
SHORT COMMUNICATION

Case report

Progressive outer retinal necrosis syndrome: successful treatment with a new combination of antiviral drugs

E.A. ROIG-MELO, T.A. MACKY, M.L. HEREDIA-ELIZONDO, D.VIRGIL ALFARO III

Department of Ophthalmology, Hanna Retina Research Center, Storm Eye Institute, Medical University of South Carolina, Charleston, S.C. - USA

PURPOSE. *To describe a case of progressive outer retinal necrosis syndrome, successfully treated with a new combination of antiviral drugs.*

METHODS. *The patient was treated with a combined therapy of antiviral drugs that includes: intravenous acyclovir 10 mg/kg, three intravitreal injections of foscarnet (1200 µg) and a ganciclovir implant in the right eye.*

RESULTS. *The progressive outer retinal necrosis appeared to respond dramatically with the combination of antiviral agents used over a period of 2 weeks with a final visual acuity of 20/80 at 3 months of follow up.*

CONCLUSIONS. *Intravitreal foscarnet combined with IV acyclovir and ganciclovir implant may represent an effective alternative treatment for PORN. (Eur J Ophthalmol 2001; 11: 200-2)*

KEY WORDS. *Progressive outer retinal necrosis, Treatment, Foscarnet, Ganciclovir, Acyclovir*

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INTRODUCTION

The progressive outer retinal necrosis syndrome (PORN) is a distinct form of necrotizing herpetic retinopathy observed in patients with AIDS. Engstrom et al have standardized the diagnostic criteria for the disease, these include: multifocal lesions characterized clinically by opacification of the deep retinal layers, with or without areas of confluence; lack of granular borders, minimal or no intraocular inflammation; and rapid progression of lesions. PORN should be differentiated from three clinical entities; CMV retinopathy, Acute Retinal Necrosis (ARN); and ocular lymphomas. Although CMV retinopathy is the most common type of necrotizing retinitis to occur in AIDS patients, PORN is found to be a much more devastating disease. To date few reports on diverse treatment modalities for PORN have been published. We present a case of PORN successfully treated with a different combination of antiviral drugs.

Case Report

A 40-year old male presented in August 1998 with pain and acute loss of vision in his right eye over the past few weeks. He had no symptoms in his left eye. The patient had a previous ocular history of herpetic keratitis and herpes zoster ophthalmicus in August 1996 in the left eye that was treated with oral acyclovir. The patient was diagnosed HIV positive in 1993, and had a history of sickle cell anemia, *staphylococcus aureus* lymphadenitis, and hepatitis B. His social history included intravenous drug use.

At the time of admission his CD4 cell count was 9 cell/ml. On ocular examination, he had visual acuity of 20/50 in the right eye and 20/20 in the left eye. Biomicroscopy revealed a right injected eye with no signs of corneal involvement; however, small corneal opacities from previous herpetic keratitis episodes were found in the left eye.

There was no anterior chamber inflammation, and the intraocular pressure was normal. Fundus exam of the right

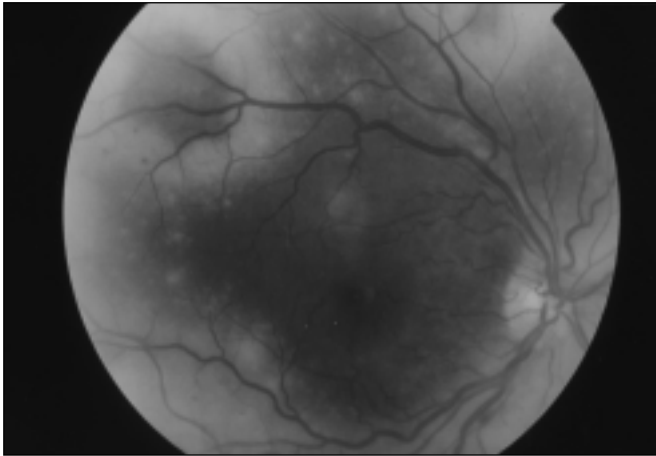


Fig. 1a - Fundus photograph of the right eye at presentation. Note the deep, active, retinal lesions outside the arcades.

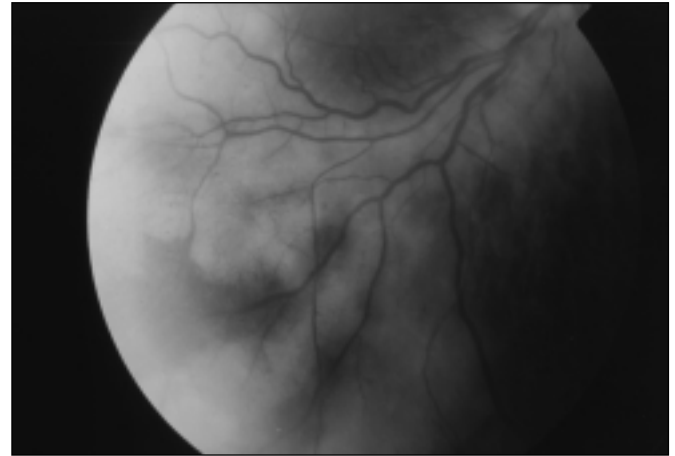


Fig. 1b - Fundus photograph of the inferotemporal quadrant of the right eye at presentation. The retinal lesions extended to the periphery.

eye showed multifocal retinal lesions characterized by deep yellow-white opacification and edema of the outer retinal layers. Lesions were located in the peripapillary, temporal and nasal mid-periphery (Fig. 1) in a perivascular distribution. Vitreous inflammation was mild. Fundus exam of the left eye was normal (Fig. 2). A clinical diagnosis of progressive outer retinal necrosis was made.

The patient was admitted for administration of intravenous acyclovir, 900 mg (10 mg/kg) three times a day.

One day after admission, there was evidence of disease progression, and the next day the vision was 20/80 with confluence of the lesions and involvement of the previous paravascular spared areas. On the third day after admission, intravitreal foscarnet injection was given; 1200

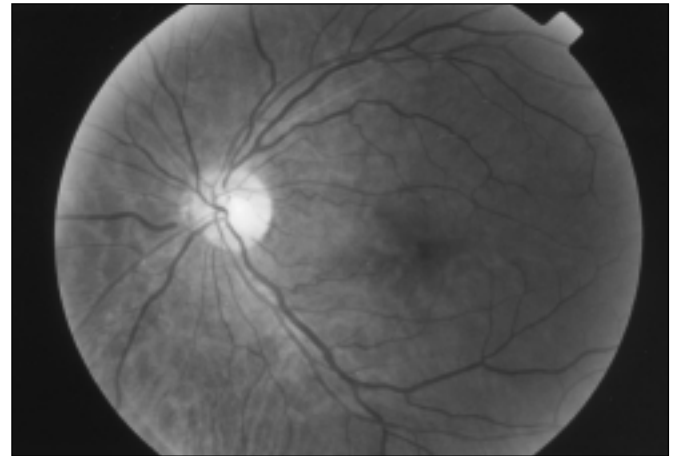


Fig. 2 - Fundus photograph of the left eye. Normal fundus.

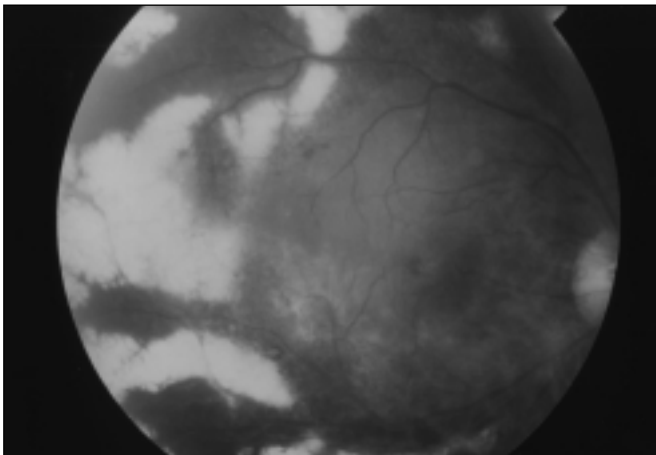


Fig. 3a - Fundus photograph of the right eye 2 weeks after treatment. The lesions have healed, with distinct margins and no inflammation.

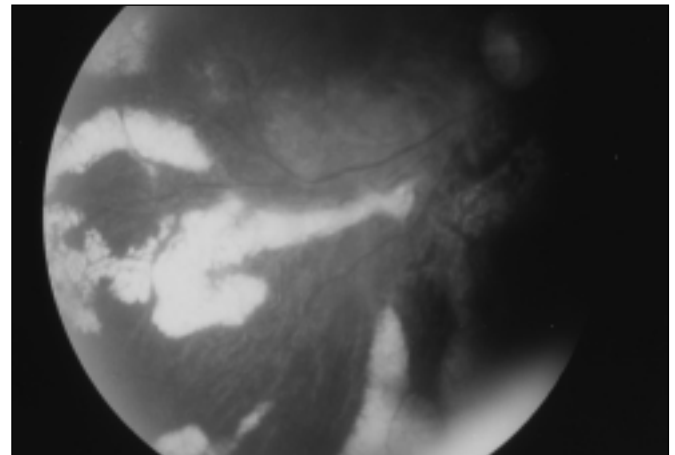


Fig. 3b - Fundus photograph of the inferotemporal quadrant of the right eye 2 weeks after treatment.

µg/ 0.1 ml with continuous IV acyclovir therapy. On the fourth day, the vision went down to 20/100. A second and third intravitreal foscarnet injections were given on the next two days (5th and 6th). The disease progression started to slow down over the next 3 days. However, a ganciclovir implant was inserted to augment the antiviral treatment. The implant was placed in the eye 4 days after the last intravitreal injection. The intravenous acyclovir was discontinued at this point. One day after the implantation, the fundus of the right eye showed decrease disease activity and stable Vitrasert implant. The patient was discharged for follow up with a visual acuity of 20/100. Two weeks later the visual acuity was 20/100 and the fundus exam showed cleared vitreous with decreased retinal edema and stabilization of disease activity (Fig. 3) with stable Vitrasert implant. One month later, the patient maintained the same visual acuity and the lesions had healed with distinct margins and no retinal edema. The patient was followed for 3 months and showed complete healing with final visual acuity of 20/80.

DISCUSSION

Treatment of PORN is disappointing in many cases, though a variety of treatment modalities has been published (1-3). Most of the experience is based on a combined therapy of intravenous and intravitreal antivirals, which include: acyclovir, ganciclovir, foscarnet, vidarabine and sorivudine. Engstrom and associates (1) have shown the poor response of progressive outer retinal necrosis to antiviral therapy. In their study, which included 38 patients including 65 eyes, 47% of his patients showed progression of the disease process in spite of the antiviral therapy initiated. However

the study also showed that combined therapies had a better response than single antiviral agents did.

Patients with AIDS often receive prolonged oral acyclovir maintenance therapy for cutaneous or systemic herpes virus infections, and subsequently develop acyclovir resistance. Ganciclovir has been shown to be effective in some acyclovir-resistant varicella-zoster isolates (4), which explain the enhanced efficacy of combined acyclovir and ganciclovir, despite similar structure and pharmacological action. Unlike the nucleoside analogs ganciclovir and acyclovir, foscarnet is a pyrophosphate analog that selectively inhibits viral DNA polymerase at the pyrophosphate binding site so it does not require phosphorylation for conversion to its active form. This may partly account for its efficacy against ganciclovir- or acyclovir-resistant herpes viruses explaining the enhanced efficacy of combined therapy (5,6).

The treatment of progressive outer retinal necrosis must be aggressive and prolonged. Systemic acyclovir therapy alone appeared unable to halt progression of the retinal lesions in our patient. Through the treatment of our patient we could highlight two points. One, the use of intravitreal foscarnet could be helpful to enhance the antiviral therapy against this devastating disease and two, the successful maintenance therapy with ganciclovir implant alone, although the follow up was limited to 3 months. However further studies are needed to confirm these results.

Reprint requests to:
Tamer A. Macky, MD
Storm Eye Institute, Medical University of South Carolina
167 Ashley Avenue
P.O. Box 250676, Charleston
S.C, USA 29425-2236
e-mail: mackyta@musc.edu

REFERENCES

1. Engstrom RE Jr, Holland CN, Margolis TP, et al. The progressive outer retinal necrosis syndrome: a variant of necrotizing herpetic retinopathy in patients with AIDS. *Ophthalmology* 1994; 101: 1488-502.
2. Spaide RF, Martin DF, Teich SA, et al. Successful treatment of progressive outer retinal necrosis syndrome. *Retina* 1996; 16: 479-87.
3. Perez-Blazquez E, Traspas R, Mendez Martin I, Montero M. Intravitreal ganciclovir treatment in progressive outer retinal necrosis syndrome. *Am J Ophthalmol* 1997; 124: 418-21.
4. Coen D, Fleming H, Leslie L, et al. Sensitivity of arabinosyladenine-resistant mutants of herpes simplex virus to other antiviral drugs and mapping of drug hypersensitivity mutations to the DNA polymerase locus. *J Virol* 1985; 53: 477.
5. Jacobson M, Drew W, Feinberg J, et al. Foscarnet therapy of ganciclovir-resistant cytomegalovirus retinitis in patients with AIDS. *J Clin Microbiol* 1992; 30: 2917-20.
6. Safrin S, Assaykeen T, Folansbee S, et al. Foscarnet therapy in five patients with AIDS and acyclovir resistant varicella zoster virus infection. *Ann Intern Med* 1990; 115: 19.