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Case Report

Cyclosporine-Induced Alopecia in Childhood Nephrotic Syndrome – A Case Report

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Abstract

Drug-induced alopecia, typically presenting as diffuse, non-scarring hair loss, is often reversible upon discontinuation of the offending medication. Cyclosporine A, an immunosuppressive agent frequently causing hypertrichosis, has been paradoxically reported to induce alopecia in rare cases. We report a 20-month-old girl with steroid-resistant nephrotic syndrome who developed severe alopecia due to a mistakenly taken high dose of cyclosporine. Upon discontinuation of cyclosporine, her hair began to regrow within a week. This case underscores the complexity of drug-induced alopecia and highlights the need for further research into the immune dysregulation associated with alopecia areata.

Introduction

Drug-induced alopecia typically manifests as diffuse, non-scarring hair loss. This hair loss is likely caused by the abrupt cessation of mitotic activity, which weakens the partially keratinized proximal portion of the hair shaft.[1] Consequently, this can result in the narrowing and eventual breakage of the hair canal, potentially leading to a complete failure of hair formation. Drugs associated with alopecia include androgen hormones, anticoagulants, antimitotic agents, psychotropic drugs, retinoids, and antithyroid agents.[2] Cyclosporin A (C_SA) is an immunosuppressive agent that inhibits the activation of helper T cells and is commonly used in transplantation medicine and the treatment of autoimmune diseases. One of the most frequent dermatological side effects of oral C_SA is dose-dependent hypertrichosis.[3] The dual properties of C_SA as a hypertrichotic and immunosuppressive drug have led researchers to use it for managing alopecia areata (AA). Here, we report a case that highlights a patient who experienced oral C_SA induced alopecia.

Case report

A one and half year old female toddler, born to non-consanguineous parents, developed childhood-onset nephrotic syndrome. Initially treated with oral corticosteroids at 2 mg / kg, she was labeled steroid-resistant when remission wasn't achieved after four weeks. Subsequently, she received intravenous methylprednisolone and oral enalapril for two weeks without achieving remission, confirming steroid resistance. Renal biopsy revealed minimal change disease without tubulointerstitial chronicity, leading to the initiation of C_SA at a dose of 5 mg / kg. Whole exome sequencing revealed a heterozygous variant of uncertain significance in the $LAMA_5$ gene, which is associated with nephrotic syndrome type 26 (NPHS26).

During the fourth week of follow-up, the patient presented with drowsiness, difficulty walking, and severe alopecia (Figure 1a and 1b). Despite these symptoms, her urine

output remained normal. A urine dipstick test showed 2+ proteinuria. Her creatinine level was 0.57 mg / dL, potassium level was 5.25 mEq / L, and albumin level was 1.73 gm / dL. Her cyclosporine C_0 level was 1483.21 ng / ml, which is considered highly toxic (Therapeutic levels are typically < 150 ng / ml). It was discovered that the mother had mistakenly been giving a dose of cyclosporine that was 10 times higher than prescribed (2.5 ml twice daily instead of 0.25 ml twice daily for three weeks). As a result, C_SA was promptly discontinued. After one week, the patient's creatinine level was 0.51 mg / dL, potassium level was 4.99 mEq / L, and the cyclosporine C_0 level was 32.6 ng / mL. She had good hair growth before the disease onset and after starting corticosteroids and enalapril. After discontinuing C_SA, new hair patches appeared within seven days. C_SA has since been restarted, and her hair growth continues.

To accurately characterize the type of hair loss dermoscopy and scalp biopsy were performed. Dermoscopy revealed exclamation mark hairs, black dots, and yellow dots, consistent with AA. Histopathological examination of the scalp biopsy showed a peribulbar lymphocytic infiltrate, confirming the diagnosis of AA.

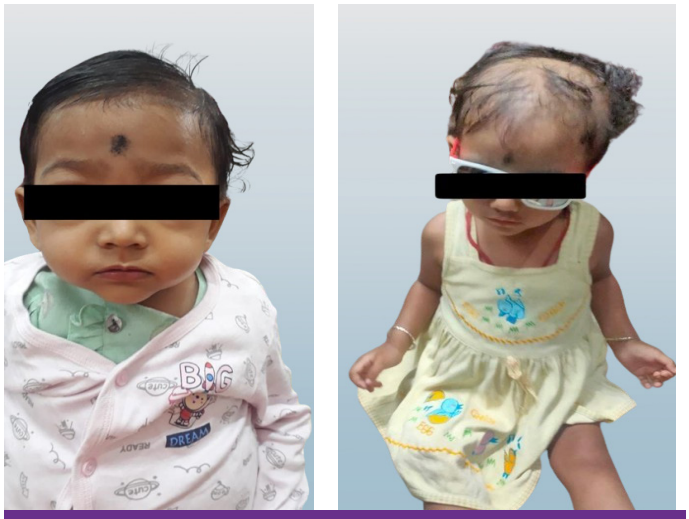

Figure 1a: Before C_SA - This image shows the patient's hair condition. **Figure 1b:** After C_SA - This image illustrates the patient's hair condition after cyclosporine treatment.

Discussion

We report this case of alopecia because it occurred in an unexpected context. Since immunosuppression is generally considered an effective treatment, the development of AA during C_SA therapy is contrary to expectations. Our curiosity led to a literature review, which revealed only a few cases of AA in patients receiving cyclosporine.[4,5]

Drug-induced alopecia is primarily caused by monoclonal antibodies, particularly TNF-alpha inhibitors and dupilumab. The mechanism involves autoantigen presentation to CD4+ Th1 cells, CD8+ T-cells, and natural killer cells at the hair bulb, leading to inflammation and hair loss.[6] TNF-alpha inhibitors can exacerbate alopecia by promoting autoimmunity through an increase in CD4+ regulatory T cells.

C_SA induced alopecia is rarely reported in the literature.[5] Hypertrichosis, however, is a well-known side effect of C_SA, though its pathogenesis is not fully understood. It is described as a dose-dependent effect, inducing the anagen phase and inhibiting the catagen phase of hair follicles. In animal models, C_SA has been shown to stimulate hair growth by promoting matrix cell proliferation and increasing the expression of vascular endothelial growth factor (VEGF).[7] Additionally, the potential induction of alpha-reductase enzyme activity, which increases the conversion of androgens to dihydrotestosterone in tissues, also contributes to hair growth.

AA is infrequently reported in cases of depressed immunity and is rare in childhood nephrotic syndrome. Given that AA is considered a CD4+ T-cell-mediated disease, its occurrence in patients taking C_SA is paradoxical and intriguing. The occurrence of alopecia areata in patients under long-term immunosuppression is a fascinating phenomenon that highlights our limited understanding of this disease. The causal relationship between drug exposure and AA remains uncertain. Further research is needed to elucidate the various aspects of immune dysregulation leading to this clinical phenotype of AA.

Conclusions

This case report highlights the paradoxical occurrence of AA in a patient undergoing C_SA therapy, a drug usually associated with hair growth. It underscores the complexity of drug-induced alopecia and the need for further research into the immune dysregulation involved in such cases, especially in paediatric patients with conditions like nephrotic syndrome.

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