Severe Darkening of a Facial Skin Graft From Latanoprost

Latanoprost is a 17 phenyl-substituted analogue of prostaglandin F₂₀ (PGF₂₀), which decreases intraocular outflow 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.

Figure 2. 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.

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 F₂₀ stimulates the activity and expression of tyrosinase, the rate-limiting enzyme in melanin synthesis, and the PGF₂₀ 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 E₂ and PGF₂₀, 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 darkening and intraocular inflammation decreased in response to antiviral agents, suggesting that HHV-6A has some role in the pathogenesis of the ocular inflammation. To our knowledge, this is the first report of a case of HHV-6A associated with intraocular inflammation. These observations suggest that HHV-6A infection may have a role as a causative agent in severe intraocular inflammation.

Sunao Sugita, MD, PhD
Norio Shimizu, PhD
Tastushi Kawaguchi, MD
Nobuaki Akao, PhD, DVM
Tomohiro Morio, MD, PhD
Manabu Mochizuki, MD, PhD

Correspondence: Dr Sugita, Department of Ophthalmology and Visual Science, Tokyo Medical and Dental University Graduate School of Medicine, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8519, Japan (sunaoph@tmd.ac.jp).

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Duplication of the optic disc and fovea is known to occur in lower vertebrates. Although additional optic discs usually serve no purpose, bifoveate birds (eg, swallows) use the additional fovea for limited conjugate binocular movements. Doubling of the optic disc, true diastasis as well as coloboma, has been described in the human eye. We report the unusual clinical finding of 2 foveae in 1 eye of a patient.

**Report of a Case.** A 25-year-old man had experienced diminished vision in the right eye for several months. There was no history of ocular injury or inflammation. His perinatal and family histories were unremarkable. Best-corrected visual acuity was 20/80, N12 OD and 20/20, N6 OS, with low myopic correction. The anterior segment was unremarkable in each eye. Fundus examination of the right eye revealed macular pucker and peripheral telangiectasia with exudation, suggestive of Coats disease. Fundus examination of the left eye revealed 2 parafoveal halos with 2 foveal reflexes; the temporal reflex was slightly distorted (Figure, A). No other ocular structure exhibited duplication. Optical coherence tomography using a Stratus OCT 3 (Carl Zeiss Meditec, Dublin, California) supported the clinical appearance of foveal duplication: the temporal fovea demonstrated a similar slope of clivus and the recession of inner retinal layers as the central fovea. However, the recession was not complete; a thin layer of inner retinal neurons remained above the photoreceptor layer, the probable cause of blunted foveal reflex. Despite additional layers, the central fovea (thickness, 163 µm) and the accessory fovea (thickness, 160 µm) were similar in thickness, probably owing to less-elongated photoreceptors in the latter (Figure, B). Fundus fluorescein angiography demonstrated only 1 foveal avascular zone, corresponding to the central fovea. A nonspecific mottled hypofluorescence was observed in the area of the temporal fovea (Figure, C). Fundus fluorescein angiography of the right eye revealed leaking telangiectasia and avascular areas in the inferotemporal periphery. Orthoptic evaluation revealed no fixation abnormalities in the left eye; the patient fixed consistently with the central fovea. Automated perimetry using the central 10-2 threshold test protocol (model 720i, Humphrey Field Analyzer II; Carl Zeiss Meditec) showed a normal foveal threshold (31 dB) at the fixation point, with a typical gradient of reducing sensitivity toward the

Figure 1. Darkening of a 6-month-old facial skin graft in a 68-year-old woman together with subtle periorcular hyperpigmentation and eyelid-margin hyperemia. She had been using topical latanoprost in both eyes for the past 3 years.

Figure 2. Significant lightening of the skin graft together with resolution of the periorcular hyperpigmentation and eyelid-margin hyperemia 1 month after stopping topical latanoprost treatment.