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. Diagnostic criteria for ARN include (1) one or more discrete foci of peripheral retinal necrosis (2) circumferential spread (3) arterial 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, scotoma, and associated pain. Intraocular acyclovir, the mainstay of therapy since its introduction by Blumenkranz et al. 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. Oral corticosteroids are commonly added 2 to 3 days later to control inflammation, with unproved benefit. Intravitreal antiviral therapy has been used, usually as adjunct to systemic therapy. 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. 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, arterial narrowing, and peripheral retinal whitening in two inferior quadrants OD (Figure 1A and B), and normal OS. Intravenous fluorescein angiogram showed hyperperfusion of the optic nerve, arterial occlusion and leakage from arterioles (Figure 2). He was admitted for induction therapy with intravenous acyclovir 10mg/kg q 8h for 8 days, aspirin 325 mg PO, topical 1% prednisolone every two hours and topical 1% atropine eye drops q hs. 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.

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 vitreos resolved over the next two weeks. Lesions showed decreased edema starting day #3, pigmentation around day #5, and healed by day #9 (Figure 3).

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.

Discussion

Our patient would probably have had a poor outcome with conventional treatment not only due to poor presenting visual acuity of 20/400 but also due to a delayed initiation of therapy (Figure 1A and B). Intravitreal antiviral therapy with ganciclovir or acyclovir has been associated with significant improvement in visual acuity and visual field in ARN. Supportive therapy with intravenous acyclovir (10 mg/kg q 8h for 8 days), aspirin, topical 1% prednisolone, and topical atropine might improve outcome in ARN. Treatment for ARN has not been very successful because inflammation has not been targeted sufficiently in the past. Conventional treatment with oral prednisone might be too slow in the face of rapidly progressing inflammatory vitreous exudation. 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 therapeutic and retinal necrosis by using high dose intravitreal acyclovir, where acyclovir is ineffective suggesting that intravitreal ganciclovir might be more effective in inhibiting viral multiplication than acyclovir.

We believe that adjunctive therapy with intravitreal ganciclovir 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.

Bibliography