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Anna Otlewska[1], Agnieszka Otlewska[2], Grzegorz Szpotowicz[3]

# Alopecia areata

## Łysienie plackowate

[1] Department of Physiology, Wroclaw Medical University, Wrocław, Poland
[2] Department of Dermatology, Venereology and Allergology, Wroclaw Medical University, Wrocław, Poland
[3] Department of Normal Anatomy, Wroclaw Medical University, Wrocław, Poland
Correspondence: Anna Otlewska, Wiązowa 7/1, 53-127 Wrocław, Poland, tel.: +48 500 074 744, e-mail: a.otlewska@gmail.com

## Abstract

Alopecia areata is a disorder with an estimated lifetime risk of 1 to 2%. The prevalence is the highest in the age group of 10 to 25 years. The exact aetiopathogenesis of alopecia areata is not precisely known, however, some factors that seem to play an important role in the development of the condition include autoimmune processes, stress or genetic vulnerability. Also, alopecia areata often coexists with depressive or anxiety disorders. The clinical presentation of alopecia areata includes sharply demarcated patches of hair loss, though the skin remains otherwise unaffected by any pathological changes. The severity of the condition varies greatly, and symptoms may range from isolated areas of hair loss on the scalp to total hair loss of the scalp – or even total loss of body hair. The most important differential diagnosis to consider in patients with suspected alopecia areata is androgenetic alopecia, i.e. the most common form of hair loss. The course of alopecia areata remains difficult to predict. In the majority of cases, the hair grows back spontaneously, but relapses are common. Treatment involves a variety of drugs, mainly immunomodulatory agents – either the types generating an allergic reaction or producing immunosuppressive effects. There are, however, no established treatment regimens for alopecia areata. It is worthwhile to note that antidepressants and non-pharmacologic interventions such as psychotherapy are also frequently used for treatment. Patients with alopecia areata often experience an impaired quality of life secondary to the disease. This fact, combined with the potential contribution of stress to the development of the condition, seems important from the viewpoint of considering psychological support in this group of patients.

**Keywords:** alopecia areata, autoimmune thyroid disease, hirsutism, glucocorticosteroids

## Streszczenie

Łysienie plackowate jest schorzeniem występującym z częstością około 1–2% w ciągu życia. Większość przypadków dotyczy pacjentów między 10. a 25. rokiem życia. Przyczyna rozwoju tej choroby nie jest jednoznacznie znana. U jej podłoża mogą leżeć procesy autoimmunologiczne, stres lub czynniki genetyczne. U pacjentów z łysieniem plackowatym często obserwuje się zaburzenia depresyjne bądź lękowe. Charakterystyczne jest występowanie ostro odgraniczonych obszarów skóry pozbawionych włosów, przy czym skóra nie jest zmieniona chorobowo. Nasilenie łysienia plackowatego charakteryzuje się dużą rozpiętością objawów: może być ograniczone do pojedynczych obszarów pozbawionych włosów na skórze głowy, może dotyczyć wszystkich włosów na głowie, a nawet wszystkich włosów na ciele. Istotną rolę odgrywa przeprowadzenie diagnostyki różnicowej, w tym wykluczenie najczęstszego typu łysienia, jakim jest łysienie androgenowe. Przebieg choroby jest trudny do przewidzenia. W większości przypadków następuje spontaniczny odrost włosów. Często występują jednak nawroty. W leczeniu zastosowanie znajdują różne leki, przede wszystkim działające immunomodulująco, zarówno te, które mają na celu wywołanie reakcji alergicznej, jak i te, które działają immunosupresyjnie. W terapii łysienia plackowatego nie ma jednak ustalonych schematów postępowania. Warto zwrócić uwagę na częste wykorzystywanie w leczeniu także psychoterapii bądź leków przeciwdepresyjnych. U pacjentów z łysieniem plackowatym jakość życia, wtórnie do choroby, często jest obniżona, co przy uwzględnieniu potencjalnego wpływu stresu na rozwój schorzenia wydaje się istotne pod kątem ewentualnego wdrożenia wsparcia psychologicznego tej grupie chorych.

**Słowa kluczowe:** łysienie plackowate, autoimmunologiczna choroba tarczycy, hirsutyzm, glikokortykosteroidy

## INTRODUCTION

Alopecia areata (AA) is a condition that causes patches of hair loss on the body. The skin within the patches is normal. The condition may involve the loss of all hair on the scalp (*alopecia areata totalis*) or all body hair (*alopecia areata universalis*)[1]. In order to better understand the pathogenesis of AA, it is important to know the hair growth phases – anagen, catagen and telogen – and how they relate to hair loss. The longest phase is anagen[2], lasting between 1 and 8 years, in which the hair actively grows. Anagen is followed by catagen, when apoptosis and involution of hair follicles take place. The catagen phase lasts about a few weeks. It is followed by telogen, i.e. the resting stage. After the telogen phase the hair follicles progress back into the anagen phase[3].

## EPIDEMIOLOGY

The lifetime risk of AA is estimated to be approximately 1–2%[4]. Although the disease can occur at any age[5], it is more prevalent in children[6]. Approximately 70% of cases are diagnosed between 10 and 25 years of age[7]. The condition has a similar prevalence in men and women[1], though some sources report that the course of the disease is more severe in men[7]. Alopecia areata is the second most common form of alopecia in humans after androgenetic alopecia[8]. It is believed to account for 25% of all cases of alopecia[9].

## PATHOGENESIS

The pathogenesis of AA has not yet been fully elucidated. A variety of factors have been identified as being associated with its development. One of the main possible causes underlying the condition is believed to be the autoimmune mechanism. The theory is justified by the fact that AA may coexist with other conditions with an autoimmune basis including vitiligo, autoimmune thyroid disease, systemic lupus erythematosus[10], type 2 diabetes mellitus, rheumatoid arthritis, pernicious anaemia[2], and atopic diseases, especially eczema[11]. It is estimated that 8–28% of AA patients have a concomitant thyroid disease[12,13], and 3–8% are affected by vitiligo[12]. Bin Saif has shown that patients with total loss of hair on the scalp or in other parts of the body are more likely to have thyroid dysfunction[14]. Also, Thomas and Kadyan claim that patients with relapsing forms and more severe course of AA should be screened for thyroid dysfunction[15]. It must be noted that AA may also be linked to autoimmune polyendocrine syndrome (APS), representing one of the components of the condition[16].

According to the autoimmune theory, T cells are directed against hair follicles which, in this case, act as autoantigens[17], and are located near the hair follicles which are in the anagen phase[18]. They include primarily CD4 and CD8 cells, but also Langerhans cells and macrophages[19]. Rarely performed biopsies of affected skin reveal the presence of lymphocytic infiltrates[20]. Mononuclear cell infiltrates are referred to as "swarms of bees"[12]. An important role in the pathogenesis of the disease is also attributed to cytokines secreted by immune system cells[21].

In addition, the development of AA has been linked to genetic and environmental factors, mainly stress[22]. Patients with AA often report anxiety disorders or depression[23]. It is estimated that individuals affected by AA have a 39% lifetime prevalence rate of depressive disorder. Also, patients with AA are more likely to experience low self-esteem, anger or anxiety[24]. However, available data on the impact of mental stress on the onset of disease are conflicting[25].

The findings of studies on AA show that the disease can be inherited in a multigenic manner, as evidenced by the high prevalence of family history of the condition[7]. Positive family history in patients with AA has been reported to range from 10 to 42% of all cases[26].

Bhat et al. have demonstrated that the development and severity of AA may also be linked to vitamin D deficiency (found at vitamin D levels <30 ng/mL)[9].

Prie et al. consider oxidative stress as one of the contributory factors to the pathogenesis of AA. Consequently, they suggest antioxidants as adjunctive therapy for AA[27].

## SYMPTOMS AND DIAGNOSTICS

Alopecia areata is characterised by well-circumscribed patches of hair loss. The skin within the patches is normal, unaffected by atrophy[22] or scarring[28]. Alopecia areata may start as a single patch of hair loss, but in the course of time it may spread into multiple patches[29]. The patches of hair loss are usually round or oval[30], and exclamation mark hairs may be seen at the margins of the bald patches[31]. The hair follicles remain undamaged. Hair loss may affect limited areas of the scalp, all scalp hair (including eyebrows and eyelashes), or all hair on the body. Hair loss is mainly seen in pigmented hair, with white hair less frequently affected[32]. The hair pull test is positive in patients with AA[28]. Alopecia areata may also be associated with changes in the nails[18,33], and their occurrence is thought to be correlated with a more severe disease course[34]. Alopecia areata may reduce the quality of life[35,36], and cause emotional and social discomfort[37].

The diagnosis is based on trichoscopic evaluation which reveals exclamation mark hairs and yellow dots corresponding to dystrophic epithelial cells and sebaceous glands[38]. Initially, hair regrowth is observed in the centre of the areas of hair loss[39]. Regrowing hair may have a different structure or be of a different colour[40]. Also, new hair often initially has no pigment[39].

Crucially, AA has to be differentiated from alopecia of different aetiology, primarily androgenetic alopecia which is characterised by hair thinning in androgen-related areas, and may be accompanied by other symptoms



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of hyperandrogenism[41]. The differential diagnosis should also include trichotillomania, scalp mycosis, systemic lupus erythematosus, telogenic alopecia, anagenic alopecia, drug-induced alopecia, and scarring alopecia. In case of doubt as to the diagnosis it may be necessary to perform additional differential diagnostic examinations[42].

## COURSE

The course of AA is unpredictable. It has been reported that spontaneous hair regrowth occurs in 50–80% of affected patients within a year[8,39,43]. However, in some patients with AA symptoms may persist for months or even years[22]. In the majority of cases, the disease has a relapsing nature[43]. In approximately 14–25% of patients AA progresses, resulting in the loss of all hair on the scalp or body[44]. When total hair loss occurs, regrowth can only be achieved in approximately 10% of patients[45]. Severe AA is diagnosed when more than 50% of scalp hair is lost[29].

Prognostically adverse factors have been reported to include positive family history of AA, early onset of the disease[4], persistence of symptoms for more than a year[40], coexistence of atopy and other autoimmune disorders[46] as well as, as mentioned above, the presence of nail lesions[32]. Furthermore, You and Kim have found the male sex to be a risk factor for the development of severe AA[47].

## TREATMENT

Currently, there are no established therapeutic regimens for AA[35]. As mentioned above, spontaneous hair regrowth is observed in most cases, so the management in patients with limited lesions often involves only observation or topical steroids[48].

The treatment of AA is based on drugs having a modulatory effect on the immune system[49], including both topical and systemic agents[50].

Immunomodulatory therapies use substances triggering an allergic reaction which leads to a decrease in the CD4 to CD8 cell ratio, and induce suppressor lymphocytes. An example of a substance producing such an effect is diphenylcyclopropenone (DPCP)[30]. DPCP solution is applied to patches of hair loss once a week, in gradually increasing concentrations, until a mild inflammation develops[44], manifesting as erythema or pruritus[51]. Adverse effects associated with this therapy include cervical or occipital lymphadenopathy, urticaria and pigmentation disorders[44]. Other substances triggering an allergic reaction are, for example, dinitrochlorobenzene (DNCB) solution or squaric acid dibutyl ester (SADBE)[47].

Another option available for the treatment of AA is intravenous or oral glucocorticosteroid therapy. The therapeutic efficacy of glucocorticosteroids is greater in patients with shorter disease duration and lower severity of hair loss[52]. Glucocorticosteroids can also be given by injection to affected skin areas[44,53]. One example of glucocorticosteroids used in injectable form is triamcinolone[4].

Other therapeutic modalities include anthralins, immunosuppressive drugs, phototherapy or biologics[16]. The main immunosuppressive drug used in AA therapy is cyclosporin, however, treatment with this drug may be associated with the risk of adverse effects such as nephrotoxicity, hypertrichosis, or hypertension[50]. It needs to be considered that immunosuppressive therapy does not eliminate relapses, while immunosuppressive drugs may produce significant complications[54].

Less commonly used pharmacotherapeutic agents include azathioprine, methotrexate, sulfasalazine and biologic drugs[2]. Some medical centres also use phototherapy with concurrent topical psoralen treatment[55], and McElwee et al. report that therapeutic benefits can also be achieved with antihistamines[56]. Another drug proposed by some authors is minoxidil, an agent extending the duration of the anagen phase[19].

Cognitive behavioural psychotherapy can also be used as adjunctive treatment. The benefits of this modality are associated with the pathogenesis of AA, i.e. the contributory effect of stress, anxiety and depressive disorders, as well as the prevalence of impaired well-being in patients with the disease. Hair regrowth can be additionally stimulated by the use of antidepressant therapy[57].

## CONCLUSIONS

Alopecia areata has been increasingly addressed in the literature in view of the marked prevalence of this condition. There are no established treatment regimens for AA, though in the majority of cases hair regrows spontaneously, without therapy. On the other hand, it needs to be noted that AA typically has a relapsing and remitting course. Another aspect to consider is that the disorder may lead to impairment of the quality of life. Consequently, some patients may require adjunctive psychotherapy or pharmacological treatment with antidepressants.

### Conflict of interest

*The authors do not declare any financial or personal links with other persons or organizations that might adversely affect the content of the publication or claim any right to the publication.*

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