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CASE REPORT

Tumor Necrosis Factor-Alpha Inhibitor-Associated Psoriatic Alopecia in a Patient with Ulcerative Colitis: A Case Report and Review of the Literature

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Paradoxical reactions in patients treated with tumor necrosis factor-alpha inhibitors (TNFis) have an estimated prevalence of 1.5% to 5%. Such reactions usually present as psoriasiform eruptions on the trunk and extremities along with palmar and flexural involvement. When affecting the scalp, new-onset psoriasis induced by TNFi can result in non-scarring or scarring alopecia. Although the paradoxical reaction was first reported in 2003, this TNFi-associated psoriatic alopecia (TiAPA) has been recently reported with increasing frequency. This condition is characteristically reversible and requires clinical and histopathological identification from other diseases for proper treatment. The cessation of TNFi therapy may not be mandatory, and decision to continue TNFi therapy depends on the severity of TiAPA and the risk-benefit ratio of treatment modification on the underlying disease. Herein, we report a case of TiAPA in a patient with inflammatory bowel disease whose alopecia improved following suspension of TNFi. We also describe the clinical and histopathological diagnostic criteria based on review of the literature. **(Ann Dermatol 33(1) 82～85, 2021)**

-Keywords-
Alopecia, Psoriasis, Tumor necrosis factor-alpha

INTRODUCTION

Tumor necrosis factor-alpha inhibitors (TNFis) have been used to successfully treat numerous autoimmune and chronic inflammatory conditions[1]. With the increasing use of TNFis, a wide array of adverse reactions is emerging. One of the most intriguing adverse reactions is *de novo* psoriasiform eruptions. Although this paradoxical reaction was first reported in 2003, TNFi-associated psoriatic alopecia (TiAPA) has been recently reported with increasing frequency. Nevertheless, TiAPA has not been reported in Asia, and this may be due to the lower incidence and prevalence of ulcerative colitis (UC) in Asia than in Western countries[2]. However, since they have rapidly increased over the past decades, reports of TiAPA are expected to increase. We summarize the clinical and histological features of TiAPA, present the first case of TiAPA in Korea, and review the literature.

CASE REPORT

A 38-year-old male with UC abruptly developed shedding of hair from his scalp along with lightly-scaly psoriasiform patches. Dermoscopic findings showed background erythema with red dots and twisted red loops. In addition, similar psoriasiform patches were present on his bearded facial area (Fig. 1). The patient had been on adalimumab therapy for about two years, and his cutaneous symptoms started two weeks prior to presentation. He denied personal or family history of psoriasis or alopecia.

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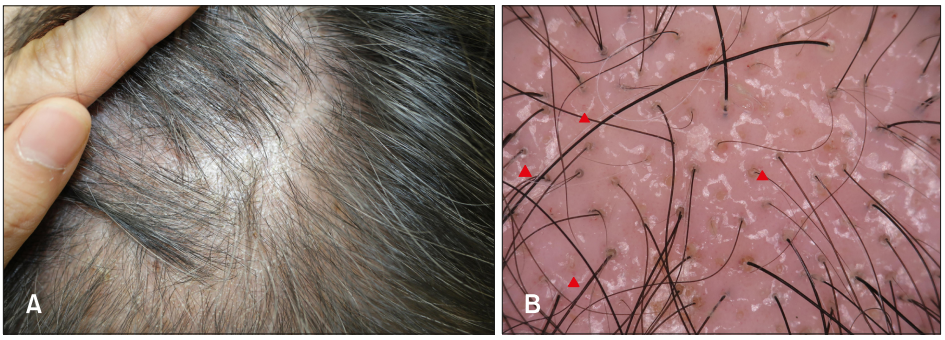

Fig. 1. (A) Scaly erythematous psoriasiform patches on the face and scalp with decreased hair density. (B) Dermoscopic findings from the scalp lesions showed background erythema and scale with red dots and twisted red loops (arrowheads) (non-polarized ×7.5).

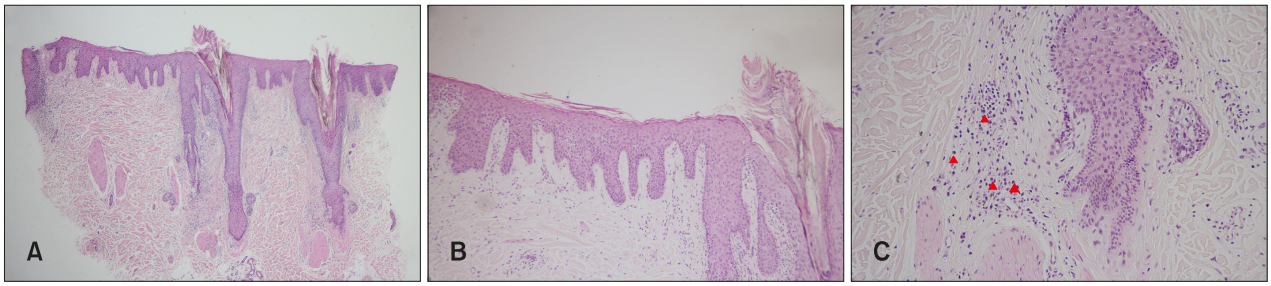

Fig. 2. The scalp biopsy showed psoriasiform epidermal hyperplasia, miniaturized hair, and perifollicular lymphocytic and plasmacyte infiltrations (arrowheads) on vertical sections (A: H&E, ×40; B: H&E, ×100; C: H&E, ×200).

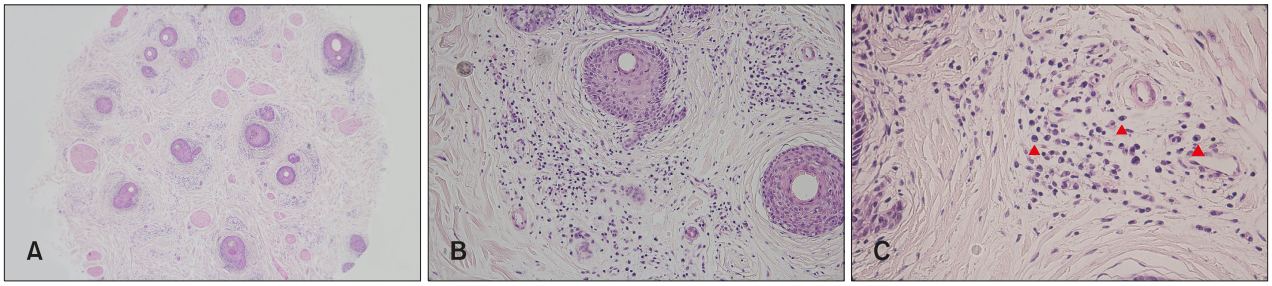

Fig. 3. The scalp biopsy showed miniaturized hair follicles, atrophy of sebaceous glands, and perifollicular lymphocytic and plasmacyte infiltrations (arrowheads) on the horizontal section (A: H&E, ×40; B: H&E, ×200; C: H&E, ×400).

The biopsy specimen from the lesion showed epidermal hyperplasia with parakeratosis, decreased granular layer, perifollicular lymphoplasmacytic infiltration, miniaturized hairs, and atrophy of sebaceous glands in both the vertical and horizontal sections (Fig. 2, 3). After considering the combination of history, temporal association of hair loss with use of TNFi, hair shedding with psoriatic eruptions, and the histopathologic findings, we diagnosed TiAPA. Given the patient's well-controlled UC symptoms but progressive TiAPA, adalimumab was stopped, and mesalazine was introduced to maintain treatment. Approximately two weeks later, the psoriatic skin lesions were improved, and the degree of improvement of hair loss continues under observation (Fig. 4).

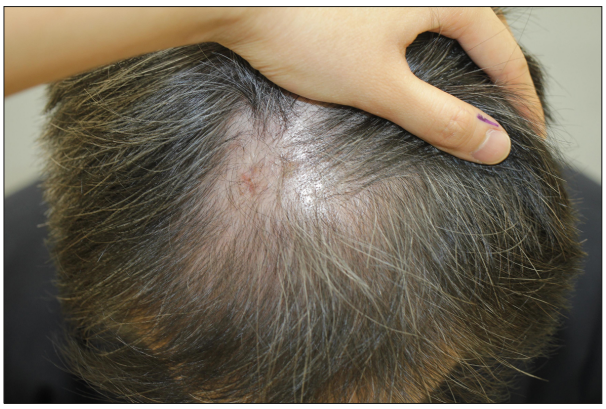

Fig. 4. Two weeks after discontinuation of the tumor necrosis factor-alpha inhibitor, the psoriatic skin lesions improved, and the degree of improvement of hair loss continues under observation.

DISCUSSION

Psoriasiform eruption during TNFi therapy has an estimated prevalence of 1.5% to 5% and usually presents as chronic plaque or guttate, pustular psoriasis, or palmoplantar psoriasis[3]. Although the pathophysiology of this paradoxical side effect is not fully understood, two mechanisms have been proposed. In the first, TNF-α blockade increases interferon-α production by plasmacytoid dendritic cells, resulting in activation and amplification of pathogenic T-cells. In the second mechanism, TNF-α blockade induces a Th17 immune response and down-regulation of Treg cells[4]. Although psoriasiform skin eruption secondary to TNFis is well known, TiAPA has been increasingly reported. TiAPA usually presents as a psoriatic plaque on the scalp, but it may be associated with simultaneous psoriasiform eruptions on the trunk and extremities. TiAPA may also show clinical and histologic features of idiopathic psoriatic alopecia (iPA) or combined psoriasiform and AA-like features. Recently, efforts have been made to distinguish TiAPA as a single disease entity.

The clinical diagnostic criteria for TiAPA proposed by Doyle et al.[5] are as follows: (1) recent initiation of TNFi, (2) no prior history of psoriasis, (3) flare of psoriasis after starting TNFi, (4) alopecic plaque(s) on the scalp, and (5) often, erythematous, scaly patches and/or pustular lesions on the scalp and elsewhere. However, we suggest a change in these clinical criteria. The first clinical criterion (recent initiation of TNFi) is not necessary because there have been some controversies on the latency period between initiation of drug and occurrence of symptoms. The latency time varies widely, suggesting that an environmental trigger may also be involved[6]. The median time from TNFi to psoriatic eruption observed in one report was 12 months for adalimumab and 17 months for infliximab varying over several months to years[7].

The histologic features of TiAPA, described by Afanasiev et al.[8], are as follows: (1) psoriasiform changes of the epidermis, (2) increased ratio of catagen/telogen phase follicles, (3) miniaturization of follicles, (4) atrophy or loss of sebaceous glands, (5) peribulbar lymphocytic infiltrate, (6) presence of plasma cells or eosinophils in the inflammatory infiltrate, (7) scarring, and (8) naked hair shaft with granuloma, if present, can be a distinguishing feature from iPA[5,8]. Among these features, atrophy or loss of sebaceous lobules, which is also a common finding in iPA, is the most striking and distinguishing feature of TiAPA from other alopecic diseases[8]. For the pathologist, loss of sebaceous lobules on histology is usually an indicator of scarring alopecia. However, based on hair regrowth after proper management, most cases of TiAPA and iPA have been reported as non-scarring[9]. Nevertheless, undisputed scarring alopecia may occur in both TiAPA and iPA, and at least with iPA, the likelihood of scarring seems to relate to duration of alopecia because the longer-duration diseases are more likely to scar[10]. Therefore, physicians must ensure a fast diagnosis and rapidly initiate appropriate therapy. In the present case, histopathologic examination showed psoriatic epidermal change, AA-like dermal features, and sebaceous gland atrophy. Additionally, plasma cell infiltration was observed. Thus, the clinical and histological data suggested a diagnosis of TiAPA.

Although there is yet to be consensus on the management and treatment of this entity, cessation of TNFi therapy may not be mandatory, as alopecia has showed significant improvement with topical treatment alone[5]. However, some cases will require discontinuation of the TNFi. In this situation, switching to a different TNFi may suffice, although TiAPA may recur and require a different treatment strategy[8]. The decision to continue TNFi therapy depends on the severity of TiAPA and the risk-benefit ratio of treatment modification on the underlying disease. Although topical treatment with moisturizers and steroids was initially attempted in the present case, the patient's symptoms gradually deteriorated, so that treatment modality was replaced considering the stable condition of his underlying disease.

TiAPA is a relatively rare but potentially reversible side effect of TNFi therapy, and it has conspicuous histopathologic findings. Specialists who manage patients treated with TNFis should be aware of this drug-associated complication to ensure faster diagnosis, prevent needless treatments, and rapidly initiate appropriate therapy.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

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