Identification of Human Herpesvirus 6 in a Patient With Severe Unilateral Panuveitis

Human herpesvirus 6 (HHV-6) is a member of the HHV family and has been associated with immunodeficiency disorders and neurologic diseases. This widespread virus can be classified into 2 groups: variant A (HHV-6A) and variant B (HHV-6B). Although HHV-6B is the known causative agent in exanthema subitum, the association of HHV-6A with clinical entities is still unknown. We describe a patient with severe right-sided panuveitis and multiple subretinal lesions. The HHV-6A genome was detected in the ocular fluid of this patient.

Report of a Case. A 75-year-old man developed a sudden decrease in vision in the right eye in 2005. Slit-lamp examination of the right eye disclosed ciliary hyperemia, moderate mutton-fat keratic precipitates, and severely inflamed anterior chamber cells with hypopyon. Funduscopic examination of the right eye revealed dense vitreous opacities, optic disc swelling, yellowish-white massive retinal lesions measuring approximately 1.5 optic disc diameters, and whitish retinal exudates (Figure 1). The left eye was normal. Results of all systemic examinations, including serologic testing for human immunodeficiency virus, were negative, and results of serologic testing for HHVs (herpes simplex virus, varicella zoster virus, Epstein-Barr virus, cytomegalovirus, and HHV-6) were positive except for varicella zoster virus. On the basis of the ocular manifestations, a viral infection was suspected. After informed consent was obtained, an aliquot of aqueous humor and an aliquot of peripheral blood were collected and examined for further investigations. Immunoglobulin G for *Toxocara* larval excretory-secretory antigen in the aqueous humor and serum was detected using an anti-*Toxocara* antibody detection kit. A multiplex polymerase chain reaction demonstrated HHV-6 genomic DNA in both samples but not other HHVs (herpes simplex virus type 1 or 2, varicella zoster virus, Epstein-Barr virus, cytomegalovirus, HHV-7, or HHV-8). To acquire quantitative data, a real-time polymerase chain reaction was performed at different stages of the clinical course. In the acute phase with active inflammation, a high copy number for the HHV-6 DNA was detected in the samples (aqueous humor: $2.4 \times 10^6$ copies/mL; serum: $5.4 \times 10^6$ copies/mL). Because the patient indicated that there was progression of intraocular inflammation, right eye diagnostic pars plana vitrectomy was performed. A high copy number for the HHV-6 genome was detected in the vitreous fluid, retinal membrane, and peripheral blood mononuclear cells. In addition, IgG for *Toxocara* larval excretory-secretory antigen in the vitreous was also detected. These data led us to make the diagnosis of panuveitis related to a *Toxocara canis* larva or an HHV-6 infection. Next we examined whether the HHV-6 infection was indicative of variant A or variant B. A high number of copies of HHV-6A was detected in the samples, and the HHV-6A genome decreased after antiviral valganciclovir hydrochloride treatment associated with systemic corticosteroids, whereas the HHV-6B genome was not detected (Figure 2). After treatment, funduscopic examination of the right eye revealed resolution of the vitreous opacities, optic disc swelling, and retinal exudates.

Comment. It is difficult to be certain whether HHV-6 was the causative agent in intraocular inflammation in this patient. Anti-*Toxocara* antibodies were also detected in serum and aqueous humor and vitreous samples, the significance of which is difficult to interpret. Another hypothesis could be that HHV-6 favored *Toxocara*-generated inflammation. However, the vi-

Figure 1. Fundus photographs of the right eye of a patient with a human herpesvirus 6 variant A infection. A, Whitish retinal exudates (white arrow), optic disc swelling (black arrow), and dense vitreous opacities are seen. B, Retinal yellowish-white massive lesions (black arrowhead) and optic disc swelling (black arrow) are seen.
Serial measurement of aqueous humor human herpesvirus 6 variant A (HHV-6A) and variant B (HHV-6B) DNA levels by means of real-time polymerase chain reaction.

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Severe Darkening of a Facial Skin Graft From Latanoprost

Latanoprost is a 17 phenyl-substituted analogue of prostaglandin F2α (PGF2α), which decreases intraocular pressure by increasing uveoscleral outflow. Since its introduction as a topical eye medication, several authors have reported adverse effects, like subtle hyperpigmentation of periorcular skin and eyelid-margin hyperemia. Herein, we present a case of a patient using latanoprost who developed severe darkening in a facial skin graft.

Report of a Case. A 68-year-old woman was diagnosed with primary open-angle glaucoma in September 2002. Topical latanoprost was commenced in both eyes, with a good control of intraocular pressure. In April 2005, a malignant melanoma was surgically excised from the left side of the patient’s face and skin was grafted to this area from her neck behind the ear. Histology confirmed a low-risk, superficial, spreading malignant melanoma in situ, which was excised with adequate margins. In September 2005, severe darkening of the skin graft was noted together with subtle bilateral periorcular hyperpigmentation and eyelid-margin hyperemia (Figure 1). Her medication was switched from latanoprost to topical brinzolamide in both eyes with a good control of the intraocular pressure. One month after stopping latanoprost, the skin graft had lightened significantly and the subtle bilateral periorcular hyperpigmentation and eyelid-margin hyperemia had resolved (Figure 2).

Comment. Prostaglandins increase both melanocyte dendricity and melanin synthesis in the skin. Prostaglandin F2α stimulates the activity and expression of tyrosinase, the rate-limiting enzyme in melanin synthesis, and the PGF2α receptor has been shown to be up-regulated by UV radiation in melanocytes in vitro and in human skin in vivo. Researchers have shown how proteinase-activated receptor 2 in keratinocytes plays an important role in skin pigmentation. Activation stimulates uptake of melanosomes through phagocytosis and also stimulates release of prostaglandin E1 and PGF2α, which stimulate melanocyte dendricity. Prostaglandins have also been implicated in postinflammatory skin hyperpigmentation.

Significant lightening of the skin graft together with the resolution of subtle bilateral periorcular hyperpigmentation and eyelid-margin hyperemia 1 month after stopping latanoprost implies that a local adverse drug reaction to latanoprost occurred in this patient. Absorption of latanoprost into facial skin is likely to occur from tear spillover during topical application. The severe dark-