28-Year-Old Female with Diffuse Thinning of the Scalp after Isotretinoin and Oral Contraceptives

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Abstract

Drug-induced alopecia can be difficult to diagnose as determining a causative link between the introduction of a drug to the onset of hair loss requires both a detailed patient history as well as a clear understanding of hair growth cycling. Clinical history taking should include a comprehensive time frame dating back at least 3 months. The difficulty in diagnosis lies in detecting the specific offending agent. New case reports and studies are continually being published linking hair loss to a specific drug, however, these studies are routinely correlative in nature without a definitive biological linkage. Despite this, there are well-studied and reported classes of medications with strong evidence of causing alopecia that should be considered when there is high clinical suspicion of drug-induced alopecia. While drug-induced alopecia is often reversible upon cessation of the offending agent, this is often not an acceptable approach for life-saving and long-term use drugs such as chemotherapy agents, anticoagulants, and psychotropics. Furthermore, the emotional and psychological impact of hair loss without intervention poses serious risks to patient well-being and drug regimen compliance. For chemotherapy-induced alopecia, several targeted therapies exist with promising results such as scalp cooling. Topical and oral minoxidil may be used in those experiencing a drug-induced cause of telogen effluvium. More recent therapies focus on the use of growth factors such as VEGF and keratinocyte growth factor. Despite limited evidence-based therapies for the treatment of

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drug-induced alopecia, a high degree of interest remains in the field for continued investigations into new treatments.

Keywords

Drug-induced alopecia · Telogen effluvium · Anagen effluvium · Hair loss · Scalp cooling

A 28-year-old female presented with diffuse thinning of her hair on the scalp. She noticed that it started about 3–4 weeks after starting isotretinoin for her acne. At the same time she started taking isotretinoin, she also began an oral contraceptive pill to prevent pregnancy. She reported that it feels like her hair comes out in clumps at times. She denied hair loss elsewhere.

On physical examination, diffuse thinning of the scalp was noted with widening of the mid-line part (Figs. 5.1 and 5.2). A hair pull test was positive. A laboratory evaluation was negative for anemia, thyroid disease, or nutritional deficiency.

Based on the clinical case description, what is the most likely diagnosis?

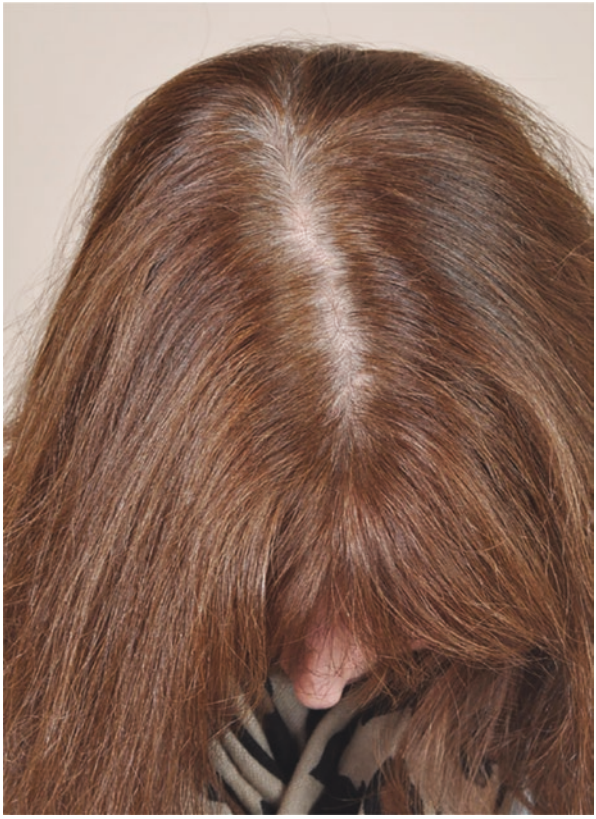

Fig. 5.1 Widening of the mid-line part. Image courtesy of Dr. Melissa Piliang and Janine Sot, MBA medical photographer

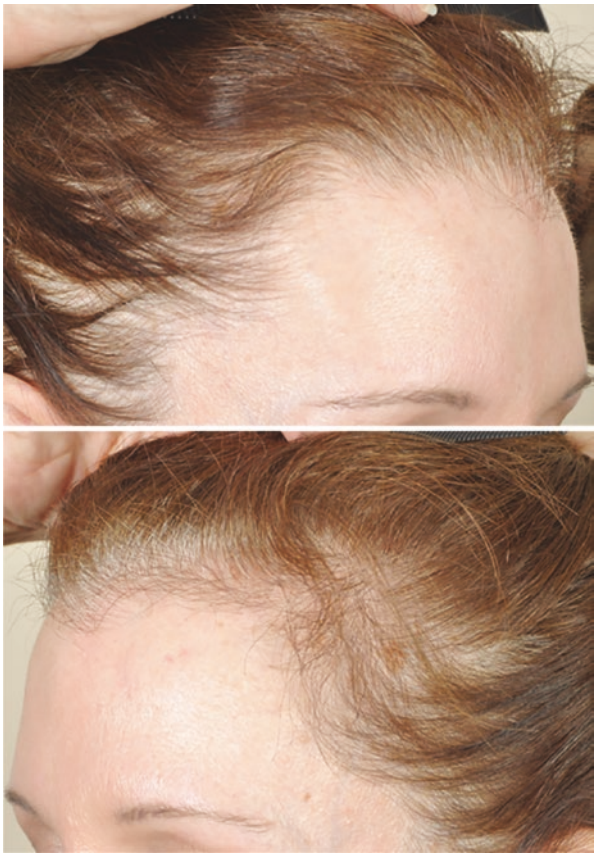

Fig. 5.2 Diffuse thinning along the frontal scalp. Image courtesy of Dr. Melissa Piliang and Janine Sot, MBA medical photographer

1. Alopecia areata
2. Androgenetic alopecia
3. Alopecia due to nutritional deficiency
4. Drug-induced alopecia (telogen effluvium)

Diagnosis

Drug-induced alopecia (telogen effluvium).

Discussion

Drug-induced alopecia can often represent a challenging clinical diagnosis. Determining a causative link between the introduction of a drug to the onset of hair loss requires both a detailed patient history as well as a clear understanding of hair

growth cycling. Briefly, hair growth is understood to consist of 3 phases: a growth (anagen) phase, a regression (catagen) phase, and a resting (telogen) phase [1]. The length of each phase and the percent of human scalp hairs in each cycle varies. Hairs can remain in anagen for up to 6 years with approximately 90% of scalp hairs being in the anagen phase at any given time [2, 3]. Thus, when considering a diagnosis of drug-induced alopecia, clinical history taking should include a comprehensive time frame dating back at least 3 months. Once an initial history and physical exam have ruled out other potential causes such as systemic autoimmune diseases and new environmental stressors, consideration can be made for linking medications to the onset of hair loss. However, even after diagnostic exclusion of other causes, identifying a single drug as the underlying cause can remain challenging. Part of this difficulty lies in the often unclear linkage of specific drugs in the literature to hair loss. New case reports and studies are being continually published linking hair loss to a specific drug, however, these studies are routinely correlative in nature without a definitive biological linkage. Despite this, there are well-studied and reported classes of medications with strong evidence of causing alopecia that should be considered when there is high clinical suspicion of drug-induced alopecia.

Drugs can induce hair loss through either anagen effluvium or telogen effluvium. Both processes present with distinct clinical characteristics and linkages to specific drug classes allowing narrowing of causative factors. Anagen effluvium presents with rapid (weeks) and significant (>80%) hair loss due to inhibition of cellular proliferation and will be discussed in a subsequent chapter. Unlike anagen effluvium, telogen effluvium presents insidiously (months after drug therapy initiation) [4, 5]. A range of drug classes have been linked to this presentation of alopecia including anticoagulants, psychotropics, antibiotics, retinoids, non-steroidal anti-inflammatory drugs, and beta-blockers. Evidence for drug-induced alopecia with anticoagulants such as warfarin, low molecular weight heparins, and new direct oral anticoagulants is reviewed in detail by Watras and colleagues [6]. Notably, there is significant uncertainty in the direct link between anticoagulants and hair loss given the limited number of case reports from the past 70 years. Part of this may be due in part to underreporting by clinicians and patients given the difficulty in linking anticoagulant use with the delayed onset of hair loss seen in telogen effluvium. Psychotropics have a more definitive linkage to telogen effluvium hair loss with lithium having a reported 12%–17% incidence of hair loss [7, 8]. Antidepressants such as selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) have additionally been described in the literature in limited case reports including fluoxetine, sertraline, trazodone, and imipramine [8–11]. Valproic acid induced hair loss has been reported to have an incidence ranging from 3.5%–28% with it notably being dose dependent [12, 13]. Reports of antibiotic induced alopecia remain rare/limited, possibly in part due to the often short duration of traditional antibiotic therapy. Of the available studies, antibiotics used to treat tuberculosis such as isoniazid are more frequently reported [14–16]. This may be in part due to the prolonged course required to effectively treat tuberculosis.

Treatment

While drug-induced alopecia is often reversible upon cessation of the offending agent, this is often not an acceptable approach for life-saving and long-term drugs such as chemotherapy agents, anticoagulants, and psychotropics. Furthermore, the emotional and psychological impact of hair loss without intervention poses serious risks to patient well-being and drug regimen compliance.

For chemotherapy-induced alopecia (CIA), several targeted therapies exist with promising results. Scalp cooling has been reported since the 1970s to induce vasoconstriction of the scalp reducing chemotherapy drug uptake by hair follicles as well as decreasing the biochemical activity of the follicles [17]. One of the earliest reports utilized a simple crushed ice in bags approach to cool the scalp with more recent devices from Paxman and Dignitana being commercially available for this indicated use [17–19]. A recent meta-analysis found scalp cooling to reduce the relative risk of CIA by ~33% indicating it as an effective treatment for preventing CIA in patients about to undergo or currently undergoing chemotherapy [20]. Topical application of 2% and 5% minoxidil, a readily available and affordable agent known to be effective in treating androgenic alopecia, has not shown similar success in treating CIA [21]. More detailed reviews do not recommend its use for treating CIA given the limited evidence of effectiveness [22, 23]. Interestingly, however, oral minoxidil has been shown to reduce hair loss in women with telogen effluvium, indicating a possible use for drug-induced causes of telogen effluvium [24].

Beyond these two classically described treatment modalities, more recent therapies have emerged with varying degrees of evidence. The use of a cocktail of growth factors such as VEGF, bFGF, and kGFG (QR 678 Neo) showed success in promoting hair growth in a limited number of patients with CIA [25]. Topical vitamin D3 analogues, thought to act directly on keratinocytes to promote differentiation, have been repeatedly investigated in the past 20 years for the treatment of CIA. Results have been inconclusive with no definitive evidence of its usefulness, but interest remains as illustrated by the recent completion of a phase I clinical trial [26–28]. Despite limited evidence-based therapies for the treatment of drug-induced alopecia, a high degree of interest remains in the field for continued investigations into new treatments. Approximately 15 clinical trials are currently registered under ClinicalTrials.gov investigating treatments such as platelet rich plasma, photobiomodulation, and keratinocyte growth factor [ClinicalTrials.gov respective identifiers: NCT04459650;NCT04036994;NCT04554732].

Key Points

- Drug-induced alopecia is largely a clinical diagnosis of exclusion based on a detailed patient history dating back at least 3 months.
- Classifying hair loss as drug-induced through either anagen effluvium or telogen effluvium based on the patient presentation can narrow suspicion for the potential offending drug class.

- Chemotherapy agents, anticoagulants, psychotropics, and select antibiotics have shown the greatest linkage to drug-induced alopecia in the literature.
- For clinical situations where drug cessation is not an option, or preventative hair loss prior to drug initiation is desired, scalp cooling therapy has shown the greatest clinical promise.

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