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Iris Heterochromia and Unilateral Eyelash Hypertrichosis

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Abstract

An 87-year-old female with a history of open-angle glaucoma presented with longer, thicker eyelashes on the right side compared to the left. Her irides were also different colors, as the right iris was brown and the left was hazel (green-brown). The patient had noticed a gradual darkening of her right iris and lengthening of her eyelashes over the last year, but denied visual changes or foreign-body sensation. Past medical history included a remote history of breast cancer treated by lumpectomy and radiation therapy, cerebrovascular accident, hypercholesterolemia, and hypertension. Her medications included bimatoprost, atenolol, atorvastatin, and clopidogrel.

What would you do next?

- A. Obtain eye and orbit computed tomography
- B. Order serologic studies including erythrocyte sedimentation rate, antinuclear antibody, complete blood count, and basic chemistry panel.
- C. Reassure patient
- D. Refer to an ophthalmologist urgently for slit-lamp and dilated examination

Diagnosis

Iris hyperpigmentation and eyelash hypertrichosis secondary to topical prostaglandin analogue (PGA) agent, bimatoprost (Lumigan, Allergan Inc. Irvine CA), to the right eye for unilateral open-angle glaucoma.

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What to do next

Reassure patient.

Iris hyperpigmentation and eyelash hypertrichosis are side effects of bimatoprost, a PGA agent.

Since this patient had glaucoma in one eye, the side effects from PGA use was clearly seen when compared to the unaffected eye, which had not been treated with a PGA. Thus, a careful history and review of medications revealed the culprit: unilateral bimatoprost use. The other diagnostic approaches, such as serological workup and imaging, could be indicated if the history, review of systems, or medications suggested congenital, ocular or systemic inflammatory, infectious, traumatic or neoplastic etiologies, but these should not be the first step in workup. Should such causes be suspected, prompt referral to an ophthalmologist would be warranted.

Discussion

PGAs are common agents used for the treatment of open-angle glaucoma, a leading cause of irreversible blindness worldwide.¹ Benign side effects associated with bimatoprost, a type of PGA agent, include eye pruritus, conjunctival hyperemia, periorbital lipodystrophy, and darkening of the iris, eyelashes, and periocular skin.^{2,3} Changes related to lipodystrophy include periorbital fat atrophy, deepening of the upper eyelid sulcus, relative enophthalmos (posterior displacement of the globe into orbit), and loss of lower eyelid fullness. Darkening of the iris pigmentation and eyelash hypertrichosis are classic findings associated with PGA use, and can occur in 1.5–1.9% and 42.6–53.6%, respectively, among patients using bimatoprost.² With the exception of permanent iris color changes, the other side effects may be reversible following discontinuation of the agent. Similar side effects have been noted to occur with other PGAs, including latanoprost and travoprost, but are more severe in bimatoprost users.⁴

Topical bimatoprost (sold as Latisse, Allergan) was FDA-approved for cosmetic eyelash growth in 2008. However, outside of the ophthalmology and dermatology communities, it is not widely known that bimatoprost and other PGAs can not only cause eyelash growth but also induce irreversible iris color changes, skin hyperpigmentation, and lipodystrophy. Since these features can also be associated with inflammation, infection, hemorrhage, and malignancies, a familiarity with medication-associated changes of the eye and surrounding structures, such as the eyelids and orbital fat, remains important for the general practitioner.

The pigmentation changes associated with PGA use are a result of increased melanin content in melanocytes present in the iris, eyelash hair follicle, and skin.^{5,6} Hypertrichosis is due to stimulated transition of hair follicles from telogen (resting phase of growth) to anagen (growing phase).⁷

The differential of iris heterochromia includes sympathetic dysfunction (congenital Horner's syndrome or neuroblastoma in children), retained intraocular metals secondary to trauma (e.g. iron, copper), intraocular hemorrhage (e.g. traumatic hyphema or neovascular

glaucoma), local and systemic inflammation (e.g. Fuch's heterochromatic iridocyclitis, sarcoidosis), and neoplasms (e.g. metastases, iris nevus, uveal melanoma, lymphoma, leukemia, or retinoblastoma).⁸ Iris heterochromia can also been seen in certain hereditary conditions such as Waardenberg syndrome, a group of genetic conditions associated with hearing loss and pigmentation changes of the hair, skin, and eyes.⁹

Eyelash hypertrichosis has a broad differential diagnosis, including congenital disorders (e.g., Oliver-McFarlane syndrome involving long eyelashes and pigmentary degeneration of the retina, oculocutaneous albinism type 1 characterized by hypopigmentation and reduced iris pigment); acquired inflammatory, infectious causes (e.g., dermatomyositis, systemic lupus erythematosus, HIV, paraneoplastic syndrome (renal cell cancer)); and medication-related findings associated with interferons, anticonvulsants (topiramate), immunosuppressives (cyclosporine, tacrolimus), and anti-epidermal growth factor agents (cetuximab, erlotinib, and gefitinib).¹⁰

Patient outcome

The patient was reassured that the condition was related to PGA use since the unilateral changes occurred after initiation of medication. Because these changes are generally benign, the patient continues PGA use, and her glaucoma remains stable.

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Figure 1.

(A) Upper facial profile showed iris heterochromia and eyelash hypertrichosis. (B) Right eyelid and eye showed thick, long eyelashes (arrowhead) with brown iris. (C) Left eyelid and eye showed thin, shorter eyelashes (arrowhead) with hazel (green-brown) iris.

Figure 2.

(A) Right upper eyelid on downgaze showed thick, long eyelashes, following bimatoprost use. (B) Left upper eyelid showed thinner, shorter eyelashes compared to the right eyelid. (C) Magnified view of brown right iris following bimatoprost use. (D) Magnified view of hazel (green-brown) left iris. There is a small brown iris nevus (arrowhead). The left eye was not treated with bimatoprost.