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Cyclosporine A Eye Drop-Induced Elongated Eyelashes: A Case Report

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Key Words
Cyclosporine A · Eyelash elongation · Giant papillary conjunctivitis · Side effect

Abstract
Purpose: The most common ocular adverse event following the use of cyclosporine A (CsA) 0.05% ophthalmic emulsion is ocular burning (17%). Other adverse effects that have been reported include conjunctival hyperemia (1–5%), discharge, epiphora, eye pain, foreign body sensation, pruritus, stinging and blurred vision. Here, we report a specific side effect of CsA, namely eye drop-induced eyelash elongation in a patient with refractory giant papillary conjunctivitis.
Design: Observational case report.
Methods: Case report and review of the literature.
Results: A 32-year-old female with giant papillary conjunctivitis on the left eye, who had undergone papillectomy 3 years previously and was refractory to topical steroid therapy, was treated with CsA 0.05% ophthalmic emulsion (Restasis) 4 times a day, preservative-free artificial tears and gentamicin ophthalmic solution in the left eye. After 5 months of topical CsA treatment, elongated eyelashes of her left eye were observed without other adverse effects.
Conclusion: Although hypertrichosis and trichomegaly have been documented in the literature as side effects of systemic CsA, topical CsA 0.05% eye drop-induced elongated eyelashes have not been reported, and we believe ophthalmologists should be mindful and inform patients about this specific side effect.

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Case Report

A-32-year-old Asian female patient, who had received conjunctival papillectomy on the left eye in 2002, visited our ophthalmic outpatient department in 2007 complaining of a swollen eyelid and discharge from her left eye. The ocular examination revealed notable injected conjunctiva, especially over the superior part, and multiple papillae with injected and engorged vessels on the left eye (**fig. 1**).

Due to the suspicion of giant papillary conjunctivitis, she was started on topical steroid medications including fluorometholone 0.1% and prednisolone acetate 1% ophthalmic solutions for 2 months. However, steroid treatment was discontinued due to poor response and an elevated intraocular pressure. Therefore, her treatment was switched to topical cyclosporine A (CsA) 0.05% ophthalmic emulsion (Restasis) 4 times a day, preservative-free artificial tears and gentamicin ophthalmic solution. After 5 months of topical CsA treatment, she came back to our clinic complaining of elongated and darkened eyelashes on her left eye without other adverse effects (**fig. 2**). According to the patient, no systemic medications such as calcium channel blockers, erythropoietin or minoxidil were used during the treatment period.

Discussion

CsA is a hydrophobic, cyclic polypeptide produced as a metabolite by the fungus *Tolypocladium inflatum.* CsA functions as an immunomodulating agent that binds to cyclophilin, a cytoplasmic protein, thus interrupting the signaling for interleukin (IL)-2 production, in addition to inhibiting the proliferation of CD4 T lymphocytes [1]. It also has direct inhibitory effects on both eosinophil and mast cell activation [2], which has established its role in the treatment of allergic inflammation [2, 3]. In the early 1980s, topically applied CsA was first used to inhibit experimental corneal allograft reaction [4]. Meanwhile, CsA eye drops were also prescribed for patients with inflammatory ocular surface disorders, particularly dry eye syndrome and severe allergic keratoconjunctivitis [5]. The current literature supports the safety of topical CsA [6].

The major side effect of systemic CsA is nephrotoxicity that is reversible with dosage reduction. Other documented adverse reactions to systemic CsA include mild hepatotoxicity, hypertension, dose-dependent hypertrichosis and trichomegaly, tremor, infection, gum hyperplasia, gastric irritation symptoms and neuropathies [7]. On the other hand, adverse events following the use of CsA 0.05% ophthalmic emulsion include ocular burning (17%), conjunctival hyperemia (1–5%), discharge, epiphora, eye pain, foreign body sensation, pruritus, stinging and blurred vision [6]. However, to our knowledge, no CsA ophthalmic emulsion-induced hypertrichosis has been reported in the literature to date. The factors that regulate the growth cycle of the eyelash hair follicles remain unclear. Paus et al. [8] suggested that CsA induces telogen follicles to enter an anagen growth phase, implying a role of CsA in regulating the hair follicle immune system and its cellular components through the release of inhibitory/stimulatory cytokines [8, 9]. The experiments also indicated that the rate of anagen induction is dependent on the dose, time course, and method of administration [8].

In summary, although rarely encountered, CsA 0.05% ophthalmic emulsion may induce the growth of eyelashes, and we believe ophthalmologist should be mindful and inform patients treated with topical CsA about this side effect.

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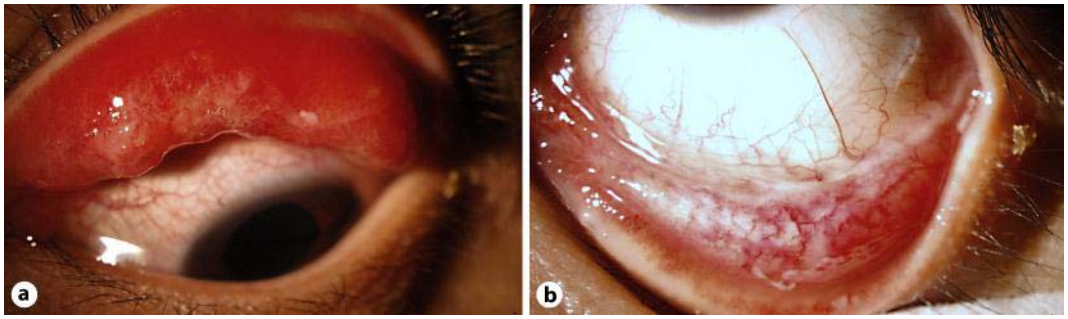

Fig. 1. External photographs showing multiple papillae with conjunctival injection (**a**) and engorged vessels (**b**) over tarsal conjunctiva on the left eye.

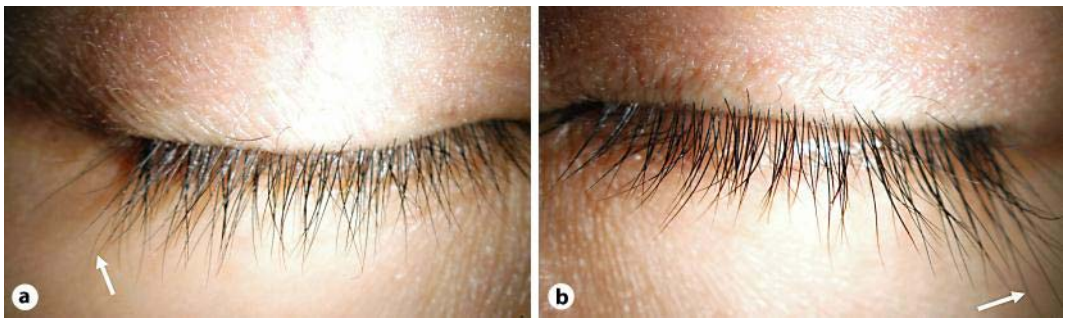

Fig. 2. External photographs demonstrating the normal eyelashes of the right eye (**a**, arrow) as compared to the elongated and darkened eyelashes on the left eye (**b**, arrow) after 5 months of topical CsA treatment.

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