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Hydroxychloroquine for granuloma annulare: A case report on secondary hair growth in alopecia universalis

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Abstract

Alopecia areata is an autoimmune disease resulting in non-scarring hair loss. Alopecia areata can progress to become alopecia totalis (loss of hair from the entire scalp) or alopecia universalis (loss of hair form the entire body), with the progression estimated to range from 7% to 30%. There are no universally proven therapies that both induce and sustain remission, and furthermore, the course of alopecia areata tends to be unpredictable, with ~80% of patients achieving spontaneous remission within 1 year. We herein present the case of a 61-year-old female who presented with a 20-year history of alopecia universalis, and biopsy confirmed widespread granuloma annulare. Hydroxychloroquine was initiated to treat her granuloma annulare, with subsequent significant hair regrowth on her scalp, eyebrows, eyelashes, and arms. A review of the literature is presented showing that hydroxychloroquine has variable success in treatment of alopecia areata, alopecia totalis, and alopecia universalis.

Keywords

Non-scarring, hydroxychloroquine, hair growth, alopecia universalis, granuloma annulare

Introduction

Alopecia areata (AA) is an autoimmune disease resulting in non-scarring hair loss. It is a T-cell-mediated autoimmune condition.[1] AA can progress to become alopecia totalis (AT, loss of hair from the entire scalp) or alopecia universalis (AU, loss of hair form the entire body), with the progression estimated to range from 7% to 30%.[1] It is thought that AA, AU, and AT are part of the same spectrum of disease, though AT and AU tend to be more refractory to treatment.[2] AA tends to be multifocal, with round or oval patches of hair loss that are smooth to the touch, often sparing gray hairs. Exclamation mark hairs are often seen clinically along with yellow dots on dermoscopy. While typically not required to make the diagnosis, biopsy will show a lymphoid inflammatory pattern around the hair bulb.[1] AA can be associated with other autoimmune conditions including vitiligo and thyroid disorders and occurs more frequently in people with affected family members.[1] There are no universally proven therapies that both induce and sustain remission, and furthermore, the course of AA tends to be unpredictable, with ~80% of patients achieving spontaneous remission within a year.[1] Treatment is often chosen based on disease extent, activity, duration, and age of the patient. First-line treatment involves topical or intralesional corticosteroids and systemic corticosteroids for more rapidly progressive disease.[1] Other therapies include topical minoxidil and local sensitizing agents—such as squaric acid dibutylester and diphenylcyclopropenone.[1] JAK inhibitors such as tofacitinib and ruxolitinib have gained traction for immune-mediated and inflammatory diseases in dermatology and have been shown to be effective for AA in various case reports, case series, pilot studies, and open-label trials, though large-scale studies are limited, and the cost of these drugs is high.[3,4] Hydroxychloroquine is an anti-inflammatory drug that has been shown to have variable success in treatment of AA, AT, and AU.[5–10]

We herein report a 61-year-old female who presented with a 20-year history of AU, and biopsy confirmed widespread granuloma annulare. Hydroxychloroquine was initiated to treat her granuloma annulare, and she was subsequently noted to have significant hair regrowth on her scalp, eyebrows, eyelashes, and arms.

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Case report

A 61-year-old woman presented for dermatologic assessment due to a 5-year history of an asymptomatic rash on the right thigh that had spread to involve the torso and legs in the preceding 18 months. Past medical history was significant for a 20-year history of AU and tinnitus. The patient had a Severity of Alopecia Tool (SALT) score of 100,[11] or severe alopecia per the new alopecia severity assessment.[12] She noted that she had previously received treatment for her AA over a decade earlier with topical steroids, intralesional triamcinolone acetonide, methotrexate, and diphenylcyclopropenone with no benefit but had not been on any treatment in recent years. The patient was on no medications. On examination, she had annular erythematous plaques on the lateral trunk and medial thighs, and erythematous circular papules on the inner arms and lateral right shin. Biopsy of a plaque on the left thigh showed a dermal perivascular and interstitial lymphohistiocytic infiltrate, with histiocytes in a palisaded arrangement and focal areas of increased dermal mucin. The diagnosis of granuloma annulare was made based on the clinical presentation in addition to histopathologic features.

Hydroxychloroquine (5 mg/kg/day) was initiated in addition to narrowband ultraviolet B (nbUVB) phototherapy for treatment of her granuloma annulare. This treatment regimen led to resolution of the majority of her granuloma annulare plaques, and concurrent regrowth of hair on her scalp, eyebrows, eyelashes, and arms was noted at follow-up, 7 months after initiation. Of note, the patient had been recently vaccinated against COVID-19 with two doses of the Moderna vaccine (the second dose was a month prior to her follow-up visit), but no other changes had been made to her medications or health. After 1 year on hydroxychloroquine, the patient had no ophthalmologic concerns, normal bloodwork, and continued to have hair regrowth on her scalp, with a SALT score of 70% (Figure 1).

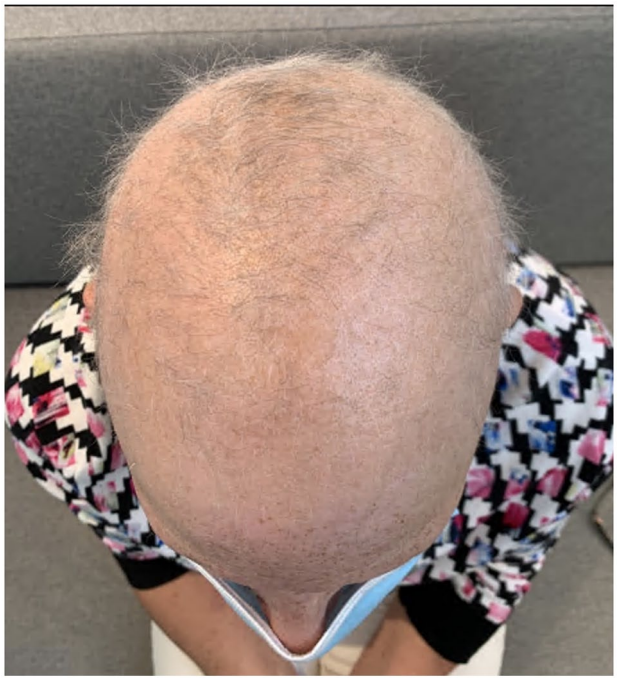

Figure 1. Patient's scalp after 7 months of treatment with hydroxychloroquine for granuloma annulare.

Discussion

There are multiple reports in the literature detailing the use of hydroxychloroquine for treatment of alopecia with varying success in the form of case reports and case series (Table 1). There is significant variation in the effectiveness of hydroxychloroquine, and the case by Nissen and Wulf demonstrated initial hair growth; however, there was relapse of disease, even while on treatment with hydroxychloroquine.[10] Of the 26 cases in the literature, 12 cases (46%) were reported to have regrowth while on treatment with hydroxychloroquine, with 3 of those 12 cases experiencing relapse in hair growth.

With respect to the association between the COVID vaccine and hair growth in this case, this was likely coincidental. There are no reports in the literature highlighting hair growth following COVID-19 vaccination. In fact, there is literature detailing the opposite. Multiple case reports have been published on patients who developed AA following vaccination,[13–15] and upon reviewing the Centers for Disease Control and Prevention Vaccine Adverse Event Reporting System database, there were 2592 cases of alopecia, 293 cases of AA, 18 cases of AT, and 20 cases of AU reported after both Moderna and Pfizer vaccination as of 27 May 2022.[16]

Hydroxychloroquine is an antimalarial agent that acts as a lipophilic weak base and, therefore, can enter lysosomes and raise the pH.[17] This rise in pH induces cell dysfunction by debilitating protein processing. Consequently, there is reduced lymphocyte and autoantibody production, in addition to reduced natural killer cell activity. More recently, hydroxychloroquine has been demonstrated to inhibit endosomal toll-like receptor (TLR) activation by binding to nucleic acids, and thereby masking the TLR binding site. This ultimately blocks immune activation. These immunomodulating and anti-inflammatory effects are the mechanisms by which hydroxychloroquine is postulated to result in hair growth in patients suffering with AA/AT/AU.[17]

We herein present a case of a 61-year-old woman with long-standing AU who presented with newer onset granuloma annulare. Initiation of hydroxychloroquine resulted in resolution of her granuloma annulare (in conjunction with nbUVB) and significant secondary hair regrowth on her scalp, eyebrows, eyelashes, and arms. The literature available is variable in its support for the successful use of hydroxychloroquine for the management of AA; however, it is worth considering as a relatively low-risk treatment option for patients with refractory AA until more effective treatments are readily available.

Table 1. Review of the literature assessing hydroxychloroquine for treatment of alopecia including AA, AT, AU, and lupus alopecia.

Reference	n	Age (years), sex	Alopecia subtype	Comorbidities	Previously trialed therapies	Time to response with hydroxychloroquine	Concomitant therapies	Response	Relapse
Stephan et al.[9]	2	40, F	AA, AT	None	• Narrowband UVB	2 months	Topical clobetasol and pimecrolimus	Hair growth	None
		23, F	AA, AT	None	• Topical clobetasol • Intralesional corticosteroids • Topical minoxidil methotrexate	5 months	Intralesional corticosteroids	Hair growth	None
Yun et al.[5]	9	12, M	AA	None	• Topical clobetasol • Minoxidil • Intralesional corticosteroids	24 months	Minoxidil	Hair growth	None
		14, M	AA	None	• Topical clobetasol • Minoxidil • Intralesional corticosteroids	18 months	Minoxidil	Hair growth	None
		14, F	AA	Atopic dermatitis	• Topical clobetasol • Intralesional corticosteroids	6 months	Topical clobetasol	No response	None
		14, F	AA	Atopic dermatitis, acne	• Topical clobetasol • Fluocinonide • Minoxidil • Intralesional corticosteroids	6 months	Topical clobetasol	No response	None
		13, F	AA	Atopic dermatitis	• Topical clobetasol • Systemic corticosteroids	4 months	Topical clobetasol	No response	None
		14, M	AA	Acne	• Topical betamethasone • Fluocinonide • Minoxidil • Intralesional corticosteroids	6 months	Minoxidil	Hair growth	None
		16, F	AA	Asthma	• Topical clobetasol • Minoxidil • Squaric acid • Anthralin • Intralesional corticosteroids	6 months	Topical clobetasol, minoxidil	None	None
		6, M	AA	Atopic dermatitis	• Topical clobetasol • Minoxidil • Systemic corticosteroid pulses • Squaric acid • Excimer laser • Anthralin	8 months	Topical clobetasol, minoxidil	Hair growth	None
		15, F	AA	Vitamin D deficiency	• Topical clobetasol • Minoxidil • Squaric acid	21 months	Topical clobetasol, minoxidil	Hair growth	None

(Continued)

Table 1. (Continued)

Reference	n	Age (years), sex	Alopecia subtype	Comorbidities	Previously trialed therapies	Time to response with hydroxychloroquine	Concomitant therapies	Response	Relapse
Paudel et al.[6]	1	35, F	AU	Hyperthyroidism	• Systemic corticosteroids • Topical fluocinolone acetonide • Minoxidil • Carbimazole	1 month	Azathioprine	Hair growth	None
Nissen and Wulf[10]	8	30.2 (mean), 6 F, 2 M	6, AT 2, AA	Not reported	• Topical corticosteroids • Intralesional corticosteroids • Topical immunotherapy • Phototherapy	161 days (mean)	None	No hair regrowth (5 patients) Hair growth (3 patients)	Relapse in all 3 patients with hair growth
Akdogan and Ersoy-Evans[8]	6	26, M	AU	Cataracts	• Systemic corticosteroids • Topical corticosteroids • Tofacitinib	6 months	None	No hair regrowth	None
		28, M		Allergic rhinitis	• Systemic corticosteroids • Cyclosporine • Diphenylcyclopropenone • Azathioprine • PUVA • Tofacitinib			No hair regrowth	
		17, M		Hashimoto's thyroiditis	• Systemic corticosteroids • Topical corticosteroids • Methotrexate • Diphenylcyclopropenone			No hair regrowth	
		6, M		Atopic dermatitis, ADHD	• Systemic corticosteroids • Diphenylcyclopropenone • Topical corticosteroids			Hair regrowth (S4 to S3)	
		9, M		None	• Diphenylcyclopropenone • Topical corticosteroids			No hair regrowth	
		22, F		Hashimoto's thyroiditis	• Systemic corticosteroids • Topical corticosteroids • Diphenylcyclopropenone • Cyclosporine • Intralesional corticosteroids			No hair regrowth	

AA: alopecia areata; AT: alopecia totalis; AU: alopecia universalis; UVB: ultraviolet B; PUVA: psoralen + ultraviolet A; ADHD: attention deficit/hyperactivity disorder.

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Ethics approval

Signed patient consent was obtained prior to reporting the following case.

Informed consent

Informed and written consent was obtained by the patient prior to publication.

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