Journal of Pakistan Association of Dermatologists. 2022;**32(2)**:425-429.

Case Report

Alopecia areata universalis showing excellent response to combination treatment modalities

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Abstract Alopecia areata (AA) is a non-scarring alopecia with mainly an autoimmune etiopathogenesis. The most severe AA variant is alopecia areata universalis (AAU), characterized by a total loss of scalp and body hair. AAU poses a significant psychosocial impact and may require combination therapy to provide satisfying results. A 15-year-old male presented with total loss of scalp and body hair in the last three years. Physical examination showed total alopecia with no terminal hairs nor scarring. Dermoscopic examination exhibited black dots, yellow dots, and empty follicles. The patient's laboratory examination also indicated reactive anti-CMV IgG, anti-toxoplasma IgG, and anti-rubella IgG. The patient was then given combination treatment consisting of pulse-dose oral antivirus, inosine pranobex, topical corticosteroid and minoxidil, intralesional steroid injection, and light-emitting diode (LED) therapy. A course of 8-month-therapy showed significant improvement marked by hair regrowth. Diagnosis of AAU was established clinically, with viral infection thought to be one of the main triggering factors. The use of combination therapy was considered safe and effective for AAU patients, although the treatment might be continued long term. AAU is a disease that significantly impacts a patient's quality of life. Its management requires comprehensive treatment and may need a combination of several treatment modalities.

Key words
Alopecia areata universalis, intralesional steroid injection, combination therapy.

Introduction

Alopecia areata (AA) is a non-scarring alopecia with mainly an autoimmune etiopathogenesis. AA tends to affect children and young adults more frequently, although it can occur at any age. It is one of the most common form of hair loss seen by dermatologists. There is generally no sexual predilection in AA, with the scalp as the most commonly affected area. AA may be associated with other comorbidities such as lupus erythematosus, vitiligo, autoimmune hemolytic anemia, atopic dermatitis, thyroid disorders, allergic rhinitis, and asthma.[1] Etiology of AA is multifactorial. Genetic susceptibility, stress, hormones, diet, vaccination, and infectious agent have been incriminated in the pathogenesis of AA.[2] Reactivation of CMV was thought to be one of the pathogenic mechanisms in AA.[3] Approximately 5% of all AA cases will progress into alopecia areata totalis (AAT) or alopecia areata universalis (AAU). These subtypes of AA have a worse prognosis and they pose a therapeutic challenge for clinicians.[4]

In AAU, there is a total loss of scalp and body hair. The likelihood of complete spontaneous regrowth in AAU is less than 10%. Moreover, there is no FDA-approved treatment for AA, although several topical and systemic therapies have been used with variable success. Therapeutic options for AA include corticosteroid, contact immunotherapy,

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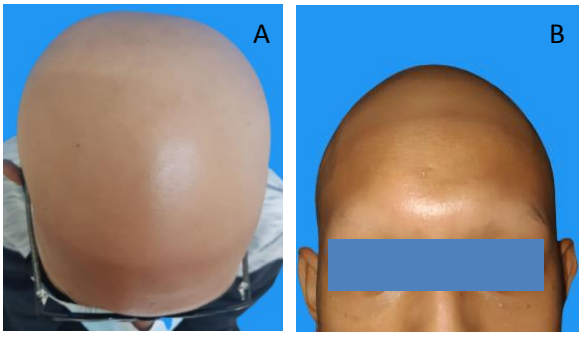

Figure 1 Physical examination on the initial visit showed total alopecia of the scalp and eyebrow

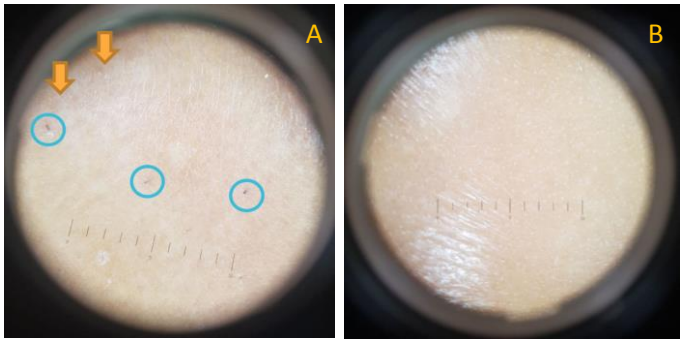

Figure 2 Dermoscopic examination showed black dots (blue circles), yellow dots (orange arrows), and empty follicles

minoxidil, ultraviolet light therapy, methotrexate, cyclosporine, and PDE4 inhibitor.[1] Even though the pathogenesis of AA remains unclear, the psychological impact it gives to the patient is often very substantial.[5] The significant psychosocial impact, especially to the patient's quality of life, requires a continuous search for efficacious and safe treatments for AA patients. In this case report, we present a case of a 15-year-old male with AAU showing excellent response to combination treatment modalities.

Case Description

A 15-year-old male presented with hair loss in the last three years. The hair loss started from the scalp, followed by the eyebrows, underarm hair, and pubic hair. There was no erythema, itch or pain before, during or after the hair loss. The hair loss continued until the patient completely lost all his scalp and body hair. Due to his condition, the patient felt embarrassed and went to a pediatrician and dermatologist to seek treatment. He had also received topical minoxidil, but the treatment showed no improvement. A history of similar symptoms had never been experienced by the patient before. Also, there was no history of alopecia in the patient's core and extended family.

Physical examination on the patient's scalp and body hair showed total alopecia, with no terminal hairs nor scarring. There were no abnormal findings on the patient's nails. Dermoscopic examination showed black dots, yellow dots, and empty follicles. The patient had undergone laboratory examination that showed negative anti-nuclear antibodies. We asked the patient to complete the TORCH panel to rule out viral infection as one of the trigger factors for AAU. The TORCH panel later yielded reactive anti-CMV IgG, anti-toxoplasma IgG, and anti-rubella IgG.

After establishing the diagnosis of AAU, combination treatment was given to the patient consisting of topical therapy, systemic therapy, intralesional corticosteroid injection, and light-emitting diode (LED) therapy. The topical therapy included topical 5% minoxidil and hydrocortisone butyrate scalp lotion; both were administered twice a day. The systemic therapy consisted of valacyclovir 3x500 mg (10 mg/kg BW) given in a pulse dose for every first ten days in a month and inosine pranobex 3x500 mg twice a week for three weeks each month. Intralesional steroid injection was given on each side of the scalp using triamcinolone acetonide 10 mg/ml diluted into 5 mg/ml on a two-week to one-month interval. Lastly, LED therapy was used after every intralesional steroid injection.

During the 8-month-therapy course, remarkable improvement was shown regarding hair regrowth. Terminal hairs were seen on the

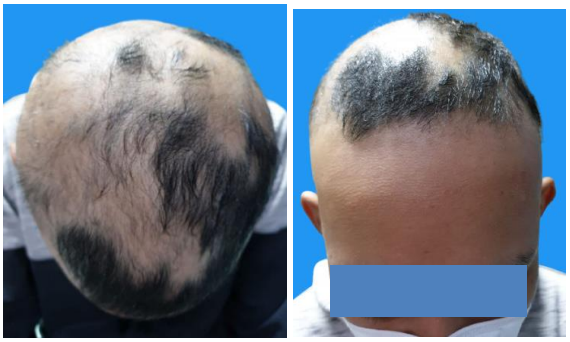

Figure 3 Physical examination on the latest visit showed regrowth of scalp and eyebrow hair.

patient's scalp and on other body parts such as eyebrows, underarms, and pubic areas. Laboratory examination was performed to confirm side effects caused by the pulse-dose antivirus, and the patient's blood results indicated normal liver and kidney function. All topical and systemic therapies were continued, and intralesional corticosteroid injection and LED therapy were administered in a one-month interval.

Discussion

This patient's diagnosis of AAU is established based on clinical and dermoscopic examination. Physical examination of the scalp shows total alopecia with no scarring and hair loss in other body parts such as eyebrows, underarms, and pubic areas. Dermoscopic examination supported the diagnosis by showing black dots indicating hair that breaks off when it reaches the skin surface, yellow dots, and empty hair follicles.[6] Other investigations, such as histopathology examination, are not needed to confirm the diagnosis because this case tends to be typical and obvious.[2]

Treatments of children with AA are limited because of less tolerability and potential side effects.[2] A numerous therapies have been reported, the evidence is mostly weak. The use of topical minoxidil and topical steroid twice a day, as well as intralesional steroid injection, is one of the first-line therapy for AA.[7] We preferred a medium potency topical steroid to minimize possible side effects even though high potency steroid has the highest efficacy for pediatric AA.[8] Intralesional steroid injection is probably one of the most effective treatments in AA. This injection may stimulate hair growth at the injection site in some patients, although multiple injections are usually needed. In this case, we did not find atrophy, hypopigmentation, or telangiectasia as side effects of intralesional steroids. Atrophy can be minimized by avoiding superficial injections, minimizing the volume and concentration, and giving space between the injection sites.

Minoxidil effectively induces hair regrowth by stimulating proliferation at the base of the bulb and differentiation above dermal papilla. Minoxidil 5% solution twice daily is more effective than the 2% concentration. Minoxidil is more responsive in young patients and provides better results when combined with a topical or intralesional steroid.[2] It was well tolerated, and there was no adverse effect such as pruritus or dermatitis in this case. The efficacy of LED therapy, especially involving the use of infrared and red wavelengths at 655 nm, has also been recognized as excellent adjuvant therapy in AA.[9] An increased number of hair follicles with the majority in the anagen phase and decreased inflammatory infiltrates were found in AA treated with LED therapy.[10]

The etiology of AA consists of several hypotheses such as infectious agents, genetic susceptibility, and various triggering factors such as stress, hormones, diet, vaccinations and many others.[2] Immunogenetics appeared to be the principal factor affecting patient susceptibility to AA. Environmental factors, including viral infections, are also thought to play an important role. After viral infection, Th1 immune responses result in a supraphysiologic

interferon production.[11] Reactivation of CMV was thought to be one of the pathogenic mechanisms in AA, although it was still debatable.[3] Reactive anti-CMV IgG and anti-rubella IgG found in this patient might indicate the role of the virus as one of the triggering factors of AAU. Thus, the administration of oral antivirus can be considered in this patient. Oral inosine pranobex is a synthetic immunomodulator with antiviral effects. Studies had shown that the administration of inosine pranobex induced complete hair regrowth in AA cases compared to placebo.[12] Valacyclovir is a nucleoside analog DNA polymerase inhibitor. Valacyclovir hydrochloride is rapidly converted to acyclovir which has demonstrated antiviral activity. Valacyclovir is better absorbed than acyclovir which contributes to less frequent administration and has been used for CMV prophylaxis.[13]

Although spontaneous regrowth may occur in many patients, AA in children tends to be worse and more progressive.[2] Several poor prognostic factors were attributed to this patient, including extensive hair loss, early-onset, and onset duration that lasted more than one year.[14] Counseling and psychological support might be needed during the treatment course, as therapy might be lifelong with a high chance of treatment failure.[7]

Conclusion

AAU is a disease with a significant impact on health-related quality of life. Etiopathogenesis remains unclear, with many factors that can be defined as an important contributor and precede the disease. Its management requires comprehensive treatment and may need a combination of topical, systemic, and other treatment modalities such as intralesional steroid injection and LED therapy. Further investigation is necessary to evaluate the effect of immunomodulator and antiviral in AAU.

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