

IN-DEPTH REVIEW

Isotretinoin and Hair Loss: A Clinical Perspective and Literature Review

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ABSTRACT

Isotretinoin, used for the treatment of moderate-to-severe acne, has many side effects due to its potent nature. While hair loss has been reported with isotretinoin use, there is limited data on the type and extent of hair loss. As hair loss poses a significant physical and psychological side effect to patients, it is important for dermatologists to consider and discuss this risk with their patients. According to a review of the literature, telogen effluvium is the most common type of hair loss reported, with some mention of androgenetic alopecia, lichen planopilaris, alopecia areata, and Darier disease.

We present the case of a 14-year-old male with moderate to severe acne, unresponsive to multiple topical and oral treatments, who was started on isotretinoin. After several months, he developed alopecia areata, which was initially treated with intralesional triamcinolone acetonide while continuing isotretinoin. Due to his worsening hair loss, isotretinoin was ultimately discontinued. Additional treatments, including topical steroids, oral dexamethasone, oral minoxidil, and an oral JAK inhibitor were introduced. While treatment remains ongoing, the patient has had near complete hair regrowth.

The onset of alopecia areata in our patient highlights the development of a unique form of alopecia that is not classically associated with isotretinoin use. While it is hypothesized that retinoids mediate hair loss via effects on the hair cycle and immune system, there is no direct explanation linking isotretinoin and alopecia areata.

INTRODUCTION

Acne is the most common skin condition in the United States (US), affecting up to 50 million people every year.¹ It affects many adolescents and young adults, with minor acne affecting approximately 85% of those aged 12 to 24.² Among those diagnosed with acne, patients may figure experience mild, moderate, or severe form of the condition. Mild acne includes non-inflammatory lesions (comedones), a few inflammatory (papulopustular) lesions, or both. Moderate

acne includes more inflammatory lesions, occasional nodules, or both, as well as mild scarring. Severe acne includes widespread inflammatory lesions, nodules, or both, as well as scarring. Severe acne also encompasses moderate acne that has not improved within 6 months of standard treatment, or acne of any severity with psychological upset.³

Patients with mild acne can be treated with topical therapies, however those with moderate to severe acne often require systemic therapy including oral antibiotics, hormonal therapies, and isotretinoin. A

retrospective study⁴ conducted by Skroza et al. in 2018 reported that up to 1% of teenage females and males, 1% of adult females, and 3% of adult males experienced severe acne. Up to 10% of teenage females, 22% of teenage males, 7% of adult females, and 15% of adult males experienced moderate acne. Due to the prevalence of moderate-to-severe acne, the indication for systemic therapies is high.

Isotretinoin is considered the most effective long-term treatment of acne and prevention of acne scarring.⁵ As of 2021, the estimated number of patients prescribed isotretinoin was around 500,000.⁶ Although treatment is generally considered very effective, isotretinoin has many reported side effects, including birth defects, dryness of the skin, lips, or eyes, and photosensitivity. Hair loss has also been noted as a potential side-effect, although this has been reported infrequently in the literature.⁵ Due to limited published information on the mechanisms and types of hair loss related to isotretinoin, it is important for clinicians to recognize unique presentations of hair loss and adequately educate patients on the potential side effect.

CASE PRESENTATION

A 14-year-old male was initiated on isotretinoin for moderate to severe acne following treatment failure with several topical and oral therapies, including adapalene gel, tretinoin cream, clindamycin gel, oral minocycline, oral doxycycline, and oral azithromycin. The patient was started on a dose of 0.5 mg/kg/day and titrated up to a dose of 1 mg/kg/day after one month. The patient tolerated the first several months of isotretinoin, experiencing anticipated side effects of xerosis and dry eyes. Approximately fourth months into the treatment course, at a cumulative dose of

103 mg/kg, the patient developed two alopecic patches on the scalp (**Figure 1**), consistent with alopecia areata. The lesions were treated with intralesional triamcinolone acetonide (3 mg/ml) and isotretinoin was continued. Because the alopecia areata continued to progress despite treatment, a decision was made by the patient and treating physician to discontinue the course of isotretinoin early (at a total cumulative dose of 118 mg/kg) in the event that isotretinoin was contributing to his worsening alopecia. Affected lesions were again injected with intralesional triamcinolone acetonide (this time at a dose of 5 mg/ml), and the patient was started on topical augmented betamethasone 0.05% lotion and pulse-dose oral dexamethasone 4 mg daily on Saturday and Sunday.



Figure 1. Month 1 of hair loss

The following month, the patient reported progressive worsening of his alopecia. Oral minoxidil 1.25 mg daily and tofacitinib 5 mg twice daily were added to his treatment regimen (tofacitinib was chosen over other on-label medications due to insurance formulary preference). Upon follow up, minoxidil was later increased to a dose of 2.5 mg daily. During this period, the patient was

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also initiated on fluoxetine 20 mg daily by his pediatrician following a diagnosis of Generalized Anxiety Disorder. The patient's anxiety symptoms corresponded to the development and progression of his alopecia areata (**Figures 2-3**).

While treatment remains ongoing, the patient has noticed almost complete hair regrowth (**Figures 4-5**). Unfortunately, during this time, the patient developed exacerbation of his acne, likely due to the oral JAK inhibitor therapy.



Figure 2. Month 3 of hair loss



Figure 4. Month 7 of hair loss



Figure 3. Month 6 of hair loss



Figure 5. Month 12 of hair loss

DISCUSSION AND LITERATURE REVIEW

Although evidence is limited, the potential for isotretinoin-induced hair loss warrants further investigation. Awareness of this possible side effect is important, as even temporary hair changes can impact a patient's quality of life and treatment satisfaction. Our case presentation highlights the development of severe alopecia areata during a course of isotretinoin. While it remains unclear if this patient's hair loss was a direct result of the

isotretinoin or simply an unfortunate coincidence, we sought to better understand the characteristics of hair loss associated with isotretinoin use.

According to a review of the literature, telogen effluvium is the most common type of hair loss reported, with some mention of androgenetic alopecia, lichen planopilaris, alopecia areata, and Darier disease. Nineteen articles were included in the review, and **Table 1** summarizes the category of hair loss as well as key findings.

Authors	Year	Method	Types of Hair Loss Reported	Key Findings
Lytvyn et al.	2022	Systematic Review	Unspecified	3.2 to 5.7% of people taking isotretinoin report hair loss, depending on the dose. Increased isotretinoin dosage demonstrated increased hair loss frequency. Low dose isotretinoin is an alternative approach to drug discontinuation.
Tran et al.	2022	Retrospective Review	Telogen effluvium, androgenetic alopecia, lichen planopilaris, alopecia areata, Darier disease	19 out of 40 patients who were on isotretinoin regimens experienced some form of hair loss during or after their isotretinoin course. Hair loss diagnoses included telogen effluvium (10 out of 19), androgenetic alopecia (5 out of 19), lichen planopilaris (3 out of 19), alopecia areata (2 out of 19), and Darier disease (1 out of 19), with some patients having more than 1 one of the listed diagnoses.
Vardhan et al.	2022	Case Report	Unspecified	A 23-year-old female presented with a bald patch 1 month after starting isotretinoin 50 mg twice daily for acne; the patch was not associated with itching or redness.

Abdelmaksoud et al.	2022	Letter to the Editor	Telogen effluvium	Isotretinoin-induced telogen effluvium is transient and improves spontaneously even without drug discontinuation.
Kapala et al.	2022	Review	Telogen effluvium, androgenetic alopecia	Isotretinoin causes telogen effluvium, which can occasionally lead to further evaluation and diagnosis of androgenetic alopecia, and hair loss may continue even after stopping the medication. The studies reviewed did not look at reversal of hair loss after isotretinoin treatment, but patients with a diagnosis of telogen effluvium were more likely to experience hair regrowth after treatment ended.
Aksac et al.	2021	Clinical Trial	Telogen effluvium, androgenetic alopecia	Addition of 10 mg/day biotin to isotretinoin has increased the rate of anagen hair and reduced the rate of telogen hair and could eventually decrease the risk of isotretinoin-induced hair loss.
Gupta	2020	Case Report	Alopecia areata	A 24-year-old female patient was on treatment with isotretinoin (0.6 mg/kg) for acne vulgaris; the dose was increased to 30 mg after 3 months. After 6 months of treatment, she presented with a localized patch of hair loss. Alopecia areata is an uncommon side effect of isotretinoin; it is mostly seen in children and affects about 1% of the population. The beginning of alopecia areata in acne patients could be regarded as a side effect of retinoids due to anti-acne therapy.

Tkachenko et al.	2019	Review	Unspecified	932 cases of alopecia were reported as an adverse event during isotretinoin use over a 20-year period (1997 and 2017). Alopecia represented 9% of all dermatological adverse event reports. • 68.7% of reports occurred in women. • 29.7 % of reports occurred in men. • Most reports occurred from age 15-19.
Islamoglu & Altinyazar	2019	Prospective Cohort Study	Telogen effluvium, androgenetic alopecia	Isotretinoin does not alter hair growth parameters in the short term when 0.5 mg/kg per day is used.
Faghihi et al.	2017	Clinical Trial	Unspecified	Hair loss and thinning hair were more frequent in the high-dose group receiving isotretinoin than the low-dose group.
Brzezinski et al.	2017	Retrospective Study	Unspecified	Hair loss was described in 154 patients on isotretinoin and persistent hair loss was seen in some patients even after completing treatment.
Demirseren et al.	2017	Prospective Cohort Study	Unspecified	20% of 300 patients experienced hair loss, with a median time of onset at 4 weeks and a wide range of 1 to 24 weeks.
Kmiec et al.	2013	Prospective Cohort Study	Telogen effluvium	Isotretinoin reduced the amount of total hair count, its density and the proportion of anagen hair, which suggests a pattern consistent with telogen effluvium.
Gan et al.	2013	Retrospective Study	Unspecified	Hair loss was temporary in 33 patients who experienced hair loss on high-dose isotretinoin.
Duncan et al.	2013	Clinical Trial	Alopecia areata	Vitamin A regulates both the hair cycle and immune response to alter the progression of alopecia areata.

Tosti & Pazzaglia	2007	Review	Telogen effluvium, alopecia totalis	High doses of Vitamin A have been associated with hair loss. Concurrent administration of Vitamin E may potentiate vitamin A toxicity.
Foitzik et al.	2005	Clinical Trial	Telogen effluvium	Topical TGF- β 2/TGF- β receptor II antagonists deserve to be explored for the prevention and management of retinoid-induced hair loss.
Hull	2000	Prospective Cohort Study	Unspecified	Hair loss increased from 7% in the fourth month of treatment to 14% at the end of treatment in a study on 124 adolescents and adults using isotretinoin for acne. Hair loss was experienced in a small percentage but was rarely noted on more than one occasion (only reported at one visit out of the treatment course).
Berth-Jones & Hutchinson	1995	Retrospective Cohort Study	Telogen effluvium	Arrest at the onset of anagen phase and follicular anchorage defect in telogen phase appear to be related to the mechanism of alopecia associated with retinoid treatment.

The cyclical pattern of hair growth, influenced by periods of quiescence and regression driven by apoptotic signals, includes three key phases: anagen (growth), catagen (transition), and telogen (rest).²⁶ The anagen phase includes active growth and differentiation of hair cells, which can last several years. The catagen phase, which lasts a few weeks, is characterized by transition into quiescence during which the hair follicle undergoes apoptosis-driven regression and loses about a sixth of its diameter. Lastly in the telogen (resting) phase, the hair follicle is dormant, and growth of the hair shaft does not occur for a variable amount of time depending on the location of the follicle. Overall, the mechanism by which

the follicle transitions between these phases remains unclear.

Although not fully understood, retinoids are thought to arrest the onset of the anagen phase of the hair cycle and impair the anchoring of hair during the telogen phase, thus increasing hair shedding and hair loss.²⁵ Another prospective cohort study demonstrated the effect of isotretinoin on the reduction in the amount of total hair count, its density and the proportion of anagen hair, which suggested telogen effluvium hair loss.¹⁹

Retinoids are also thought to have some role in the initiation of alopecia areata, though their exact effect is unknown. One study

found that the rate of alopecia areata) in mice consuming vitamin A in their diet was seven times higher than mice without vitamin A.²¹ However, the same study also reported that mice with vitamin A in their diet were partially protected against the development of alopecia through the effect of vitamin A on the immune response. These conflicting findings suggest a complex, potentially dose-dependent role of vitamin A in both the hair cycle and immune regulation, which may influence the development of alopecia areata.

The limited evidence-based explanations for the molecular mechanisms of various types of hair loss, especially alopecia areata, warrants further research to verify causal relationships between isotretinoin and hair loss. Additionally, in cases where isotretinoin is used to treat conditions like Darier disease or lichen planopilaris – which themselves cause alopecia – it can be difficult to determine whether hair loss is due to the drug or the disease.

Strategies to Reduce Hair Loss

While it is important to educate patients on the risk of hair loss, it is also important to educate them on strategies to reduce each type of hair loss. A primary approach to reducing hair loss while on isotretinoin would be to lower the daily dose, which is an alternative to discontinuing the drug.⁷ Additionally, a study found that TGF- β 2/TGF- β receptor II antagonists have potential therapeutic effects in retinoid-induced hair loss.²³ While this topical therapy is not yet commercially available, it shows potential as a focus for future studies.

Micronutrients and vitamin supplementation have also been shown to help in telogen effluvium, androgenetic alopecia, and alopecia areata.²⁷ Most authors agree on supplementing Vitamin D in patients with hair

loss or vitamin D deficiency, as well as those with alopecia areata (which has been associated with low Vitamin D levels). Vitamin C is strongly recommended in patients with hair loss that is associated with iron deficiency.²⁸ Most authors also agree on iron supplementation in patients with iron or ferritin deficiency and hair loss (for telogen effluvium and androgenetic alopecia), while iron deficiency reported in females with alopecia areata is likely coincidental. Supplementation with Vitamin A is discouraged during isotretinoin use due to the risk of hypervitaminosis A. Meanwhile, there is not sufficient evidence to recommend use of other micronutrients such as Vitamin E, zinc, and folic acid. Other strategies to reduce hair loss include stress reduction and reducing exposure to harmful chemicals for hair health.^{29,30}

Furthermore, it is important to consider the psychological impact of hair loss on patients. In our case presentation, the development of alopecia areata caused our patient significant anxiety, and he was subsequently diagnosed with generalized anxiety disorder. The potential for psychological impact (including anxiety and depression) of acne and alopecia makes discussing strategies to reduce hair loss crucial. Treatment and prevention of these dermatological conditions, especially when they may happen concurrently, can limit the negative psychosocial impact.³¹

CONCLUSION

The onset of alopecia areata in our patient highlights the development of a unique form of alopecia that is not classically associated with isotretinoin use. While there are some hypotheses about the role of retinoids in hair loss and alopecia areata through effects on the hair cycle and immune system, there is

no direct explanation linking isotretinoin and alopecia areata.

To our knowledge, this patient is the second case of alopecia areata developing after isotretinoin use published in medical literature. This warrants further investigation into the mechanisms of retinoids and how they can result in various types of hair loss.

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