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Psoriasis and Alopecia: Unveiling the Links

Mohammad Reza Pourani[1*], Yasaman Khajeamiri[2*], Fahimeh Abdollahimajd[3,4,5], Omid Zargari[1]

1 Skin Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2 School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3 Clinical Research Development Unit of Shohada-e Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
4 Department of Dermatology, Shohada-e Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
5 Research Center of Artificial Intelligence in Health, Shohada-e Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
* These authors contributed equally to this work and are considered as co-first authors.

Key message: Psoriasis and alopecia are related through several pathways, which can be classified as follows: psoriatic alopecia; drug-induced alopecia, especially from TNF-α inhibitors; concomitant psoriasis and alopecia areata.

Key words: Psoriasis, Alopecia, Alopecia areata, Lichen planopilaris, Hair loss

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***Corresponding Author:** Fahimeh Abdollahimajd, Clinical Research Development Unit of Shohada-e Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran; E-mail: fabdollahimajd@yahoo.com; ORCID: 0000-0002-9463-0665

Co-corresponding Author: Omid Zargari, Skin Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran; E-mail: ozargari@gmail.com

ABSTRACT

Introduction: Psoriasis is a chronic inflammatory disease that may lead to scalp involvement, with a significant impact on patients' quality of life. Although most patients with scalp psoriasis do not experience alopecia, alopecia in the context of psoriasis is a multifaceted issue on which studies are limited.

Objectives: The purpose of this review was to investigate different types of alopecia in psoriasis and the potential mechanisms.

Methods: A thorough literature review was performed, focusing on the relationship between psoriasis and alopecia areata (AA), drug-induced alopecia, and psoriatic alopecia.

Results: Psoriasis and alopecia are related through several pathways. Regarding psoriatic alopecia, in most cases of psoriasis patients with scalp involvement, hair loss is attributed to telogen effluvium. In late-stage lesions, destruction of the hair follicle, perifollicular fibrosis, and free bare hair shafts in the dermis are revealed. However, hair loss in psoriasis is almost always non-scarring and reversible. In drug-induced alopecia, both conventional systemic treatments and biologics may cause hair loss in psoriatic patients. Specific side effects have been reported with TNF-α inhibitors and IL-17 blockers. TNF-α inhibitors may cause several types of alopecia: i) TNF-α inhibitor-associated psoriatic

alopecia, ii) TNF-α inhibitor-associated AA, and iii) TNF-α inhibitor-associated lichen planopilaris. In concomitant psoriasis and alopecia areata, there is strong and convincing evidence that patients with psoriasis are at increased risk of developing AA, suggesting a complex interplay of autoimmune mechanisms.

Conclusion: Understanding the types and causes of alopecia in patients with psoriasis is crucial to proper management, thus highlighting the need for more research.

Introduction

Psoriasis is one of the most common inflammatory cutaneous diseases, affecting around 2% of the population. Scalp is a common site of involvement in psoriasis, with a frequency of 50–80%. Classic scalp psoriasis typically presents as well-defined erythematous lesions which are covered with silvery scales; in severe cases, the entire of the scalp may be involved [1, 2].

While the majority of patients with scalp psoriasis do not experience alopecia, hair loss is one of their main concerns and can occur due to different causes. The relationship between psoriasis and alopecia has not been fully investigated. Alopecia may be related to the psoriasis itself, the treatment modalities, or to related autoimmune conditions. In this review, we aimed to investigate the association between psoriasis and alopecia and to discuss the possible causes of hair loss in patients with psoriasis.

Psoriasis and alopecia are related in different ways, which can be classified as: i) psoriatic alopecia; ii) drug-induced alopecia; iii) concomitant psoriasis and AA.

Psoriatic Alopecia

The true frequency of hair loss directly related to psoriasis is unknown and appears to be uncommon [3]. Alopecia and other hair abnormalities in patients with psoriasis were first reported about 50 years ago; however, psoriatic alopecia is still a little-known condition [3, 4]. In psoriasis patients with scalp involvement, hair loss is a common complaint, but telogen effluvium is believed to be the cause in most cases due to the inflammatory process and trauma from scratching itchy lesions [4, 5]. Histological findings of psoriatic alopecia have shown features of psoriasis in the interfollicular epithelium, with perifollicular inflammation and atrophy or loss of sebaceous glands [3, 5, 6]. Also, in late-stage lesions, destruction of the hair follicle, perifollicular fibrosis, and free bare hair shafts in the dermis are revealed [7, 8] (Figure 1).

The main cause of hair loss in psoriasis is telogen effluvium (TE), which can be both localized or generalized. The localized telogen effluvium is more common in psoriasis. In fact, in involved areas of the scalp, there is a higher proportion of telogen and catagen hairs, which is responsible for a localized telogen effluvium in some patients [6]. Also, generalized TE is a well-known consequence of severe forms of psoriasis, including erythrodermic psoriasis and generalized pustular psoriasis [6]. As mentioned, hair loss in psoriasis is almost always non-scarring and reversible. However, there are several reports of scarring alopecia in psoriatic patients such as the first case of "destructive alopecia" described by Shuster in 1972 [9].

One of the largest case series of alopecia among psoriatic patients was reported by Runne and Kroneisen-Wiersma in 1992. They described 47 patients with acute and chronic hair loss in patients with scalp psoriasis, in which five patients had clinical and histopathological features of scarring alopecia [5]. The severity and duration of scalp involvement in psoriasis is correlated with the risk of scarring alopecia [10]. Remarkably, familial cases of scarring alopecia in psoriatic patients have also been reported [11].

Drug-Induced Alopecia

Both conventional and biological therapies may lead to hair loss in psoriatic patients. Hair loss is a well-known adverse effect of some drugs, including methotrexate and systemic retinoids. Over the past decades, biologics have revolutionized the treatments of psoriasis. Although hair loss due to biologics seems to be less common in comparison with conventional treatments, it is not very rare. Indeed, alopecia secondary to biologics has been reported with both TNF-α antagonists and IL-17 blockers [12, 13]. TNF-α inhibitor may cause different types of alopecia: i) TNF-α inhibitor-associated psoriatic alopecia (TiAPA), ii) TNF-α inhibitor-associated AA (TiAAA), and iii) TNF-α inhibitor-associated LP (TiALP).

TNF-α Inhibitor-Associated Psoriatic Alopecia (TiAPA)

The overall success rate of TNF-α inhibitors (TNFi) in many individuals is remarkable, but some side effects such as increased risk of infection and paradoxical induction of psoriasiform skin lesions have been increasingly reported over the past few years [14]. TiAPA has been reported in several studies. In a review done by Baniel et al., they described six new cases of scarring alopecia following treatment with

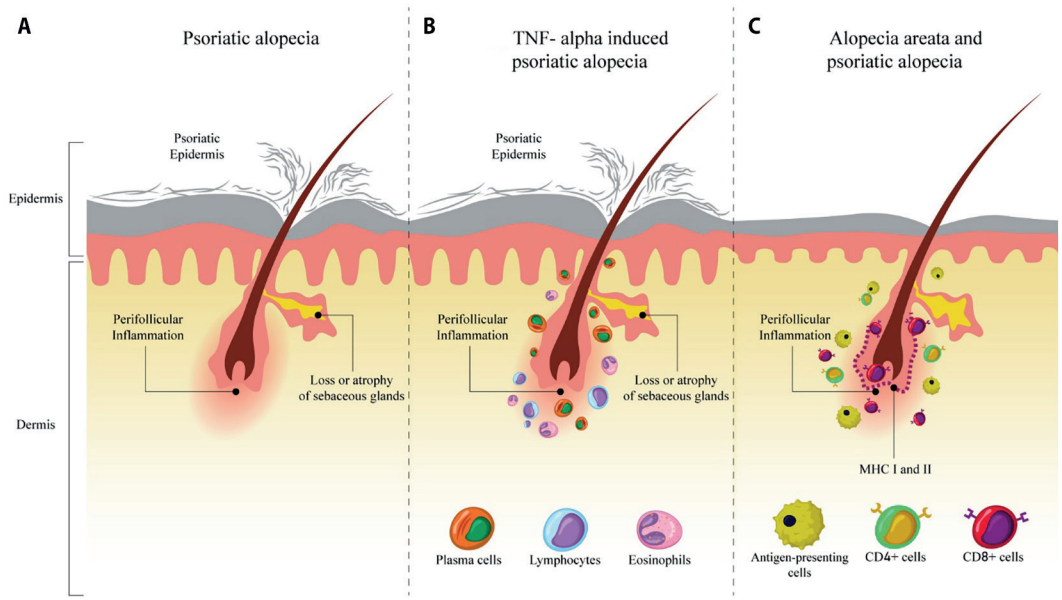

Figure 1. (A) Psoriatic alopecia. Histological findings are features of psoriasis in the interfollicular epithelium, with perifollicular inflammation and atrophy or loss of sebaceous glands. (B) Psoriatic alopecia induced by TNF-α inhibitors, atrophy of sebaceous lobules, and a brisk superficial and deep perifollicular infiltrate consisting of peribulbar lymphocytes, prominent plasma cells, and variable eosinophils; (C) Alopecia areata and psoriatic alopecia, perifollicular infiltrations of APCs, CD4+ and CD8+ T cells. APCs, antigen-presenting cells.

TNF-α blockers [15]. The authors suggest a prompt histological evaluation of alopecia in psoriatic patients and discontinuing the TNFi therapy in the presence of scarring [15]. The proposed clinical diagnostic criteria for TiAPA include recent initiation of TNFi therapy, no previous history of psoriasis, flare-up of psoriasis after initiation of TNFi therapy, alopecic plaques on the scalp, and erythematous, scaly plaques with or without pustular lesions on the scalp and other parts of the body [16, 17].

Histologically, psoriatic alopecia induced by TNF-α inhibitors has two distinctive features: atrophy of sebaceous lobules, which is a potentially reversible characteristic and conspicuous feature of TiAPA, and a brisk superficial and deep perifollicular infiltrate consisting of peribulbar lymphocytes, prominent plasma cells, and variable eosinophils [12] (Figure 1).

Although there is no guideline for the treatment of TiAPA, most cases sufficiently respond to topical steroids [16]. In general, several therapeutic options, including discontinuation of TNFi therapy, switching to a different TNFi, and medication dose adjustment, can be considered depending on the disease severity, underlying disease, and risk-benefit ratio of therapy modification [16-18].

TNF-α Inhibitor-Associated AA (TiAAA)

Alopecia areata (AA) is a non-scarring pattern of hair loss with well-circumscribed patchy areas that frequently appear on the scalp. Although AA can occur as a coincidence in patients receiving TNF-α inhibitors, it seems that there is a causal effect in at least some patients [19, 20]. The exact incidence of AA during anti-TNF-α therapy is unknown because there are no prospective controlled studies. Furthermore, the exact diagnosis of the cause of AA is debatable because AA may occur as an autoimmune manifestation in predisposed patients with chronic inflammation or as a side effect of TNF-α inhibitors. The cases of AA following treatment with TNF-α inhibitors has been reported with all of the TNF-α blockers. In a recent systematic review, the most common etiology of drug-induced AA was TNF-α inhibitors (47%), including adalimumab (18.6%), infliximab (14.7%), etanercept (11.7%), and golimumab (1.9%) [21]. The possible mechanism of TiAAA is that by increasing plasmacytoid dendritic cell production of interferon-α, the expression of the ligands CXCL9, CXCL10, and CXCL11 leading to AA will increase [18-20].

In a multicenter study, of the 29 cases with AA, 11, 11, and seven patients had psoriasis, inflammatory rheumatism, and inflammatory bowel disease, respectively. Moreover, the most common clinical presentation of cases was patchy AA affecting the scalp or beard (79% of patients). In addition to AA, vitiligo, psoriasiform eruptions, or Hashimoto's thyroiditis were observed in 24% of patients [19]. Clinical presentations of alopecia areata during anti-TNF-α therapy can vary widely, from mild limited patches to diffuse alopecia areata. Meanwhile, the onset of AA can range from one to 42 months after the initiation of TNF-α inhibitors [22].

To date, no valid clinical trial has been conducted to investigate the optimal treatment options for alopecia areata

occurring during anti-TNF-α therapy. Most patients achieved complete hair regrowth after discontinuing anti-TNF-α therapy, while some patients continued on TNF-α inhibitor therapy and still experienced some hair regrowth [19]. There are currently no accepted guidelines that indicate whether a TNF-α inhibitor should be discontinued or not in these patients, and this should be evaluated on a case-by-case basis.

TNF-α Inhibitor-Associated LP (TiALP)

Lichenoid drug reactions are a well-established adverse reaction to TNF-α inhibitors, while the reported cases of TNF-α inhibitor-induced lichen planopilaris are rare [23]. One of the first case of lichen planopilaris (LPP) secondary to anti-TNF-α therapy was reported by Garcovich in 2008 [24]. Moreover, Asarch et al. presented two cases of LP-like eruptions after infliximab and adalimumab therapy for psoriasis [23]. Since then, several similar cases with different TNF-α blockers have been reported. Some studies suggest that TNF-α inhibitors can stimulate a wide range of inflammatory diseases, including cutaneous and mucosal LP. The exact mechanism for the induction of inflammatory skin disease such as LPP during TNF-α inhibitor therapy is unknown. IFN-α increases following inhibition of TNF-α, leading to the activation of T cells and dendritic cells. It is suggested that dendritic cells, T cells, and other related factors such as T-cell mediated pathways and inflammatory cytokines, including IFN-α, play a crucial role in the occurrence of LP [25].

The onset of lichenoid reactions can vary, from a few weeks to months after the start of the responsible agent, although most cases are reported in the first two months of treatment [23]. The decision on discontinuation of TNF-α blocking agents depends on the condition of the patient.

Concomitant Psoriasis and AA

Several studies have shown that there is a greater risk of developing a variety of autoimmune diseases in psoriatic patients [26, 27]. Considering psoriasis as an autoimmune disease, several biochemical pathways may overlap with altered pathways associated with other autoimmune diseases such as Crohn's disease, type 1 diabetes, and rheumatoid arthritis [27]. The frequency of immune-related conditions is higher among patients with psoriasis than in the general population, and many inflammatory autoimmune diseases are the result of a disruption of multiple cytokine pathways [27]. Moreover, psoriasis may be associated with other immune-related conditions such as systemic lupus erythematosus, multiple sclerosis, inflammatory bowel disease, including Crohn's disease, celiac disease, autoimmune thyroid disease, vitiligo, Sjögren's syndrome, and alopecia areata [28,29]. There is strong and convincing evidence that patients with psoriasis have a higher risk of developing AA [30]. However, as mentioned above, many reports of AA were in psoriatic patients undergoing systemic treatments [19]. In a retrospective study by Wu, patients with psoriasis were at a 2.5 times higher risk of developing alopecia areata [26]. In a recent meta-analysis, the pooled prevalence and odds ratio of alopecia areata among psoriatic patients were 0.5% and 2.71, respectively. Furthermore, the pooled prevalence and odds ratio of psoriasis among patients with alopecia areata were 2.5% and 3.52, respectively [31]. Interestingly, there is a bidirectional association between psoriasis and alopecia areata [31]. Furthermore, the prevalence of psoriasis incidents in AA patients was 1.8%, with an odds ratio (OR) of 1.79 [32]. Additionally, the association between psoriasis and AA was significantly increased, with OR 2.4; however, psoriatic arthritis was not associated with AA [26].

In addition, an interesting case of the Renbök phenomenon or inverse Köbner phenomenon was reported in a female with a history of long-lasting AA who presented with new psoriasis lesions. In AA areas with psoriasis, complete regrowth of hairs was observed [33]. Furthermore, another case of the Renbök phenomenon was reported in a female with presentation of both AA and psoriasis, with a regression of psoriatic scalp lesion following the appearance of AA lesion in the same area. Also, normal regrowth of hairs was noticed in an alopecic area with new lesions of psoriasis [34].

The complex cytokine milieu plays an important role in the flare-up of psoriasis and AA. The correlation between these two diseases is plausible as psoriasis is related to a class of factors such as Th17 and Th1 pathway cytokines, including interferon-λ, interleukin (IL)-12, and IL-2, which are also important in the pathogenesis of AA [35, 36] (Figure 1). Furthermore, AA worsening after successful treatment of psoriasis in patients with concomitant AA has been reported [37].

Thus, treatment regimens for these patients are complex as they involve preventing the worsening of one inflammatory condition while treating another [38]. In addition, according to the findings of a nationwide population-based study conducted by Chu et al., the age at onset of AA provides clues for the diagnosis of specific autoimmune diseases and can be used for timely diagnosis and treatment [37].

Conclusion

Hair loss in psoriatic patients can be related to various causes. Most patients with psoriatic alopecia experience complete regrowth of scalp hair after successful treatment, although there are a few reports of scarring alopecia secondary to psoriasis. TNF-α inhibitors can induce psoriatic alopecia (TiAPA), alopecia areata (TiAAA), and lichen planopilaris (TiALP). All dermatologists should know the possible complications following the administration of TNF inhibitors. Understanding the type and cause of alopecia in patients with psoriasis is essential to the proper management

of this condition. Given the limited information in this area, more studies are needed to understand the association between psoriasis and alopecia.

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