sup>

The prognosis of individuals with ARN is dependent on the disease course but is usually poor as a result of irreversible loss of

vision, with best corrected visual acuity (BCVA) often deteriorating to between 6/60 and 6/9<sup>8,9</sup> and sometimes to no light perception. The aims of treatment for ARN are to prevent further damage and to target the causative virus by either systemic or intravitreal antiviral therapy. Furthermore, treatment with an argon laser or vitrectomy might be applied prophylactically to prevent retinal detachment. ARN usually develops in non-immunocompromised adults between 20 and 60 years of age, although it sometimes affects individuals with various degrees of humoral immune deficiency, and it often occurs as the result of reactivation of HSV-1 or HSV-2 or of VZV after chickenpox. Factors that contribute to visual prognosis of ARN include age, initial visual acuity, and retinal detachment.

During a recent 2-year period, we detected indications of a possible outbreak of ARN in elderly individuals (>80 years of age). The prognosis of ARN specifically in such individuals has not been

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characterized, although such knowledge will become increasingly important as the aged population of developed countries increases. We now describe three cases of ARN in elderly patients and compare their prognosis, including visual acuity and treatment efficacy, with that of three cases in middle-aged individuals. The elderly patients had a poor visual outcome associated with periarteritis, dense vitreous opacity, peripheral retinal exudates, and retinal detachment despite administration of antiviral, corticosteroid, and antithrombotic therapy. We also investigated the possible causal factors for such poor prognosis in the elderly by analysis of clinical characteristics of the three cases.

#### 2. Subjects and methods

Six consecutive patients (six affected eyes) with ARN who attended the Department of Ophthalmology at Yamaguchi University Hospital between 2014 and 2015 were identified and retrospectively reviewed. Clinical features, causative virus, time from symptom onset to initial physician visit, visual acuity at both presentation and final visit, and treatment were evaluated. All six patients were immunocompetent. VZV, HSV, and cytomegalovirus were examined as potential causative viruses on the basis of a Goldmann-Witmer coefficient of  $\geq$ 6 for immunoglobulin analysis or of a positive polymerase chain reaction (PCR) test of aqueous humor or vitreous fluid, with all assays being performed by SRL (Tokyo, Japan).

#### 3. Results

The patients were classified into an elderly group (>80 years of age, one man and two women) or a middle-aged group (<80 years of age, three women), and their clinical characteristics were compared (Table 1). The mean  $\pm$  SD age of the two groups was  $83.0 \pm 1.7$  and  $53.7 \pm 12.3$  years, respectively. Two of the three patients in the middle-aged group had a documented history of herpetic infection, whereas none of those in the elderly group had such a history. In all six cases, the disease was unilateral and VZV was detected by PCR analysis of aqueous humor. The mean  $\pm$  SD time from the onset of subjective symptoms to the first visit to a physician was  $18.0 \pm 8.7$  and  $8.3 \pm 1.5$  days for the elderly and middle-aged groups, respectively. The final BCVA of the elderly group was worse than that of the middle-aged group.

All patients received intravenous aciclovir treatment (600, 750, 1250, or 1850 mg/day) for 7 or 14 days after clinical diagnosis, and five of the six patients also received oral valaciclovir (500 or 1000 mg/day) for 7 or 14 days (according to clinician preference) (Table 2). All patients were treated with an oral steroid to control persistent intraocular inflammation and with a nonsteroidal anti-inflammatory drug (NSAID) to prevent coagulation (Table 2).

Five patients with posterior involvement or severe vitritis that prevented observation of the retina underwent <u>prophylactic vitrectomy</u> to avoid the development of retinal detachment vitrectomy to treat or prevent the development of retinal detachment (Table 2). All three eyes in the elderly group developed ischemic neuropathy, with onset times of 3 days, 5 weeks, or 8 months after the diagnosis of ARN. There was no recurrence in either the affected or healthy eye of any patient during follow-up.

#### 3.1. Case 1

An 81-year-old woman first presented to an ophthalmologist with complaints of ocular pain and a strange feeling in her left eye that had begun 12 days previously. Treatment with betamethasone eyedrops and oral prednisolone (30 mg/day) was started. She was referred to our department 7 days later, when her BCVA in the affected eye was 20/40 and mild inflammation, including cells, keratic precipitates (KPs) with mutton fat—type appearance, and corneal edema, was detected in the anterior chamber of the left eye. Ophthalmoscopy revealed retinal hemorrhage along her whitish vessels as well as yellowish lesions in the peripheral retina involving the supraposterior pole (Fig. 1A), whereas spectral domain—ocular coherence tomography (SD-OCT) showed a largely normal anatomy with mild vitreous opacity (Fig. 1B).

ARN was suspected and treatment with intravenous aciclovir (1250 mg/day; 15 mg/kg per day), oral prednisolone (30 mg/day), and oral bayaspirin (100 mg/day) was immediately started. Two days after her first visit to our hospital, vitreous surgery was performed on the left eve because of progressive periarteritis including retinal hemorrhage, dense vitreous opacity, peripheral retinal exudates, and retinal detachment. VZV DNA was detected in aqueous humor by quantitative PCR analysis, and the patient was therefore diagnosed with ARN due to VZV infection. Periarteritis including retinal hemorrhage, dense vitreous opacity, and peripheral retinal exudates were attenuated somewhat after vitrectomy (Fig. 1C and D), and systemic administration of aciclovir and corticosteroid was continued for a total of 14 days and 3 months, respectively. However, the necrotic lesions did not diminish, macular edema and retinal atrophy remained apparent in the posterior pole, and BCVA of the left eye had dropped to 20/400 at the patient's final visit (Fig. 1E and F).

#### 3.2. Case 2

An 84-year-old woman first presented to an ophthalmologist with complaints of visual disturbance in her left eye that had started 4 weeks previously. One month later, she visited our department because of worsening of the visual disturbance. Her BCVA was counting fingers in the left eye. Mild inflammation in the

 Table 1

 Clinical features of unilateral acute retinal necrosis in elderly and middle-aged patients.

Case	Age (years)	Sex	Virus (AC)/history of herpetic infection	Days from symptom onset to first visit	Presenting BCVA	Final BCVA	Follow-up (months)
Elderly							
1	81	F	VZV/none	12	20/40	20/400	23
2	84	F	VZV/none	28	CF	HM	26
3	84	M	VZV/none	14	20/200	LP (-)	20
	$83.0 \pm 1.7$			$18.0 \pm 8.7$ days			
Middle-aged							
4	40	F	VZV/herpetic stomatitis	7	20/15	20/15	27
5	57	F	VZV/none	10	20/100	20/50	16
6	64	F	VZV/herpes zoster	8	20/25	20/25	10
	$53.7 \pm 12.3$			$8.3 \pm 1.5$			

Abbreviations: AC, anterior chamber tap; BCVA, best corrected visual acuity; CF, counting fingers; HM, hand motion; LP(–), light perception negative; VZV, varicella zoster virus.

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