Hair follicles are important adnexal structures that have both ectodermal (hair) and mesodermal (dermal papillae) derivation. Hair cycles through various phases including anagen (growth) catagen (regression) and telogen (resting phase). Involved in the cycling includes various cytokines and growth factors such as FGF-5/7 (fibroblast growth factor), TGF-β/α (transforming growth factor), BMP-2/4 (bone morphogenetic protein), vitamin D receptor, RXR-α (retinoid X receptor-α), PTHrp (parathyroid hormone-related peptide), TNF-α (tumor necrosis factor), IL-1(interleukin-1), Follistatin, IFN-γ (interferon-γ) among others. Cyclosporine is a calcineurin inhibitor that was identified in 1976 to have potent immunosuppressive effects. Cyclosporine was originally approved for organ rejection in the United States in 1983 and then reformulated in 1995 to have better bioavailability. Cyclosporine has many adverse effects but of interest to this case report include hypertrichosis and hyperpigmentation. A literature search of cyclosporine ophthalmic drops revealed no case reports of hyperpigmentation of the scalp hairs secondary to this treatment. However, oral cyclosporine has many reported cases of both of the above side effects.

A 69-year-old female presented to the clinic complaining of her hair darkening in color. She stated this began after beginning treatment with cyclosporine ophthalmic solution for ocular dryness. The patient had grey hair since approximately the age of 60 but did have blonde hair as a child. Patient admits to dying her hair blonde after she had significant amounts of grey hair. She denied hypertrichosis, denied pruritus, or pain of the scalp. She states the change in hair color happened over a period of several months. The hairs that are hyperpigmented grow in a patchy pattern diffusely throughout her scalp. Her past medical history includes only seasonal allergies. She admits to only using cyclosporine ophthalmic solution twice a day and taking a woman’s daily vitamin. She denies any other medication and denies any herbal supplements. On physical examination, patient had no apparent areas of hair loss, no erythema and no scale of the scalp.

The mechanism of action of cyclosporine has not been fully delineated yet it is known to inhibit production of interleukin-2 (IL-2) via inhibiting calcineurin which reduces the activity of a transcription factor, nuclear factor of activated T-cells (NFAT-1). Cyclosporine has many adverse reactions but of interest is hypertrichosis and hyperpigmentation. S Lan et al. report that caspase-dependent apoptosis pathways play a vital role in transition of hair from anagen to catagen and cyclosporine decreases this cycling. Similarly, a study by Gafter-Givli et al. revealed cyclosporine may induce hair growth by increasing the amount of follicles. Cyclosporine via an intra-ocular route has not been reported in the literature to our knowledge of causing hyperpigmentation of scalp hairs. However, it has been reported as an oral preparation to cause hyperpigmentation of both the skin and hair in patients as well as hypertrichosis. Lee et al. report a microarray analysis in which they showed NFAT-2 was upregulated in white compared to black hair. Cyclosporine reduces the activity of NFAT which enhanced tyrosinase activity and melanogenesis. Authors Sadighha and Zahed report a patient that was receiving cyclosporine for the treatment of psoriasis developing hair darkening as well as hair growth two months after the initiation of treatment.

Many studies have focused on the mechanisms involved in melanogenesis to unveil new treatments for graying hair and a way to delay the aging process. Our case study may be the first report of ophthalmic cyclosporine causing hair hyperpigmentation. Further studies are needed to elucidate the exact mechanism in which cyclosporine can induce hair darkening. This is a challenging feat in that the exact mechanism of action of cyclosporine has yet to be fully understood. It is interesting as well that our patient was able to have systemic effects from a locally applied i.e. ophthalmic solution. Further research in this case report that may yield valuable information is elucidating the amount of systemic absorption via testing our patients scalp hairs for cyclosporine.

References