Periorbital Changes Induced by Prostaglandin Eye Drops

Anya Stassiy, PA-C; Amor Khachemoune, MD

PRACTICE **POINTS**

- Ask patients to provide photographs taken prior to noticed changes to assess progression if they are new to your practice.
- Take photographs of patients in good light against a solid-colored background to have a baseline. It may be helpful to update patient images annually.
- Discuss with patients the aesthetic changes that may occur with the use of prescription medications. Provide pamphlets with images to educate them on what to expect.

To the Editor:

A 42-year man presented with hollowing of the upper eyelid and skin discoloration of the left periorbital area of 10 years' duration. He was a professional mixed martial arts fighter with a history of 2 surgeries for retinal detachment of the left eye 13 years prior to the current presentation. The patient also has macular scarring in the left eye. He denied a history of facial fracture, reconstructive surgery, or other medical conditions. His visual acuity was unknown; however, he did not require corrective glasses. He used 3 prescription ophthalmic eye drops—dorzolamide hydrochloride plus timolol maleate, 10 mL; brimonidine tartrate ophthalmic solution 0.15%, 5 mL; and latanoprost ophthalmic solution 0.005%, 125 µg/2.5 mL—in the left eye to lower intraocular pressure, as therapy for glaucoma. If left untreated, glaucoma can lead to vision loss.

Physical examination revealed periorbital hyperpigmentation on the left side; hypertrichosis and eyelash trichomegaly compared to the right side; and a deep left upper orbital sulcus compared to the right side (Figure). The patient was alert and oriented to person, place, and time. Extraocular movement was intact bilaterally, and his pupillary reflex was symmetric. No tenderness was noted over the affected area on palpation; no subcutaneous masses or lesions were observed or palpated. There was no ocular discharge, the conjunctiva was pink, and the sclera was white bilaterally.

The differential diagnosis included professional trauma-induced orbital changes, nevus of Ota (oculomucodermal melanocytosis), prostaglandin-associated periorbitopathy (PAP), and melasma. Although the patient sustained an injury that caused retinal detachment, he never experienced an orbital bone fracture; additionally, a fracture would not explain the skin discoloration or longer eyelashes. Periorbital nevus of Ota most commonly manifests as a unilateral scleral and brown-bluish skin discoloration but does not cause hollowing of the orbital sulcus or affect the length and thickness of eyelashes. Melasma—bilateral skin hyperpigmentation that most commonly affects women—can be induced by oral contraceptives, antibiotics, heat, sun exposure, and pregnancy. It does not affect the color of the iris or the depth of the scleral sulcus, and it does not increase the length and thickness of eyelashes. Based on the clinical presentation and a review of the eye drops used, he was diagnosed with PAP due to prolonged use of latanoprost ophthalmic solution. The patient was referred to an ophthalmologist for consideration of a switch to a different class of medication.

Anya Stassiy is from High Point Medspa, Mountainside, New Jersey. Dr. Khachemoune is from SUNY Downstate Health Sciences University, Veterans Affairs Medical Center, Brooklyn, New York.

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Correspondence: Amor Khachemoune, MD, SUNY Downstate Health Sciences University, Veterans Affairs Medical Center, 800 Poly Pl, Brooklyn, NY 11209 (amorkh@gmail.com).

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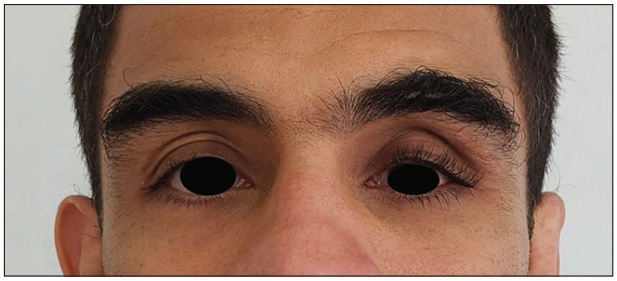
Of the 3 eye drops used by this patient, latanoprost, a prostaglandin analog, decreases intraocular pressure and is known to cause PAP. This condition comprises a constellation of changes, including upper eyelid ptosis, deepening of the upper eyelid sulcus, involution of dermatochalasis, periorbital fat atrophy, mild enophthalmos (sunken eye), inferior scleral show, increased prominence of eyelid vessels, and tight eyelids.[1] Latanoprost most often produces these findings, but all prostaglandin ophthalmic medications can, including the dual-indication bimatoprost, which was approved by the US Food and Drug Administration to reduce elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension but also is used to grow darker, thicker, and longer eyelashes. Clinicians who prescribe bimatoprost for this cosmetic indication should be mindful of the potential for PAP and discuss it with patients.

The prescribing information (PI) for bimatoprost (Latisse; Allergan) does not list PAP as an adverse reaction observed in the 4-month multicenter, double-blind, randomized, vehicle-controlled study of bimatoprost (as Latisse) in 278 adults.[2] The PI does list "periorbital and lid changes associated with periorbital fat atrophy and skin tightness resulting in deepening of eyelid sulcus and eyelid ptosis" as an adverse reaction in postmarketing experience. However, according to the PI, the frequency of these adverse reactions cannot be established, as the reporting of such incidents was voluntary and the size of the treated population was uncertain.[2]

Prostaglandins can cause periorbitopathy by several mechanisms; one speculated cause is that this group of medications might provoke smooth muscle contraction. Prostaglandin medications also have an affinity for fat cells[1]; atrophy of fat cells can lead to enophthalmos and deepening upper eyelid sulcus. In an observational study of 105 participants who were using a prostaglandin in 1 eye for longer than 1 month (the other eye was used as a control), the overall frequency of prostaglandin-associated periorbitopathy was 93.3% in the bimatoprost group, 41.4% in the latanoprost group, and 70% in the travoprost group, while the frequency of deepening of the upper eyelid sulcus was 80% in the bimatoprost group, 15.7% in the latanoprost group, and 45% in the travoprost group.[3] These changes may not be as striking when a patient is using a prostaglandin ophthalmic medication in both eyes and may not be noticed even by the patient. It is prudent for the clinician to take a baseline photograph of the patient when these medications are prescribed to observe for early signs of periorbitopathy. These adverse effects may not be reversible when the medication is discontinued[4] and have been observed as early as 4 to 6 weeks after the start of treatment.[5]



Periorbital hyperpigmentation on the left side; hypertrichosis and eyelash trichomegaly compared to the right side; and a deep left upper orbital sulcus compared to the right side that was determined to be the result of use of latanoprost ophthalmic solution 0.005%.

Our patient was counseled that his constellation of PAP findings potentially could be partially reversed over months or even a year or longer if the offending agent was discontinued. However, he was cautioned that cessation of latanoprost first needed to be discussed with his ophthalmologist, who would determine if there was a suitable alternative to a prostaglandin analog for him. The patient's only concern was the aesthetic appearance of the left periorbital area. A hyaluronic acid filler or fat grafting can be considered for correction of orbital sulcus hollowing; however, we could not locate any long-term studies in which such corrective treatments were applied for PAP. Our patient continues to use latanoprost with no change in the frequency of use. There have been no further changes or progression in the physical appearance of the left eye or periorbital area. The patient has not undergone any corrective treatments.

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