Periocular discoloration after using a prostaglandin analog for eyelash enhancement: evaluation with reflectance confocal microscopy

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Summary

A 32-year-old Caucasian woman was admitted to our outpatient department with periocular discoloration. She applied a serum with the active ingredient isopropyl cloprostenate for enhancing the growth of the eyelashes. The discoloration appeared for the first time when the patient had used the serum and gradually remitted after the discontinuation of use. Confocal laser scanning microscopy revealed small white spots in the perifollicular dermis and in the surrounding dilated vessels, which was reported earlier as a side effect of prostaglandin analogs.

Keywords: eyelash enhancement, bimatoprost, isopropyl cloprostenate, periocular hyperpigmentation

Darkening of the iris, hyperemia, and discoloration of eyelids are well-known side effects of bimatoprost therapy for glaucoma. However, only little information can be found in the literature or is available online about the side effects of prostaglandin analogs for enhancing the growth of eyelashes.

Case report

A 32-year-old Caucasian woman was admitted to our outpatient department for the evaluation of periocular discoloration which had started 4 months earlier (Fig. 1a). She had a history of acne vulgaris but was otherwise healthy. She denied taking any medication apart from drinking a Chinese tea mixture for treating acne. Seventeen months ago, she had started applying a

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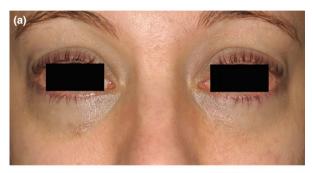
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serum with the active ingredient isopropyl cloprostenate for enhancing the growth of her eyelashes. The periorbital skin became irritated (red) after a month, and the first signs of greenish discoloration had appeared about a year later, and had gradually worsened with time. She had discontinued using the product despite its effectiveness 3 months prior to her admission, because the color of the eyelids had darkened.

A referral to our ophthalmology department revealed no ocular abnormalities apart from hyperemia of the eyelids. A CT scan was performed to exclude a tumor. No pathological changes were found. A biopsy for histological examination was declined by the patient. Therefore, confocal laser scanning microscopy (CLSM) was performed as a noninvasive alternative. Results were matched to periorbital normal skin of a healthy female control of equal age. For CLSM imaging, a commercially available device (Vivascope® 1500; Mavig GmbH, Munich, Germany) was used, which offers a lateral and axial resolution of $1.25-2.5~\mu m$ and a penetration depth of about $250~\mu m$. The CLSM has been used successfully in the diagnostics of different

diseases such as melanoma and nonmelanoma skin cancer, the rapeutic monitoring, or permanent makeup reactions. The method has been described in detail before. $^{2-6}\,$

CLSM revealed small white spots in the perifollicular dermis and in the surrounding dilated vessels, compatible with melanin granules or macrophages (Fig. 2). No such changes were found in the images of the unaffected control.



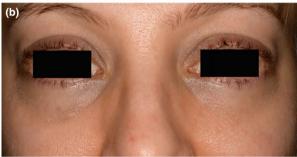


Figure 1 (a) Green discoloration and hyperemia of the eyelids on the day the patient was first admitted to the clinic. (b) Seventeen months later, after discontinuation of topical bimatoprost analog.

During follow-up, the patient did not use any cosmetics except concealer. During the following 16 months, a slow regression of the discoloration occurred. At the end of the seventeen-month follow-up, a significant reduction of the periorbital greenish color was seen (Fig. 1b).

Discussion

The fact that the discoloration appeared for the first time when the patient had used the isopropyl cloprostenate – containing eyelash enhancer – as well as the gradual remission after discontinuation of its use strongly implicates the prostaglandin analog as the cause of the discoloration. Eyelash-enhancing serums have not been thoroughly studied yet, but the possible causative relationship between topical prostaglandins and cutaneous discoloration is supported by numerous reports demonstrating similar side effects with other prostaglandins. However, the pathomechanisms by which prostaglandins stimulate discoloration and the exact nature of the pigment remain unclear so far. In our case, postinflammatory hyperpigmentation can be an explanation as well.

Unfortunately, histology was not possible in our patient as she declined a biopsy. However, confocal laser scanning microscopy revealed an image very much reminiscent of an increase in the number of melanin granules, as it has been reported as a side effect of other prostaglandin analogs. In this study, the authors found an almost 250-fold increase in melanin granule counts in the epidermis and a sixfold increase in the dermis compared to control patients. The melanin granules appeared to be mainly in the basal

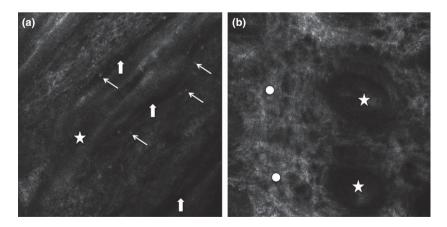


Figure 2 (a) Small white spots (arrow) and perifollicular, dilated vessels (block arrow) in the dermis. Due to tangential imaging, hair follicles are longitudinal (star). (b) Control patient: normal round, dark hair follicles (star) and bright reticular connective tissue (dot) are shown in horizontal imaging (0.5 mm 0.5 mm, Vivascope® 1500; Mavig GmbH, Munich, Germany).

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keratinocytes of the epidermis and in the melanocytes of the superficial and deep dermis.

Doshi et al. 9 analyzed 37 patients with mostly bimatoprost-induced skin darkening and found that 277 ± 138 days were required for the development of the skin changes. The therapy was discontinued when the first signs of darkening were noted. Total regression was observed in 33 patients. After the darkening appeared and the therapy were discontinued or switched, 205 ± 97 days were needed until resolution. No safe therapeutic possibility has been reported yet. In the case of our patient, the discoloration appeared after 13-14 months of use, and a regression of the symptoms occurred after 17 months; however, the greenish color did not disappear completely.

In conclusion, users of prostaglandin-containing eyelash enhancers should be aware of the possibility of unwanted, aesthetically unpleasant side effects of these products. Discoloration is usually long-lasting, persisting for at least several months, and effective treatments are unknown so far.

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