Cyclosporine A-induced hair re-pigmentation in a patient with dermatitis: A case report with a review of the literature

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Abstract

Cyclosporine A (CsA) is an immunosuppressant drug that is known to cause several side effects. One of the most common side effects is hypertrichosis, with hair repigmentation rarely presenting on this medication. Here we report a case of an Omani male patient who presented in 2020 to the Dermatology Clinic at Rustaq Polyclinic in Rustaq, Oman with exfoliative erythroderma. The patient had hair repigmentation after 3 months of treatment with CsA.

Keywords: Cyclosporine; Dermatitis/Exfoliative; Hair color; Case report; Oman

Introduction

Cyclosporine A (CsA) is a known immunosuppressant that is widely used in multiple medical specialties, such as in the treatment of multiple transplants, skin and rheumatology conditions.[1] CsA is a calcineurin inhibitor which inhibits cell mediated and humoral immune responses by binding to cyclophilin, leading to the activation of nuclear factor of activated T-cells (NFAT) and reduction in IL-2 transcription. Known side effects of this medication are renal toxicity, hypertension, hypertriglyceridemia, immunosuppression and lymphoma.[2] CsA can affect hair by causing hypertrichosis, though it is rarely reported to cause hair darkening.[3]

Here we report the case of an Omani male patient who presented to the dermatology clinic at Rustaq polyclinic in Rustaq, Oman in 2020, with reversal of his hair color from white to black after 3 months of treatment with CsA for his chronic atopic dermatitis.

Case report

A 65-year-old Omani male patient, who was a known smoker with no comorbid conditions, not on any medications, had been attending the dermatology clinic for chronic atopic dermatitis for 11 years. He first presented with itchy scaly erythematous plaques over exposed areas, which was initially controlled by topical steroids for several years. For the last 3 years he had presented with multiple flare ups, which were controlled with topical steroids, tapering oral steroid courses and antihistamines.

In mid-2020, he developed generalized exfoliative erythroderma which required admission to the hospital. A skin biopsy was done, which indicated the presence of spongiotic dermatitis and no evidence of malignancy. He underwent pan-computed tomography (CT) which showed no evidence of internal malignancy. Blood tumor markers (including alfa feto protein, carcinoembryonic antigen and prostate specific antigen) were normal. His peripheral smear was reviewed by a hematologist and was reported to be normal.

He was started on methotrexate (MTX), 7.5mg once a week titrated up slowly to 20mg. Despite being on a high dose of MTX, the patient's condition was worsening regarding his dermatitis and itching. The MTX was stopped, and the patient was changed to CsA within a month, initially 3mg/kg/day of CsA divided into two doses for 2 weeks then titrated up to 5mg/kg/day. The patient showed improvement on CsA with no major side effects noticed on follow-ups.

After 3 months of treatment, he developed hypertrichosis and reversal of his hair color from white (Figure 1) to black (Figure 2), which first appeared over scalp edges, central scalp, beard and moustache, then slowly spread to the other scalp areas.

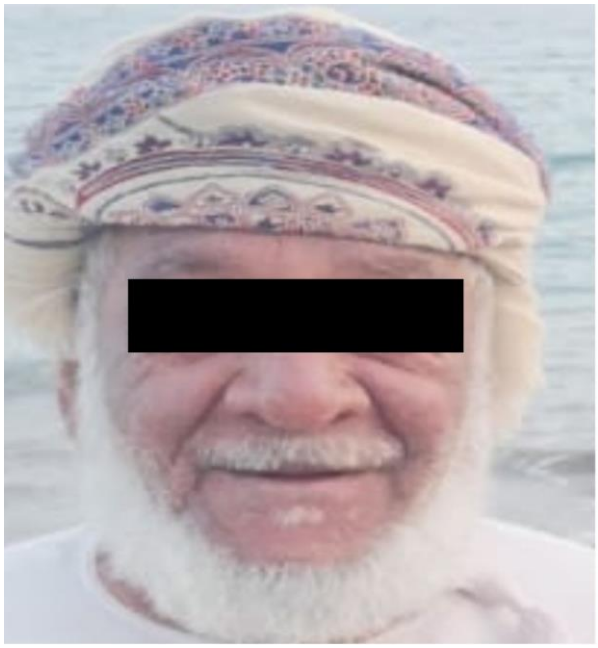

Figure 1: The patient 1 year before starting CsA.

Figure 2: The patient 3 months after starting CsA showing darkening of hair over scalp, moustache and beard areas.

Discussion

Diffuse re-pigmentation of gray hair can be induced by certain medications that inhibit inflammation or stimulate melanogenesis. From a search of the literature many drugs have been reported to cause hair darkening, including anti-inflammatory medications.[4]

CsA is known to cause dose-dependent hypertrichosis, which has been reported in approximately 50% of transplant patients who take a high dose of the drug, and in around 3%

of patients with skin conditions, especially those who have been treated with 5mg/kg/day of CsA.[5]

CsA causes hypertrichosis by inducing and prolonging the anagen growth phase, which enhances hair follicle stem cell activity, and blocks the ability of the dermal papilla cells to initiate catagen.[6] Through interfering with T-cell activity and regulation of IL-2 activity, CsA plays a role in the activation of degenerated or dormant melanocyte stem cells and recruits functional melanocyte stem cells from neighboring hairs. One randomized control study on mice involving a new compound (CsA, minoxidil, and a pigment-promoting drug) induced gray hair re-pigmentation. The increase in the pigmentation of gray mouse hairs was associated with increased melanocyte progenitor cell count in up to 80% of the hair bulbs. The study also showed that even after stopping the treatment, shaved hair was noted to regrow with continued re-pigmentation in following hair cycles.[7]

Only two cases of hair darkening after introduction of CsA have been reported in the literature.[8,9] The case by Sadighha and Zahed reported a 59-year-old man with psoriasis who presented with erythroderma and had been on MTX for 20 years. MTX was stopped because patient developed liver cirrhosis and switched to CsA 5mg/kg/day. Hypertrichosis and hair darkening occurred after 2 months of the treatment, where it first appeared on the scalp edges.[8] The case by Rebora *et al.* reported a 73-year-old man with eczematous dermatitis, who developed erythroderma and was treated with CsA, 5mg/kg/day. Hair darkening was noticed 1 month after the treatment began.[9]

The patient in this case and the other two previously reported cases shared similar backgrounds of autoinflammatory dermatological conditions progressing to erythroderma, requiring the initiation of CsA. In addition, all three patients developed hair darkening on the same dose of CsA, 5mg/kg/day, and over similar time periods.

Conclusion

CsA causes hypertrichosis and re-pigmentation of the hair, beginning as little as a month after treatment. To know whether this side effect is temporary or permanent, more case reports are needed with prolong follow up for the patients after stopping CsA. Despite some proposed mechanisms explaining the hair re-pigmentation has been published, still further studies need to be done to know the exact mechanism.

Disclosure

The authors declared no conflicts of interest.

The patient gave a written informed consent for his images and clinical information to be published in a medical journal.

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