Cytomegalovirus (CMV) retinitis is the most common opportunistic ocular infection in immunocompromised patients [1]. However, CMV retinitis can develop in immunocompetent patients after intravitreal triamcinolone acetonide (IVTA) or after implantation of fluorocinolone acetonide [2-6]. All patients with such problems have been successfully treated with intravitreal and/or intravenous, and oral administration of ganciclovir (Table 1). Spontaneous resolution of CMV retinitis has been reported in infants with congenital infection and in patients receiving highly active antiretroviral therapy (HAART); however, spontaneous resolution has not been previously reported in a patient with intravitreal steroid-induced CMV. Here we report such a case [7,8].

A 73-year-old woman underwent vitrectomy and intravitreal triamcinolone acetonide (IVTA) of the right eye and cataract surgery with IVTA of the left eye, for bilateral diabetic macular edema. The patient presented with visual loss in both eyes three-months postoperatively. The fundoscopic examination revealed white-yellow, necrotic peripheral lesions in the superotemporal quadrant of both eyes. Although bilateral acute retinal necrosis was suspected, azotemia resulting from diabetic nephropathy limited the use of acyclovir. Antiviral treatment was not started. A sample of the aqueous humor for polymerase chain reaction (PCR) analysis was obtained. One week later, the PCR results indicated the presence of cytomegalovirus (CMV). Since the retinal lesions did not progress and did not threaten the macula, the patient was followed without treatment for CMV. The retinal lesions progressively regressed and completely resolved in both eyes by six months of follow-up. Patients with IVTA-induced CMV retinitis may not require systemic treatment with ganciclovir.

Key Words: Cytomegalovirus retinitis, Diabetic retinopathy, Intravitreal injections, Triamcinolone acetonide

Received: February 2, 2010 Accepted: July 9, 2010

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weeks previously. The visual acuity was 20/200 in the right eye and counting fingers at 30 cm in the left eye. The intraocular pressure (IOP) was 30 mmHg in the right eye and 42 mmHg in the left eye. The slit lamp examination demonstrated fine keratic precipitates of the corneal endothelium, 3+ inflammatory cells, 2+ flare in the anterior chamber, and moderate vitreous haze in both eyes. The fundus examination revealed white-yellow, necrotic peripheral retinal lesions in the superotemporal quadrant of both eyes (Fig. 1A and 1B).

As bilateral acute retinal necrosis was suspected, starting intravenous treatment with acyclovir was considered. However, the patient refused hospital admission and further treatment. Moreover, azotemia resulting from diabetic

| Table 1. Previous reports of CMV retinitis after IVTA |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Age  | Sex | Systemic disease | Ocular pathology | Previous Ocular surgery | Onset of CMV retinitis following IVTA (mon) | Initial VA | Final VA | Treatment |
| 75   | M   | DM             | DME              | –                     | 4            | 0.05          | 0.05          | Diagnostic vitrectomy with intravitreal ganciclovir (2 mg), vancomycin (1 mg), ceftazidime (2.25 mg) Oral valganciclovir 900 mg twice daily for 9 months Repeated intravitreal ganciclovir (2.0 mg), twice After recurrence Repeated intravitreal ganciclovir (2.0 mg), once Oral valganciclovir |
| 77   | M   | DM             | AMD              | IOL                   | 3            | FC            | 1.8 m         | Intravitreal ganciclovir (2 mg) Intravenous ganciclovir (5 mg/kg/12 hr) for 1 week → Oral valganciclovir (900 mg twice a day) for about 3 months Subsequent RRD managed with vitrectomy, scleral buckling, photocoagulation, silicone oil tamponade |
| 69   | M   | DM             | CRVO             | PPV IOL               | 4            | 0.1           | 0.2           | Intravitreal ganciclovir (2 mg); not clearly disclosed in the article Intravenous ganciclovir (5 mg/kg/12 hr) for 1 week → Oral valganciclovir (900 mg twice a day) for about 3 months |
| 63   | M   | DM             | BRVO             | IOL                   | 7            | 0.1           | 0.6           | Intravenous acyclovir (prior to PCR result) Intravenous ganciclovir 500 mg for 3 days Oral ganciclovir for 1 week |
| 77   | F   | HTN            | CRVO             | –                     | 4            | LP            | HM            | Intravenous ganciclovir (prior to PCR result) Intravitreal gancyclovir (1.7 mg) Argon laser photocoagulation between retinitis and normal retina After 3 weeks, aggravation Repeated intravitreal gancyclovir (1.7 mg), 3 times |
| 73   | F   | DM             | HTN              | DME                   | 3            | 0.1 (OD)      | 0.2 (OD)      | Intravenous acyclovir for 7 days (prior to PCR result) No anti-CMV treatment |

CMV = cytomegalovirus; IVTA = intravitreal triamcinolone acetonide; VA = visual acuity; DM = diabetes mellitus; DME = diabetic macular edema; AMD = age-related macular degeneration; IOL = cataract surgery; FC = finger count; CRVO = central retinal vein occlusion; PPV = pars plana vitrectomy; BRVO = branch retinal vein occlusion; PCR = polymerase chain reaction; HTN = hypertension; LP = light perception; HM = hand motion; OD = right eye; OS = left eye.
nephropathy limited the use of acyclovir. Therefore, anti-viral treatment was not started and the patient was closely monitored. A diagnostic aqueous humor sample for polymerase chain reaction (PCR) analysis was obtained. PCR was carried out to test for varicella zoster virus, herpes simplex virus type 1 and 2, and CMV. Topical anti-glaucomatous and steroid medications were used for treatment.

The PCR results, available seven days later, confirmed the presence of CMV. The infectious disease consultant reported that systemic CMV infection was not possible and recommended antiviral therapy with ganciclovir for the CMV retinitis. However, one week had elapsed and the IOP and inflammatory reaction of the anterior chamber and vitreous had decreased, the peripheral retinal lesion did not increase, and the macula was not threatened in either eye (Fig. IC and ID).

The CMV retinitis was likely caused by the local (intraocular) immunosuppression caused by the IVTA and the immunosuppression might have reduced over time (already 3 months since the IVTA was administered in both eyes). The CMV retinitis did not threaten the macula. Since starting treatment with ganciclovir was not urgent, the patient was closely followed without any anti-CMV medications. The plan was close observation while maintaining the topical anti-glaucomatous and steroid therapy.

In November of 2008, two months after the initial presentation, the inflammatory reaction of the anterior chamber appeared to be resolved and the vitreous haze was much improved in both eyes. The IOP was 24 mmHg in the right eye and 28 mmHg in the left eye with topical application of timolol and dorzolamide. The necrotic retinal lesion regressed slightly without any progression of the margin of the lesion in both eyes.

In April of 2009, six months after initial presentation,
In murine studies, the possibility of the retina as a site of CMV infection is rare. CMV infection occurs in 4% of live-born infants and 50% to 80% of adults. Moreover, PCR-based studies indicate that some seronegative adults are chronic virus carriers [9-12]. The site of chronic infection continues to be debated. Sites reported have included monocytes [9], bone marrow-derived myeloid progenitors such as granulocyte-macrophage progenitor cells [13,14], endothelial cells and the smooth muscle cells of blood vessels [15-18]. In murine studies, the possibility of the retina as a site of chronic infections has been proposed [19]. However, Vogel et al. [20] showed that the human eye (retina) is not a specific site for chronic CMV and that CMV retinitis is more likely due to infiltration of virus-infected circulating cells during immunosuppression. It is assumed that CMV spreads hematologically (in mononuclear and polymorphonuclear leukocytes and/or endothelial cells) to infect the retina after reactivation [21,22]. Studies on patients with CMV retinitis have shown that retinal vascular endothelial cells can be infected with CMV in vivo. Therefore, it was assumed that CMV infected the retinal vascular endothelial cells, leading to infection of the surrounding glial and neuronal cells followed by the retinal pigment epithelium [23].

Considering the wide use of IVTA, CMV retinitis could become a not-so-rare, significant complication attributable to local immunosuppression. The clinical course of the case reported here suggests that systemic treatment with ganciclovir may not be mandatory; its use should take into consideration such factors as host immunity, macular involvement, the elapsed interval after IVTA, history of vitrectomy, and coexisting diabetic nephropathy, which can be aggravated by ganciclovir.

In previous reports, immunocompetent patients with CMV retinitis attributable to IVTA have been managed with intravenous ganciclovir similar to the treatment of immunocompromised patients (Table 1). However, the patient reported here was not treated with antiviral therapy. The IVTA-induced local (intraocular) immunosuppression was thought to decrease with time and that close observation without ganciclovir was appropriate in this patient; the intraocular concentration of triamcinolone is measurable for up to three months in the absence of a vitrectomy, and the elimination half-life would be much shorter in vitrectomized eyes after IVTA [24,25].

Immunity plays a significant role in the pathogenesis of CMV retinitis in patients with acquired immunodeficiency syndrome. Prior to the introduction of HAART, the treatment of CMV retinitis included an induction phase and maintenance phase with ganciclovir. Subsequently, prolonged use of ganciclovir was found to cause systemic adverse effects such as hematological abnormalities (neutropenia, thrombocytopenia and anemia) and renal impairment [26,27]. After the introduction of HAART with subsequent immune recovery, CMV retinitis may not recur even after maintenance anti-CMV therapy is discontinued. In addition, as this case illustrates, active CMV retinitis may spontaneously resolve in some patients that never receive specific anti-CMV treatment [28].

Conflict of Interest
No potential conflict of interest relevant to this article was reported.

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