Ixekizumab-induced alopecia areata

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INTRODUCTION

Alopecia areata (AA) is characterized by autoimmune destruction of hair follicles. Psoriasis, another autoimmune inflammatory condition, has been linked with AA. Patients with AA are 2.8 times more likely to have psoriasis than the general population (for comparison, the odds ratios for vitiligo and thyroid disease are 5.2 and 1.9, respectively).[1] AA has additionally been linked with the use of tumor necrosis factor (TNF)-α inhibitors[2] but has not been well established as a side effect of the other biologics commonly used in psoriasis. Here we report on a patient who had AA while receiving ixekizumab for plaque psoriasis and psoriatic arthritis but had hair regrowth after medication discontinuation.

Abbreviations used:

AA: alopecia areata
IL: interleukin
TNF: tumor necrosis factor

CASE REPORT

A 70-year-old white man presented with a 9-year history of plaque psoriasis mostly affecting his back and buttocks. His medical history also included factor XI deficiency, hypothyroidism, and coronary artery disease. He previously tried etanercept and ustekinumab with no effect and had an allergic reaction (hand and foot swelling) to adalimumab in the past. He was taking 17.5 mg of methotrexate weekly for psoriatic arthritis and using triamcinolone 0.1% cream 3 times a week for his skin. His other medications, which did not change throughout his treatment, included atorvastatin, duloxetine, isosorbide mononitrate, metoprolol, omeprazole, and levothyroxine. To achieve better control of his skin and joint symptoms, he was started on ixekizumab in August, 2016, and his methotrexate was tapered and eventually discontinued 7 months later. His plaque psoriasis and arthritis cleared, but after 13 months of ixekizumab, he had hair loss (Fig 1). Clinical examination found elongated patches of alopecia, prompting biopsy to determine the etiology of the hair loss. Punch biopsy of the scalp found a normal number of hair follicles with prominent catagen and telogen shift, miniaturized hair follicles, and focal peribulbar inflammation consistent with the diagnosis of AA. His laboratory values were notable for a normal thyroid-stimulating hormone level. Ixekizumab was discontinued after 15 months of total use. Three months after discontinuation, his hair began to grow back, with ultimately a complete recovery.

His psoriatic plaques returned 8 months after ixekizumab discontinuation, so he was started on guselkumab. His psoriasis cleared briefly but worsened again 2 months later, prompting a switch to tildrakizumab, on which his psoriasis cleared. He was on guselkumab for 2 months and at the time of this report has been on tildrakizumab for 4 months with no evidence of AA recurrence.

DISCUSSION

Our patient with plaque psoriasis and psoriatic arthritis on the interleukin (IL)-17A inhibitor ixekizumab had AA, which resolved after discontinuation of the drug. This observation was unexpected, as reports of elevated intralesional and serum IL-17 levels in AA patients have led to the investigation of IL-17A inhibitors as a potential therapy in the disease, although the results to date have not been promising.[3] Although there have not been previous reports of ixekizumab causing AA, there have been 2 reports involving the other IL-17A inhibitors,

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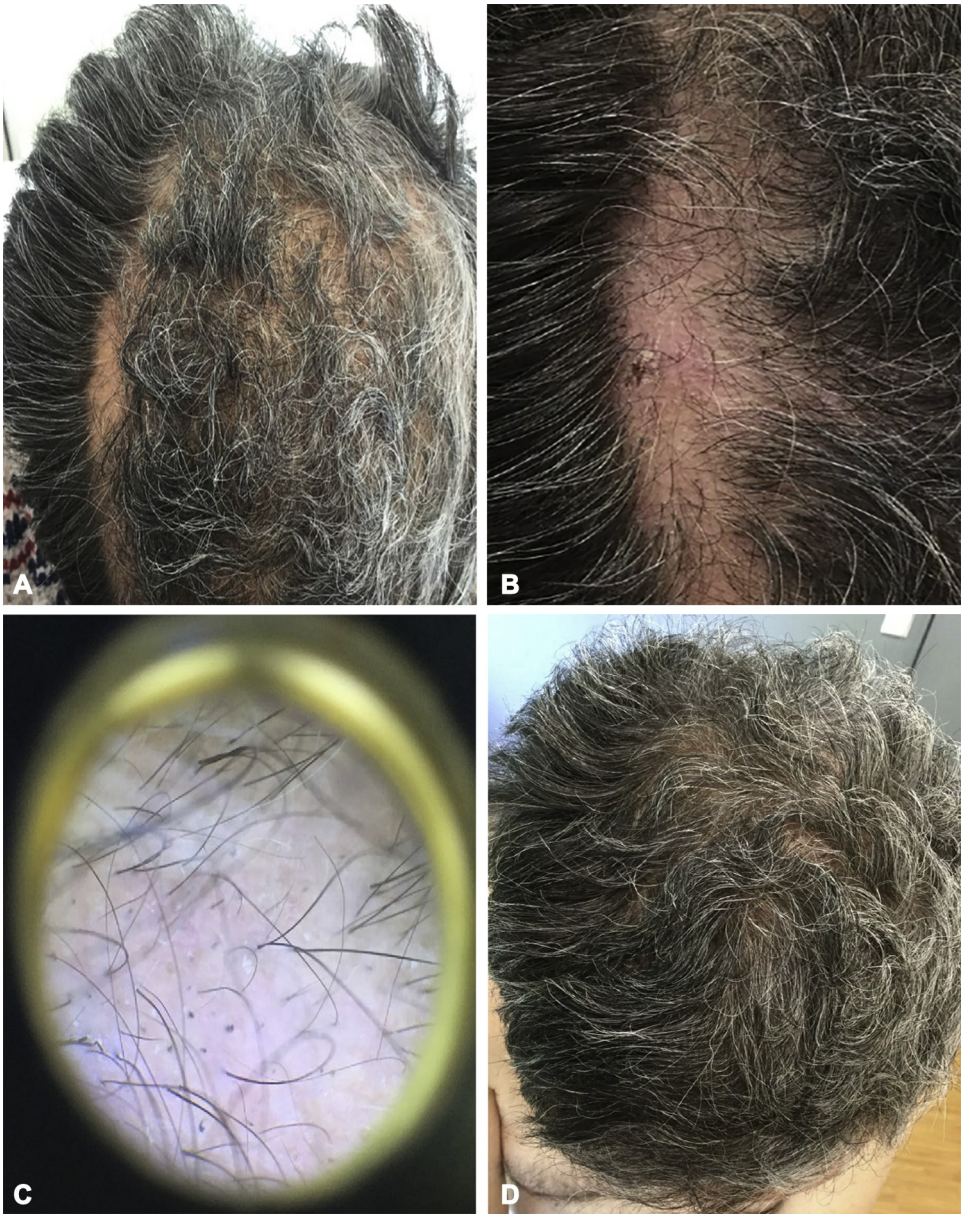

Fig 1. **A** and **B**, Hair loss after 13 months of ixekizumab. **C**, Magnified view of scalp after 13 months of ixekizumab showing "exclamation mark" hairs. **D**, Hair regrowth 3 months after discontinuing ixekizumab.

secukinumab and brodalumab. Apart from TNF-α inhibitors, the only other reports of AA developing in patients on biologics are 3 reports of patients taking ustekinumab for plaque psoriasis. In these reports, however, the patients were not trialed off the drug to observe for hair regrowth, so it is not possible to confirm whether ustekinumab was the direct cause of their hair loss (Table I).[4-6]

Over the course of his treatment, our patient received 2 TNF-α inhibitors, an IL-12/23 inhibitor, and two IL-23 inhibitors and did not experience AA while on any of these medications. It may be possible that he did not take these drugs long enough to experience AA, as he took ixekizumab for 13 months prior to AA development. From the few existing reports, it is difficult to determine the impact of treatment duration on this reaction. However, in at least two previous reports, patients recovered after switching to a different biologic, and in one case the patient recovered after switching to a different drug with the same target (secukinumab to brodalumab). Therefore, it seems that AA induced by biologics may be a drug-specific, rather than a target-specific mechanism. As an increasing number of patients are being

Table I. Cases of AA induced by biologic therapies for plaque psoriasis and psoriatic arthritis (excluding TNF-α inhibitors)

Drug	Target	Treatment duration to onset	Resolution	Study
Brodalumab	IL-17A	2 mo	Switch to ustekinumab	Yajima et al[4]
Secukinumab	IL-17A	24 mo	Switch to brodalumab + 10 mg prednisone	Yajima et al[4]
Ustekinumab	IL-12/23	7 mo	Not reported	Slowinska et al[5]
Ustekinumab	IL-12/23	5 mo	Medication continued; no resolution	Verros et al[6]
Ustekinumab	IL-12/23	10 mo	Medication continued; no resolution	Verros et al[6]
Ixekizumab	IL-17A	13 mo	Switch to guselkumab, then tildrakizumab	Current case

prescribed biologics for psoriasis, arthritis, and other conditions, it is important to understand the molecular basis of how these drugs can cause AA and the factors that put patients at risk for this side effect.

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