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Research Letter

Management of Immune-Mediated Alopecia With Tumor Necrosis Factor Alpha Inhibitors: A Report of 4 Cases

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To the Editor,

Tumor necrosis factor-α (TNF-α) inhibitors are used to treat multiple inflammatory diseases. Although these agents generally exhibit a favorable safety profile, autoimmune diseases and paradoxical immune-mediated reactions have been reported in association with their use,[1] including psoriasis, lichen planus, systemic or cutaneous lupus erythematosus, and hidradenitis suppurativa, among others.[2] These reactions may also present as alopecia, with possible psoriasiform, lupus-like, or alopecia areata-like histologic patterns.[3] Among TNF-α inhibitors, infliximab and adalimumab are the agents most frequently associated with these adverse events.[2]

We describe 4 women who developed alopecia after receiving anti-TNF-α therapy (Fig. 1, Table 1). All underwent scalp biopsy, which demonstrated either a lupus-like or psoriasiform pattern; in one case, scarring features were present. These findings were interpreted as immune-mediated alopecias, prompting discontinuation of TNF-α inhibitors and initiation of JAK-inhibitor therapy. Three months into therapy, complete regrowth of alopecic patches was achieved, along with optimal control of the underlying disease that had led to TNF-α inhibitor initiation. The validated DAS28 and BASDAI scales were used to quantify response in rheumatoid arthritis and psoriatic spondyloarthropathy, respectively.[4]

TNF-α inhibitors are known to induce paradoxical psoriasis and drug-induced lupus, which may manifest clinically as alopecia. Several cases have been published, some treated with topical agents with limited response. Other therapeutic strategies have included switching to a different TNF-α inhibitor less commonly associated with alopecia, such as certolizumab.[5] In other cases, selection of a new therapeutic target has been pursued to control the underlying disease—for example, ustekinumab in patients with Crohn disease.[6]

In our patients, treatment was switched to JAK inhibitors, which have been described in the management of cutaneous signs of lupus,[7] although not specifically for anti-TNF-α-induced lupus. Upadacitinib,

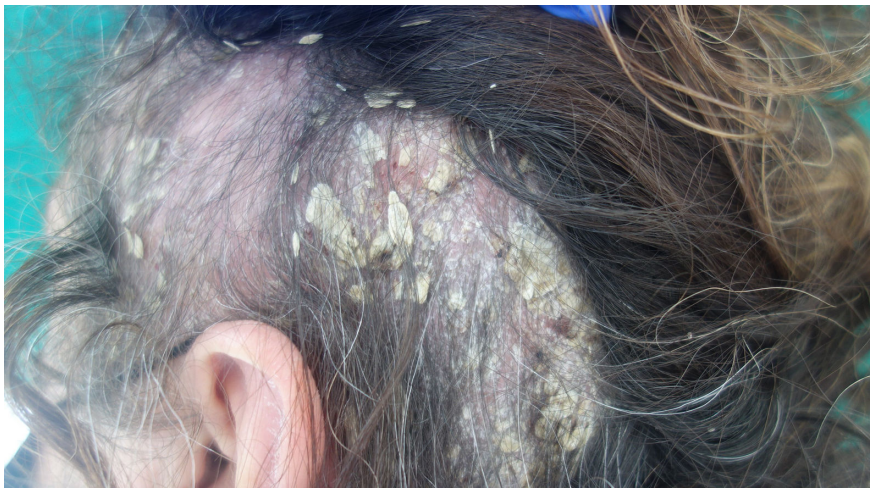

Fig. 1. Scarring alopecic plaque on the left temporal region, presenting with a pseudotinea amiantacea appearance.

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Table 1
Summary of the 4 cases and their management.

	Case #1	Case #2	Case #3	Case #4
Age (years)	57	53	50	65
Sex	Female	Female	Female	Female
Underlying condition	Rheumatoid arthritis	Crohn disease and psoriatic spondyloarthropathy	Rheumatoid arthritis	Rheumatoid arthritis
Personal history of psoriasis	No	Yes	Yes	No
Anti-TNF-α therapy	Adalimumab 40 mg every 14 days	Infliximab 5 mg every 8 weeks	Adalimumab 40 mg every 14 days	Adalimumab 40 mg every 14 days
Time from start of anti-TNF-α therapy to onset of alopecia	2 months after starting biosimilar	9 months	21 months	24 months
Clinical findings	Bilateral parietal erythema, scaling, exudation, and decreased hair density	Alopecic plaques with erythema and scaling resembling pseudotinea in bilateral parietal regions (Figure 1)	Diffuse scarring-pattern alopecia	2 alopecic plaques in the frontal and occipital regions with erythema, follicular scaling, and absence of follicular openings
Histology	Parakeratosis, neutrophilic exudate in the stratum corneum, periadnexal plasmacytic–lymphocytic infiltrate	Mild spongiosis, focal basal vacuolization, periadnexal and perivascular infiltrate	Perifollicular fibrosis, follicles lacking sebaceous glands, perivascular inflammatory infiltrate	Spongiosis, basal vacuolization, periadnexal and perivascular lymphohistiocytic infiltrate
Histologic subtype of alopecia	Psoriasiform	Lupus-like	Lupus-like with scarring changes	Lupus-like
Need for change of agent	Yes	Yes	Yes	Yes
Anti-JAK therapy	Upadacitinib 15 mg daily	Upadacitinib 15 mg daily	Tofacitinib 5 mg every 12 hours	Baricitinib 4 mg daily
Hair regrowth at 90 days	Yes	Yes	Yes	Yes
Control of underlying disease at 90 days	Disease remission (DAS-28 2.16)	Good response (BASDAI 1.8)	Low disease activity (DAS-28 2.67)	Low disease activity (DAS-28 2.89)

tofacitinib, and baricitinib were used depending on the underlying disease and comorbidities.[8]

All patients experienced regrowth of alopecic plaques, regardless of histologic pattern, including the patient with biopsy-proven scarring and fibrosis.

We believe this favorable outcome was due primarily to early initiation of therapy; however, it may also reflect the antifibrotic properties of JAK inhibitors, which could contribute to reversing follicular fibrosis. This mechanism may explain the regrowth observed even in the case with scarring alopecia on histology.

This hypothesis is supported by the use of JAK inhibitors in conditions with prominent fibrosis, such as ruxolitinib for myelofibrosis.[9]

An experimental study published in 2020 further demonstrated that JAK inhibitors modulate activation of profibrotic M2 macrophages, particularly those with activity vs JAK2.[10]

In summary, in our series, early discontinuation of the offending drug followed by initiation of JAK inhibitors was associated with robust regrowth—even in cases of scarring alopecia—as well as good control of the underlying rheumatologic disease that had originally led to TNF-α inhibitor therapy. If confirmed in additional cases, JAK inhibitors may represent a therapeutic option for immune-mediated alopecias induced by TNF-α inhibitors.

Conflict of interest

The authors declare that they have no conflict of interest.

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