Alopecia areata: What to expect from current treatments

**ABSTRACT**

Alopecia areata is relatively benign and often resolves on its own, although its psychosocial impact on children and young adults can be severe. Some form of treatment is usually required. Because current treatments may not show results for 3 to 6 months, reassuring the patient and the parents and informing them about the results that can be expected are an essential part of management. The choice of treatment depends on the patient's age and the extent of alopecia activity.

**KEY POINTS**

Alopecia areata is an autoimmune, T-cell-mediated reaction directed against hair follicles.

Other autoimmune diseases often coexist in patients with alopecia areata.

Current treatments include intralesional and topical corticosteroids, minoxidil, short-contact anthralin, and contact sensitizers.

**MAIN FEATURES**

Alopecia areata is a common cause of non-scarring alopecia, occurring in 1% to 2% of the population and affecting both sexes and all racial groups. It may present at any age but is more common in children and younger adults: 60% of patients who present with their first patch are under the age of 20.\(^1,2\) Onset in childhood may be a marker of more severe disease.\(^2,3\)

The characteristic lesion of alopecia areata is a smooth round or oval bald patch on the scalp, the most severe patch currently in the right temporal area (FIGURE 1). He has thinning of the eyebrows and mild bald patches on the forearms and legs. A previous 3-month regimen of topical steroids, intralesionally injected steroids, and minoxidil 5% resulted in only mild improvement. He has a history of acne vulgaris and allergies to ragweed, mold, grass, weeds, trees, and dust mites. He has no family history of alopecia or autoimmune disease.

In this case, the diagnosis of alopecia areata can be made on the basis of the clinical presentation. The challenge is now to select a reasonable treatment, given the history of failed treatments to date. This case highlights the key challenges of managing alopecia areata: finding a regimen that works, and making sure that the patient has realistic expectations about the effectiveness of the treatment.

In this article we briefly review the features of alopecia areata and current and future approaches to its management.
scalp or any other hair-bearing area of the body. Usually, the condition is localized when it first appears. Most patients (80%) have a single patch, 12.5% have two patches, and 7.7% have more. The number of patches at onset is not correlated with subsequent severity.1

“Exclamation-mark” hairs—short, broken-off hairs that are narrower closer to the scalp—may be seen at the periphery of each patch in alopecia areata. A hair-pull test may be positive at the margin of the patch.4 This test is done by gently but firmly tugging on a small clump (about 60 hairs), and it is positive when more than 6 hairs are pulled out by the root. A positive test helps to differentiate alopecia areata from other forms of hair loss that have a negative test, such as trichotillomania and androgenic alopecia.

Hair loss due to alopecia areata is usually asymptomatic. However, some patients describe tenderness, burning, or pruritus before a patch appears. The scalp may feel slightly depressed because of the loss of the supportive effect of the hair shafts.4

The pattern of scalp involvement is usually patchy, but may also be reticolar, band-like, or diffuse.1,3,4 In some patients with partial loss of scalp hair (alopecia areata) the condition progresses to a total loss of scalp hair (alopecia totalis) or to a loss of all scalp and body hair (alopecia universalis) during a single episode or with recurrent episodes. In fact, 55% of children with onset of alopecia areata before age 2 develop alopecia totalis or alopecia universalis.5

Nail involvement occurs in 7% to 49% of patients. Pitting is the most common nail manifestation in children.5 Beau lines (transverse grooves), trachyonychia (roughened surface), koilonychia (spooning), and red lunulae may also be present.5

■ PATHOPHYSIOLOGY:
THE ROOTS OF THE PROBLEM

Alopecia areata is strongly associated with certain human leukocyte antigen class II alleles, such as interleukin-1 receptor antagonist allele 2.6 Several genes may play a role in determining disease susceptibility. Genetic factors probably interact with environmental factors such as physical or emotional stress or microorganisms to trigger the disease.6 A family history is noted in 10% to 42% of cases.1

The autoantigen in alopecia areata remains to be identified, but results from current studies suggest that it may be derived from melanocytes. Support for this comes from clinical observations that alopecia tends to target pigmented hairs and that it is commonly associated with vitiligo.7

In 20% to 30% of patients, alopecia areata is associated with other autoimmune diseases such as Hashimoto thyroiditis, type 1 diabetes mellitus, systemic lupus erythematosus, vitiligo, and celiac disease, and also with connective tissue diseases.8,9 One study10 noted thyroid abnormalities in 17.5% of children with alopecia areata. Atopy (allergic rhinitis, asthma, atopic dermatitis) is found in more than 40% of alopecia areata patients vs a 20% prevalence in the general population.7 Thus, a complete review of systems must be done to assess for an associated disease and to determine if a laboratory workup is warranted.

■ DIFFERENTIAL DIAGNOSIS

Alopecia areata is easily distinguishable from telogen effluvium, androgenetic alopecia, and tinea capitis.4 Telogen effluvium is a form of non-scarring alopecia characterized by diffuse shedding (hair falling out by the root). Hair loss is generalized over the entire scalp as opposed to the usually patchy appearance of
alopecia areata. Androgenetic alopecia is male-pattern baldness; it tends to occur in a typical pattern, and shedding is not prominent. Tinea capitis, primarily a disease of children, usually presents as scaly erythematous lesions in addition to one or several round patches of alopecia.1

■ DIAGNOSIS BASED ON CLINICAL APPEARANCE

The diagnosis of alopecia areata is based on clinical appearance, but punch biopsy may be necessary to confirm the diagnosis in some cases, since other inflammatory scalp disorders can present as an alopecic patch. Microscopic study of the biopsy specimen in a patient with alopecia areata shows a T-cell-rich lymphocyte infiltrate surrounding the hair follicle in a pattern referred to as a “swarm of bees.”4,11 This inflammatory reaction accelerates the telogen or shedding phase of the hair-growth cycle.11

■ NATURAL HISTORY IS UNPREDICTABLE

The only thing predictable about the natural course of alopecia areata is its unpredictability. Patients may present with several episodes of hair loss and hair regrowth during their lifetime. Recovery from hair loss may be complete, partial, or none. Patchy alopecia areata is usually self-limited. Complete regrowth can be expected within 1 year in most patients, with or without treatment.4

As hair regrows in alopecia areata, the first hairs are often white, and pigmented hairs usually follow. Regrowth in one site and a worsening of alopecia at another site may occur at the same time in the same patient.12

From 7% to 10% of patients with alopecia areata eventually develop a severe, chronic form. Such patients are likely to have other autoimmune diseases, a family history of alopecia areata, a younger age of onset, nail involvement, and extensive hair loss (> 25% loss of scalp hair).1,4,5

■ TREATMENTS

Treatment is not mandatory, since alopecia areata is benign and tends to remit spontaneously, and since treatment does not prevent recurrences. Nevertheless, because alopecia areata can cause extreme psychologic distress in young people, most physicians offer treatment.

Current treatments include corticosteroids, minoxidil, anthralin, and contact desensitizers. While primary care physicians often prescribe treatments for alopecia areata, referral to a dermatologist is recommended when:

• The alopecia involves less than 25% of the scalp, but previous treatment with intralional or topical corticosteroids has been ineffective
• The alopecia involves more than 25% of the scalp
• The patient has alopecia totalis or universalis.

Treatment of alopecia areata is intended to stimulate hair regrowth and reduce inflammation. Treatment has no effect on the natural course of the condition. The choice of treatment plan depends on the age of the patient and the extent of scalp involvement (Table 1).

Intralesional steroids are first-line therapy

Table 1: Treatment plan for alopecia areata

| Age <10 years | Minoxidil 5% solution | Topical corticosteroid or short-contact anthralin |
| Age >10 years | <50% scalp involvement | Intralesional corticosteroids every month |
| | | Minoxidil 5% solution |
| | | Topical corticosteroid or short-contact anthralin |
| >50% scalp involvement | Topical immunotherapy: diphenylcyclopropenone, squaric acid dibutylerster, dinitrochlorobenzene |
| | | If good response, continue immunotherapy as needed |
| | | If poor response, consider minoxidil 5% solution and topical corticosteroid or short-contact anthralin |
| | | Consider scalp prosthesis |

Although the condition is relatively benign, the psychological impact is often severe.
patchy alopecia areata and less than 50% scalp involvement. Corticosteroids suppress the T-cell-mediated immune attack on the hair follicle. The recommended dose per treatment session is up to 3 mL of a 5-mg/mL solution injected into the mid-dermis in multiple sites 1 cm apart. The amount injected into each site is 0.1 mL.

Regrowth is usually seen within 4 to 8 weeks in responsive patients, and treatment can be repeated every 4 to 6 weeks. In patients with rapidly progressive, extensive, or long-standing alopecia areata, the response is poor. Drawbacks are the pain of the injection and the risk of permanent atrophy at the injection site. Children under age 10 are usually not treated with intralesional corticosteroids due to pain at injection sites. However, a topical anesthetic cream such as lidocaine-prilocaine can be applied to reduce discomfort. The risk of atrophy can be minimized by injecting into the mid-dermis rather than into the epidermis or the subdermal fat.

Corticosteroids should be discontinued if there is no response after 6 months of treatment.

**Topical steroids**

Topical steroids, while often used, may not be effective when used alone due to insufficient penetration into the hair bulb, but when combined with intrallesional corticosteroid injections, they are of greater benefit. A recent study of patients with alopecia totalis and alopecia universalis concluded that clobetasol propionate 0.05% applied to half the scalp under occlusion with plastic film is effective in inducing hair regrowth: 28.5% of patients had regrowth of more than 75% of terminal hairs on the treated side by 6 to 14 weeks. Hair regrowth occurred only on the treated half of the scalp. Thus, topical steroids may be a beneficial treatment option.

Adverse effects of long-term use of highly potent topical steroids include telangiectasia, skin atrophy, folliculitis, and adrenal suppression.

**Systemic steroids**

Oral corticosteroid therapy has been used to treat alopecia areata for more than 50 years, and it is effective. However, prednisone doses required to maintain hair regrowth are between 30 and 150 mg daily, giving rise to unacceptable side effects. Relapse often occurs after tapering the dose. Thus, systemic steroids are rarely used today in the treatment of alopecia areata.

**Minoxidil**

Minoxidil stimulates follicular DNA synthesis. Its specific mode of action in alopecia areata is unknown, but it does have an immunomodulatory effect. Topical minoxidil 5% solution is applied twice daily. Cosmetically acceptable regrowth has been shown in 20% to 45% of patients with 20% to 99% scalp involvement. When minoxidil is effective, initial hair regrowth is achieved after 3 months. Side effects are rare and include local irritation, allergic contact dermatitis, and facial hair growth.

**Anthralin**

Anthralin may generate free radicals, which have antiproliferative and immunosuppressive actions. Anthralin cream (0.5%–1%) may be applied overnight or can be used as short-contact therapy, initially for 30 minutes and gradually increasing to 1 hour. When anthralin is effective, new hair growth is noticed in 3 months. A cosmetically acceptable response may take longer than 6 months. Side effects include pruritus, erythema, folliculitis, and regional lymphadenopathy.

**Contact sensitizers**

Dinitrochlorobenzene (DNCB), squarc acid dibutyl ester (SADBE), and diphenylcyclopropenone (DPCP) are indicated for alopecia areata with greater than 50% loss of scalp hair. They are administered in a university or hospital setting by a dermatologist, and informed consent must first be obtained. DPCP is the most commonly used of the contact sensitizers because of its greater safety and stability and because DNCB has been shown to be mutagenic. The exact mechanism of action of contact sensitizers is unclear; however, it is hypothesized that they induce an allergic contact dermatitis, which shifts the position of T cells away from the hair follicle, thus enabling hair regrowth. Mild eczematous reactions and enlargement of
retroauricular lymph nodes are desired reactions and are inherent to treatment.\textsuperscript{14} Extension of the contact dermatitis to other body areas and postinflammatory hyperpigmentation or hypopigmentation may occur, but no long-term side effects have been reported.\textsuperscript{15}

One study with DPCP achieved a cosmetically acceptable result in 60\% of patients with 25\% to 99\% scalp involvement.\textsuperscript{14} Regrowth typically is seen after 3 months of therapy, with cosmetically acceptable results after 6 months.\textsuperscript{1} DPCP should be discontinued if there is no response after 12 months.

\section*{CASE RESOLUTION}

The patient was continued on his current treatment regimen of intralesional steroids and minoxidil with only minimal improvement. Six months later, he was started on DPCP 0.03\% twice weekly. Substantial regrowth of hair was noted 4 months later (\textbf{FIGURE 2}). The DPCP strength was then increased to 0.2\%. Nine months later, most hair had regrown (\textbf{FIGURE 3}). The DPCP was gradually increased to 0.3\% twice weekly. His current maintenance therapy is DPCP 0.3\% alternating with 0.5\% twice weekly. Any new patches are treated with 0.5\% DPCP as needed.

\section*{THE FUTURE OF TREATMENT}

Gundogan et al.\textsuperscript{18} are the first to discuss successful treatment of two patients with alopecia areata with the 308-nm xenon chloride excimer laser. The laser is thought to induce T-cell apoptosis, which is analogous to topical treatment of alopecia areata. After 11 to 12 sessions within a period of 9 to 11 weeks, the patches showed homogenous and thick regrowth. There was no relapse in the 5 to 18 months of follow-up.

Other new therapeutic developments may include incorporation of steroids into liposomes (which would produce a topical agent able to penetrate into subcutaneous fat surrounding the hair bulb), topical macrolides of the ascomycin type, anti-CD44-v10 antibodies, inhibition of the Fas-FasL system, and induction of tolerance.\textsuperscript{14}

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure2.png}
\caption{Regrowth after 4 months of diphenylcyclopropenone 0.03\% twice weekly.}
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\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure3.png}
\caption{Nearly complete regrowth after 13 months of treatment with diphenylcyclopropenone.}
\end{figure}

\section*{REFERENCES}


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