22-Year-Old Male with Several Discrete Patches of Hair Loss

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Abstract

Alopecia areata (AA) is an immune mediated, non-cicatricial, hair loss. AA may occur at any age and has an estimated lifetime incidence of 1.7%. Hair loss may range from localized, discrete patches or comprise the total body surface. The etiology of AA is multifactorial and thought to be caused by autoimmune, environmental, and genetic factors. Upon histological analysis, hair follicles afflicted by AA may reveal dense inflammatory cell infiltrate surrounding the bulbar region of anagen hair follicles. Dermatoscopic evaluation may reveal short, broken hairs with narrow proximal ends and thicker distal portions referred to as "exclamation mark" hairs. AA may be diagnosed clinically by the presence of often sharply demarcated round or oval-shaped areas of sudden, patchy hair loss. The rate of remission of AA is thought to be dependent on the amount of scalp involvement upon initial diagnosis. The general treatment approach to AA should include education regarding prognosis to facilitate informed decisions regarding treatment preferences. Patients should be directed to resources including opportunities to participate in clinical trials, products available to conceal hair loss, and psychosocial support upon initial diagnosis. Intralesional corticosteroids are considered to be first-line therapy for individuals experiencing limited disease and as adjunctive therapy in patients experiencing extensive disease. In patients with limited disease, topical corticosteroids have also shown clinical benefit particularly due to local anti-inflammatory effects. Topically applied agents may be used alone or in combination with additional treatment modalities and may be preferred over injections in the pediatric population. Minoxidil, methotrexate, or

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S. C. Trotter, S. Sampath (eds.), *Clinical Cases in Alopecia*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-15820-9_3

topical immunotherapy may also be considered based upon patient specific factors. A wide range of new therapeutic modalities with promising initial results are currently under investigation for the treatment of AA including statins, phosphodiesterase-4 inhibitors, Janus kinase (JAK) inhibitors, and platelet rich plasma (PRP).

Keywords
Alopecia areata · non-cicatricial · autoimmune · exclamation mark hairs · corticosteroids

A 22-year-old male presented with several focal patches of non-scarring alopecia on the scalp. He reported that the hair loss started after he had a cold on the right side of his scalp and gradually, more areas began to come up. He buzzed his hair short a few days ago so that we could evaluate his scalp more thoroughly. The patient denied hair loss elsewhere but reported he had a history of atopic dermatitis.

On physical examination, multiple well-demarcated patches of nonscarring alopecia were appreciated. Some patches had short, pointed hairs that were present (Fig. 3.1). Eyelashes and eyebrows appeared intact. He had a few dry, pink, scaly patches in the antecubital fossa bilaterally and on the trunk. Fingernail examination was within normal limits.

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

1. Alopecia areata
2. Anagen effluvium

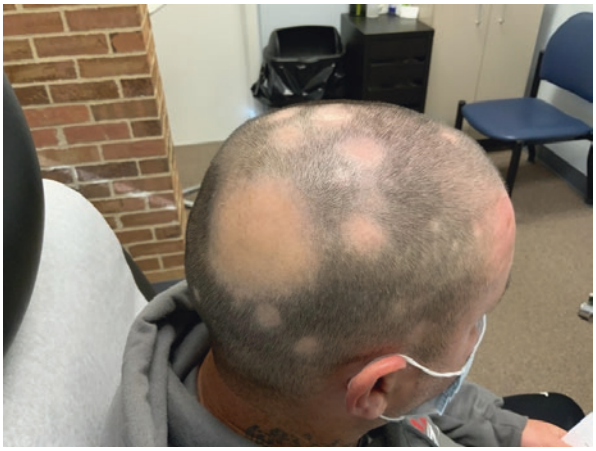

Fig. 3.1 Multiple discrete, well-demarcated patches of non-scarring hair loss

3. Androgenetic alopecia
4. Telogen effluvium

Diagnosis

Alopecia areata.

Discussion

Alopecia areata (AA) is characterized by non-scarring (also known as non-cicatricial) hair loss in localized areas. Non-scarring alopecia refers to hair loss that is due to alteration in the hair growth cycle, hair follicle size, hair breakage, or a combination of these with preservation of the hair follicle [1]. It is known that AA targets the hair follicle matrix but the condition itself has an unpredictable course with widespread phenotypic and genotypic variability. AA can be organized into three broadly distinct categories: (1) patch-type AA, characterized by round patches on the head or body; (2) alopecia totalis, defined as a near complete absence of hair on the scalp; and (3) alopecia universalis, which is described as complete hair loss on the body, face, and scalp [2]. The estimated lifetime incidence of AA is 1.7% [3]. AA can occur at any age, however, the typical age of onset is less than 25 years [4].

The etiology of AA is not entirely recognized but it is thought to be attributed to autoimmune, genetic, and environmental factors [4]. A loss of immune privilege of the hair follicle is thought to be a significant driver of the pathogenesis of AA [1]. Initiation of follicular damage is caused predominantly by CD8+ lymphocytes. CD4+ lymphocytes, natural killer cells, macrophages, Langerhans cells, and cytokines also contribute to the pathogenesis of AA, but to a lesser degree [5]. The hair follicle matrix epithelium undergoing early cortical differentiation has emerged as the primary target of cellular immune attack [1]. Localized degenerative changes within the matrix epithelium create weakness within the hair shaft and ultimately lead to breakage once the shaft emerges to the skin surface [1]. The primary histopathological feature of AA is dense inflammatory cell infiltrate surrounding the bulbar region of anagen hair follicles [1]. Dermoscopic examination of this phenomenon may reveal characteristic, although not pathognomonic, “exclamation mark” hairs, which are short, broken hairs where the proximal end of the hair is narrower than the distal portion. Additional dermoscopic features may include black dots, yellow dots, broken hairs, or short vellus hair [6]. However, preservation of the hair follicle and sparing of follicular stem cells results in the lack of ostensible scarring of the skin [7].

AA is typically diagnosed by its clinical manifestations including the presence of often sharply demarcated round or oval-shaped areas of sudden, patchy hair loss postulated to be caused by a premature transition from the anagen to the telogen phase within the hair growth cycle [8]. Hair loss may also present more diffusely and has the capacity to affect any hair-bearing region of the body. The Alopecia

Areata Assessment Tool (ALTO), a self-administered questionnaire designed to capture the hallmark features of AA and its three main phenotypes, aids clinicians in establishing a diagnosis of AA while discriminating AA from other forms of non-scarring alopecia such as androgenic alopecia, telogen effluvium and tinea capitis [9]. AA is also associated with other auto-immune mediated dermatologic diseases such as vitiligo, atopic dermatitis, psoriasis, and lichen planus.

Treatment

Patients with extensive AA, defined as >50% of the scalp, may experience lower remission rates as compared to those with limited scalp involvement, defined as <25%. Limited scalp involvement portends a better prognosis with remission rates up to 68% [10]. Counseling patients regarding disease prognosis may contribute to improved informed decisions regarding treatment preferences. Upon diagnosis, patients can use the National Alopecia Areata Foundation website (www.naaf.org) for resources including opportunities to participate in clinical trials, products available to conceal hair loss, and psychosocial support.

Intralesional corticosteroids are considered the first-line therapy for individuals experiencing limited disease and as adjunctive therapy in patients experiencing extensive disease [11]. Pilot studies have demonstrated a similar benefit of 2.5 mg/mL triamcinolone acetonide when compared to 5 or 10 mg/mL in patients experiencing patchy AA [12]. The triamcinolone acetonide dose should not exceed 20 mg per monthly session [12]. Adverse reactions to this form of therapy include skin atrophy at the site of injection. If patients fail to respond within 3–6 months, or skin atrophy is noted, therapy should be discontinued [13].

In patients with limited disease, topical corticosteroids have also shown clinical benefit particularly due to local anti-inflammatory effects. Topically applied agents may be used alone or in combination with additional treatment modalities and may be preferred over injections in the pediatric population [11]. Higher potency topical steroids may be used in adult patients, whereas less potent topical agents may be considered in pediatric patients. Side effects may include skin atrophy, acneiform eruptions, striae, telangiectasia, and skin discomfort associated with mild itching or burning [14]. In severe cases of diffuse AA, a brief course of oral corticosteroids could be considered to stimulate hair regrowth and modulate immunologic factors that contribute to AA prognosis [15]. However, relapse upon discontinuation is highly likely. Adverse reactions associated with systemic therapy which impede long-term use include hypothalamic-pituitary-adrenal axis suppression, worsening glycemic control, hypertension, and decreased bone density [11].

Topical minoxidil may assist in the maintenance of hair growth stimulated by other agents and may be used as adjunctive therapy [16]. Concentrations of topical minoxidil at 5% have been shown to be effective [17]. Adverse reactions of topical minoxidil include tachycardia, sparse vellus hairs, and scalp irritation including itching and dermatitis [18]. Notably, a recent clinical trial demonstrated that once-per-day dosing of oral minoxidil (OM) was found to be an effective and

well-tolerated treatment alternative for healthy patients encountering compliance barriers with topical formulations [19]. While not without a side-effect profile, this recent review found that OM at lower doses (<5 mg) was tolerable, with few and mild adverse effects [19]. By far, the most common adverse effect of OM was hypertrichosis, which was reported as mild and easily manageable. Other less common adverse effects include postural hypotension, dizziness, lower limb edema, and mild blood pressure changes [19].

Methotrexate as monotherapy or in conjunction with prednisone has been shown to stimulate successful hair regrowth in both pediatric and adult populations. Due to the adverse effects of methotrexate, such as abnormal liver function, gastrointestinal discomfort, and less commonly, lymphopenia and risk for pulmonary tuberculosis, methotrexate should be primarily considered in patients who have failed other standard therapies or who are suffering from severe AA [11, 20].

In adult and pediatric patients >10 years of age with extensive AA (scalp involvement >50%), evidence supports the implementation of contact sensitization. Contact sensitization involves the use of topical immunomodulators to induce localized allergic contact dermatitis and antigenic competition. Although the exact mechanism of action has yet to be elucidated, it is thought that topical immunotherapy results in the shifting of the target of T-cells from hair follicles to the epidermis through antigenic competition. An additional postulation involves an increase in T-regulatory lymphocytes through cytokine alteration resulting in a reduction of follicular inflammation [21]. Currently prescribed topical immunotherapeutic agents include squaric acid dibutylester (SADBE) and diphenylcyclopropenone (DPCP) [22]. A study demonstrated that DPCP yielded an overall response rate of up to 72.2% with efficacy further augmented by the concomitant use of anthralin [23, 24]. While efficacy has been demonstrated, DPCP possesses a high degree of relapse, resulting in the need for thorough patient education. SADBE therapy may be considered for patients refractory to DPCP therapy [11]. Topical immunotherapy with both SADBE and DPCP is contraindicated in pregnancy. Adverse reactions include localized lymphadenopathy and severe eczema [23].

Although further clinical trials and investigation are warranted, the pleiotropic effects of statin therapy were explored amongst patients with AA. In a small prospective pilot study, the administration of simvastatin at a moderate-intensity dose (40 mg) in combination with ezetimibe (10 mg) displayed hair regrowth in 14 out of 19 patients as early as 16 weeks of therapy [25, 26]. Additionally, the oral phosphodiesterase-4 inhibitor, apremilast, has shown promising results in mouse models and is currently under investigation in an ongoing clinical trial [27].

The use of Janus kinase (JAK) inhibitors is currently being explored in patients with AA. Specific agents that have been investigated include baricitinib, ruxolitinib, and tofacitinib [11]. A retrospective investigation of tofacitinib in adolescents aged 12–17 demonstrated hair regrowth amongst 69% of a study population containing 13 patients [28]. An open-label trial investigating ruxolitinib suggested that the degree of response may be variable and possesses a positive correlation with high interferon and cytotoxic T-lymphocytes levels at baseline [29]. JAK inhibitors carry a potential risk for serious adverse reactions including malignancy, infection, and

viral reactivation. Thus, larger-scale investigations of these agents are warranted and are currently underway [11].

Platelet rich plasma (PRP) isolated from venous blood samples has recently been explored in patients with AA. Bioactive molecules and growth factors within PRP have a regenerative impact on tissue, which leads to the potential use of PRP in the promotion of hair regrowth in AA [30]. A recent review highlighted a positively influential effect of PRP if at least three intradermal scalp treatments were administered at 4 to 5 week intervals for a total treatment duration of 4 to 6 months [31]. Further research is warranted to define its benefit, as limited studies have been conducted amongst patients with AA.

Key Points

- Alopecia areata (AA) is characterized by non-scarring (also known as non-cicatricial) hair loss in localized areas coinciding with varying phenotypic and genotypic presentations.
- Intralesional corticosteroids are considered the first-line therapy for individuals experiencing limited disease and as adjunctive therapy in patients experiencing extensive disease.
- A wide range of new therapeutic modalities with promising initial results are currently under investigation for the treatment of AA including statins, phosphodiesterase-4 inhibitors, Janus kinase (JAK) inhibitors, and platelet rich plasma (PRP).

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