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SHORT COMMUNICATION

Unilateral recurrent acute retinal necrosis syndrome caused by cytomegalovirus in an immune-competent adult

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PURPOSE. *To report an immune-competent patient with unilateral recurrent acute retinal necrosis syndrome caused by cytomegalovirus, and to highlight the importance of diagnostic vitreous biopsy and specific antiviral therapy in this condition.*
METHODS. *Case report.*
RESULTS. *A 75-year-old man with good general health had two episodes of acute retinal necrosis syndrome affecting his left eye. Vitreous biopsy was performed in each episode, and polymerase chain reaction analysis on the vitreous specimen was positive for cytomegalovirus and negative for varicella zoster virus and herpes simplex virus 1 and 2. On each occasion, investigations indicated past cytomegalovirus infection but no evidence of a systemic reactivation. No indication of immunodeficiency was found over a 2-year follow-up period. His management, which included systemic and intravitreal antiviral therapy, is discussed.*
CONCLUSIONS. *To the authors' knowledge, only two other cases of acute retinal necrosis syndrome caused by cytomegalovirus have been reported previously in immune-competent patients. This case illustrates the importance of vitreous biopsy for viral polymerase chain reaction studies in cases of acute retinal necrosis syndrome, in order to direct appropriate antiviral treatment. It also illustrates the role of an intravitreal antiviral drug that is effective against all three herpetic viruses. (Eur J Ophthalmol 2006; 16: 484-6)*

KEY WORDS. *Acute retinal necrosis syndrome, Cytomegalovirus, Vitreous biopsy*

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INTRODUCTION

We report an immune-competent patient with unilateral recurrent acute retinal necrosis syndrome (ARN) caused by cytomegalovirus (CMV). We highlight the importance of diagnostic vitreous biopsy and specific antiviral therapy in this condition.

Case report

A 75-year-old man presented with a 1-month history of deteriorating vision and discomfort in the left eye. Left visual acuity was counting fingers. He had marked anterior uveitis with large keratic precipitates. Intraocular pressure was high at 34 mmHg. There was an intense vitritis, and the fundus showed widespread occlusive retinal vasculitis with arteriolar involvement, scattered intraretinal hemorrhages, and two areas of active retinitis in the superotemporal periphery (Fig. 1). The right eye was normal. He was in good health, and medical examination was unremarkable.

A clinical diagnosis of ARN was made. He was treated with high-dose intravenous acyclovir (10 mg/kg tds) for 1 week without complication, followed by oral valacyclovir (1 gm tds) for 1 month. A vitreous biopsy was performed on day 2, and intravitreal foscar-

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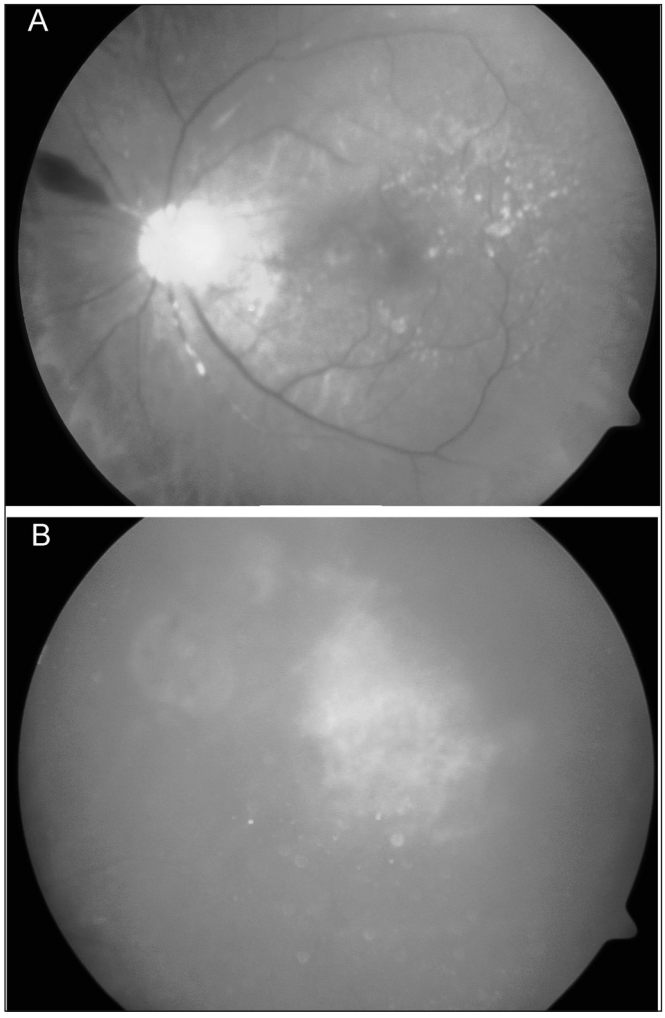

Fig. 1 - *(**A**) Fundus photograph of the left eye showing arterial attenuation and hazy view due to vitreous cells. (**B**) Area of retinal necrosis in the upper temporal periphery of the same eye.*

net was given (2.4 mg in 0.1 mL). Oral prednisolone (1 mg/kg daily) was started on day 4 to control the intraocular inflammation and was tapered over the next 6 weeks. The retinitis became inactive after 1 week, and vision improved to 6/24 at 1 month.

Polymerase chain reaction (PCR) analysis on the vitreous specimen was positive for CMV (1.65×10^5 copies DNA/mL) and was negative for varicella zoster virus (VZV) and herpes simplex virus (HSV) 1 and 2. His serology indicated past CMV infection and no recent systemic reactivation: the complement fixation test (CFT) for CMV was positive (1:64) with no rise in titre at 2 weeks, and the anti-CMV IgM and serum PCR for CMV were negative. Serology for human immunodeficiency virus (HIV) 1 and 2 and for Treponema pallidum were negative. There was no indication of immunodeficiency with a normal full blood count and white cell differential, normal lymphocyte surface markers (CD4+ lymphocyte count 535 cells/mm^3), and normal immunoglobulin levels.

Three months later, the ARN relapsed with development of fresh areas of retinitis. Vitreous biopsy and intravitreal foscarnet injection were repeated, and vitreous PCR analysis again confirmed CMV, this time with a higher viral load (8.4×10^6 copies DNA/mL). Serum PCR for CMV and anti-CMV IgM remained negative, and there was no rise in the CMV CFT. This time, he was treated with intravenous ganciclovir (5 mg/kg bd) for 3 weeks without complication, followed by oral valganciclovir (900 mg bd) for 2 weeks (discontinued because of nausea), and a tapering course of oral prednisolone. The retinitis became inactive after 2 weeks, and vision improved to 6/18. There has been no further reactivation after 18 months of follow-up.

DISCUSSION

ARN syndrome is a clinical diagnosis characterized by one or more well defined focus of retinitis in the peripheral retina; rapid and circumferential disease progression; occlusive vasculopathy with arteriolar involvement; and a prominent inflammatory reaction in the vitreous and anterior chamber (1). It typically affects healthy individuals and is usually caused by VZV or HSV 1 or 2 (2).

Acquired CMV infection in healthy adults is usually asymptomatic but may occasionally present as a Paul Bunnell negative infectious mononucleosis before entering a latent state. Recurrent infection and marked tissue destruction are rare in healthy patients. However, severe immune suppression can lead to viral reactivation, viremia, seeding to one or more target sites (retina, gastrointestinal tract, liver, lungs, or brain), and tissue destruction. In this way, CMV infection causing a retinitis is the commonest ocular opportunistic infection in acquired immunodeficiency syndrome (AIDS). It has also been implicated rarely as a cause of ARN in other immune-compromised patients (3). However, ocular CMV infection in immune-competent patients is extremely rare and to our knowledge only two other cases of ARN caused by CMV have been reported previously in such patients (4, 5).

Our patient developed a recurrent ARN due to CMV infection confirmed each time by PCR analysis of the vitreous. On each occasion, investigations indicated past CMV infection but no evidence of a systemic reactivation, possibly suggesting a localized intraocular reactivation in our patient.

His immune competence may explain the marked anterior and posterior segment intraocular inflammation usually lacking in patients with AIDS with CMV retinitis.

Initial misplaced skepticism about the diagnosis of CMV in our patient, his good response to treatment, and concerns about the toxicity of systemic anti-CMV drugs led to continued treatment with intravenous acyclovir followed by oral valacyclovir. We suspect it was the intravitreal foscarnet, a drug effective against VZV, HSV, and CMV, which initially controlled his disease (we give this drug routinely to all cases of ARN at the time of vitreous biopsy). However, the subsequent relapse of ARN and the second positive PCR prompted appropriate systemic anti-CMV treatment with ganciclovir.

This case illustrates the importance of vitreous biopsy for viral PCR studies in cases of ARN in order to direct appropriate antiviral treatment, and the role of an intravitreal antiviral drug that is effective against all three herpetic viruses.

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