Intravitreal Ganciclovir and Dexamethasone as Adjunctive Therapy in the Management of Acute Retinal Necrosis Caused by Varicella Zoster Virus

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Introduction

Acute retinal necrosis (ARN) syndrome is a distinct infectious retinitis caused by members of herpes virus family.[1] Diagnostic criteria for ARN include (1) one or more discrete foci of peripheral retinal necrosis (2) circumferential spread (3) arteriolar occlusion (4) a prominent vitreous or anterior chamber inflammatory reaction and (5) rapid disease progression in the absence of therapy. Supporting characteristics include optic neuropathy or atrophy, scleritis, and associated pain.[2]

Intravenous acyclovir, the mainstay of therapy since its introduction by Blumenkranz et al[3] in 1986, prevents formation of new lesions in the affected eye and reduces the risk of involvement of the fellow eye, but does not decrease inflammation.[1, 4] Oral corticosteroids are commonly added 2 to 3 days later to control inflammation, with unproven benefit.[1, 5] Intravitreal antiviral therapy has been used, usually as adjunct to systemic therapy.[6] Unfortunately despite treatment, visual prognosis in the affected eye remains poor.

Inflammatory vasculitis involving all layers of the eye is an important cause of tissue damage in ARN. Histological studies have demonstrated diffuse retinal arterial occlusion.[7]

We therefore hypothesized that prompt control of inflammation and viral multiplication with adjunctive intravitreal injections of dexamethasone and ganciclovir might improve outcome in ARN.

Case Report

A 40-year-old healthy male presented with a three day history of pain, redness and decreased vision OD. Examination revealed visual acuity of 20/400, conjunctival congestion, anterior uveitis, dense vitritis, optic nerve edema, arteriolar narrowing, and peripheral retinal whitening in two inferior quadrants OD (Figure 1A and B), and normal OS. Intravenous fluorescein angiogram showed hypoperfusion of the optic nerve, arteriolar occlusion and leakage from arterioles (Figure 2). He was admitted for induction therapy with intravenous acyclovir 10/mg/kg q 8h for 8 days, aspirin 325 mg/d PO, topical 1% prednisone acetate every two hours and topical 1% atropine eye drops q 8h. The following morning, a diagnostic vitreous tap was performed followed by intravitreal injections of ganciclovir (2 mg/0.1mL) and dexamethasone (400 mcg/0.1mL). PO prednisone 60 mg/day was added on day #3 and tapered over three months. Valacyclovir 1 gm PO tid was started on day #9 and continued for three months.

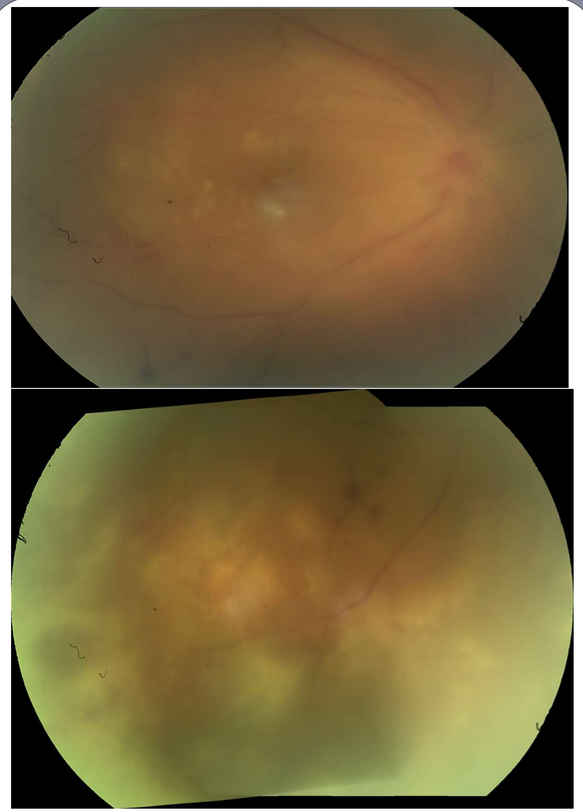

Figure 1A and B

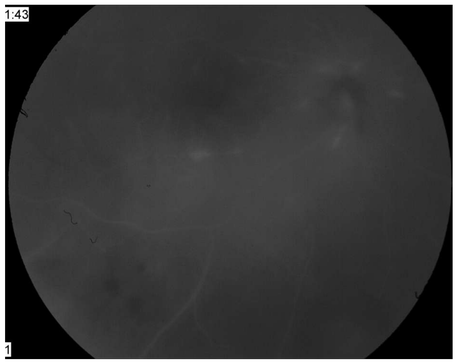

Figure 2

Results

Varicella zoster virus DNA was detected by PCR in the vitreous. Serology was negative for HIV, toxoplasmosis, and syphilis. Chest X-ray was normal. No new lesions were observed, and optic nerve edema and uveitis resolved over the next two weeks. Lesions showed decreased edema starting day #3, pigmentation around day #5, and healed by day #9 (Figure 3).

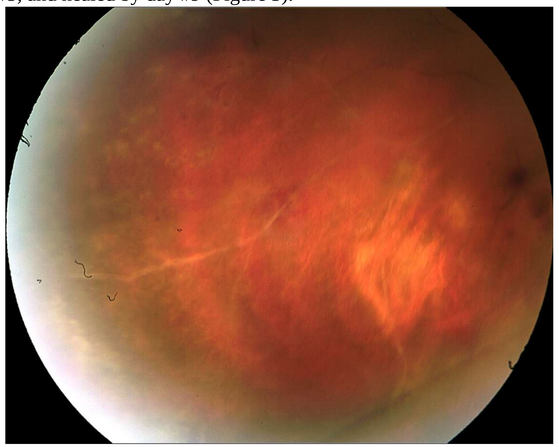

Figure 3 (Day #9)

Visual acuity improved to 20/30 at two months follow up and remained at that level for three months. Approximately five months after the onset of disease, he presented with sudden loss of vision to hand motions because of vitreous hemorrhage OD. An ultrasonography showed attached retina. A 25-g pars plana vitrectomy was done three days later. Retinal neovascularization was identified at inferior periphery. It was excised with the vitrector and panretinal photocoagulation was performed giving him a total of 1100 spots with endo and indirect laser. Visual acuity improved to 20/30 two weeks after vitrectomy. Fundus photographs two months after vitrectomy showed mild pallor of the optic nerve, sheathing of retinal arterioles, healed retinitis and good panretinal photocoagulation (Figure 4). The other eye has remained uninvolved.

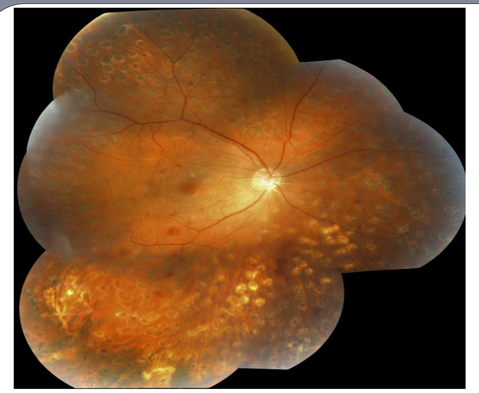

Figure 4 (Seven months)

Discussion

Our patient would probably have had a poor outcome with conventional treatment not only due to poor presenting visual acuity of 20/400,[5] but also due to generalized retinal ischemia from arteriolar occlusion,[8] optic disk involvement,[1,9] retinitis involving about 50% of the retina, and causal agent being varicella zoster virus.[6]

Inflammatory vascular occlusion involving the iris, choroid, retina and optic nerve is an important cause of tissue destruction in ARN**.** Virus has not been detected in blood vessels, optic nerve or choroid.[7] We therefore hypothesized that treatment for ARN has not been very successful because inflammation has not been targeted sufficiently in the past. Conventional treatment with oral steroid initiated a few days later might be too slow in the face of rapidly progressing inflammatory vascular occlusion.

There is obvious concern that intravitreal steroids might induce immune suppression. We therefore elected to give intravitreal ganciclovir at the same time. Intravitreal ganciclovir can achieve remission in progressive outer retinal necrosis (PORN), where iv acyclovir is ineffective suggesting that intravitreal ganciclovir might be more effective in inhibiting viral multiplication compared to iv acyclovir.[10]

We believe that adjunctive therapy with intravitreal gancyclovir and dexamethasone promptly addresses both components of tissue damage in ARN, specifically control of viral multiplication and control of inflammation, and needs to be further studied.

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Financial Disclosures: None
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