Effective use of ustekinumab in a patient with concomitant psoriasis, vitiligo, and alopecia areata

Amal Elkady, MBBCh, Lauren Bonomo, BA, Yasmin Amir, MD, Anjali S. Vekaria, MD, and Emma Guttman-Yassky, MD, PhD
New York, New York

Psoriasis is an immune-mediated disease characterized by formation of well-demarcated plaques with silver scale. Drugs such as cyclosporine and methotrexate can have deleterious side effects; however, biologic immune modifying agents now provide a safer alternative for psoriasis. Ustekinumab, an interleukin (IL) 12/23 inhibitor, is one such agent and is approved by The US Food and Drug Administration for the treatment of moderate to severe chronic plaque psoriasis. Vitiligo is an acquired autoimmune disorder resulting in depigmented patches of skin. Alopecia areata (AA) is another autoimmune disease that results in nonscarring hair loss. Current therapies for both conditions are limited, typically involving topical, intralesional, or systemic steroids.[1] Because these traditional therapies are not sufficiently efficacious, new modalities including laser and biologic agents are being explored.[2]

CASE REPORT

A 39-year-old South Asian woman weighing 94 kg presented to our clinic in February 2016 with a several-year history of moderate generalized plaque psoriasis. In addition to psoriasis, she had a 1-year history of nonsegmental vitiligo of the face, scalp, and neck, and a 2-year history of patchy alopecia of the scalp. Her medical history was significant for asthma and penicillin allergy. She had no associated joint pain or personal history of other autoimmune disorder. Her family history was, however, significant for hypothyroidism. On physical examination, the patient had well-demarcated, erythematous, scaly plaques covering approximately 10% of her body surface area. She was also noted to have 3 well-demarcated, depigmented patches ranging in size from 2 to 4 cm on the face to 5 cm on the back of her scalp. Finally, the patient had significantly decreased hair density with several round patches of nonscarring hair loss ranging from 2 to 4 cm in diameter. These findings were consistent with 3 separate diagnoses: moderate chronic plaque psoriasis, vitiligo, and AA.

In the past, the patient had been treated with etanercept for her psoriasis with no improvement. For her vitiligo, she had received intralesional triamcinolone injections with only minimal improvement. For her AA, she had received intramuscular vitamin B complex injections, also with a poor clinical response. After explaining the benefits and risk, the patient consented to treatment with ustekinumab 90 mg subcutaneous injection, initially administered at 0 and 4 weeks. Subsequent doses were administered every 8 weeks. Dose selection was based on our experience with AA in a published study where 90 mg of ustekinumab every 8 weeks proved effective.[2] Because of a lack of established protocols in the published literature for either condition, we opted for what worked for AA. No other adjuvant medications were used with ustekinumab. The patient showed significant improvement in erythema and scaling of psoriatic lesions by week 8 and complete resolution with body surface area 0% by week 16. In addition to the excellent response seen with her psoriasis, the patient showed impressive improvement in vitiligo and AA lesions of the

From the Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York.

Funding sources: None.

Dr Guttman-Yassky has served on advisory boards for AbbVie, Anaco, Celgene, Demira, Galderma, Glenmark, Leo Pharmaceuticals, Medimmune, Novartis, Pfizer, Regeneron, Sanofi, Stiefel/GlaxoSmithKline, Vitae, Mitsubishi Tanabe, Eli Lilly, Asana Biosciences, Kiowa Kirin, Janssen, and Almirall. The other authors have no conflicts of interest to declare.

Correspondence to: Emma Guttman-Yassky, MD, PhD, Icahn School of Medicine at Mount Sinai, Department of Dermatology, 5 E 98th St, 5th fl, New York, NY 10029. E-mail: emma.guttman@mountsinai.org.

JAAD Case Reports 2017;3:477-9.
2352-5126

http://dx.doi.org/10.1016/j.jdcr.2017.07.009

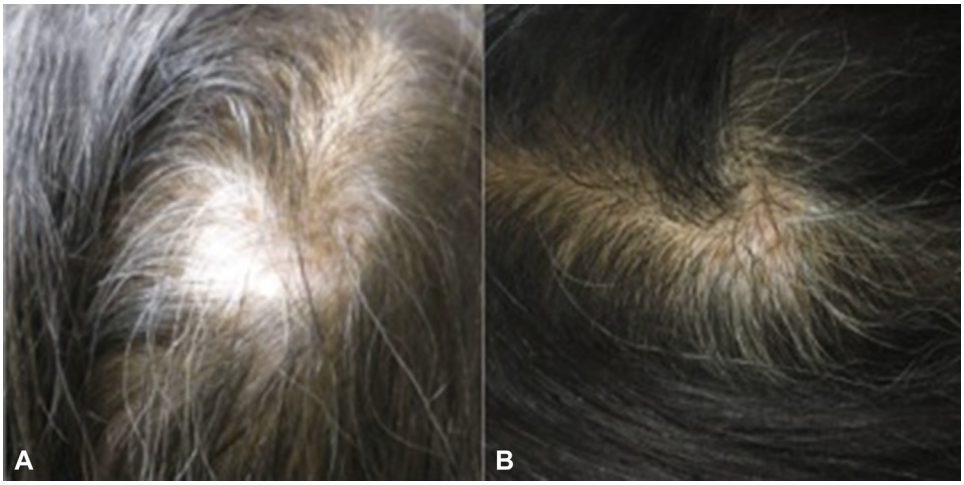

Fig 1. Patient at week 0 of ustekinumab therapy with depigmented macules on the back of scalp (**A**) compared to week 16 (**B**) of ustekinumab therapy with visible repigmentation surrounding the hair follicles.

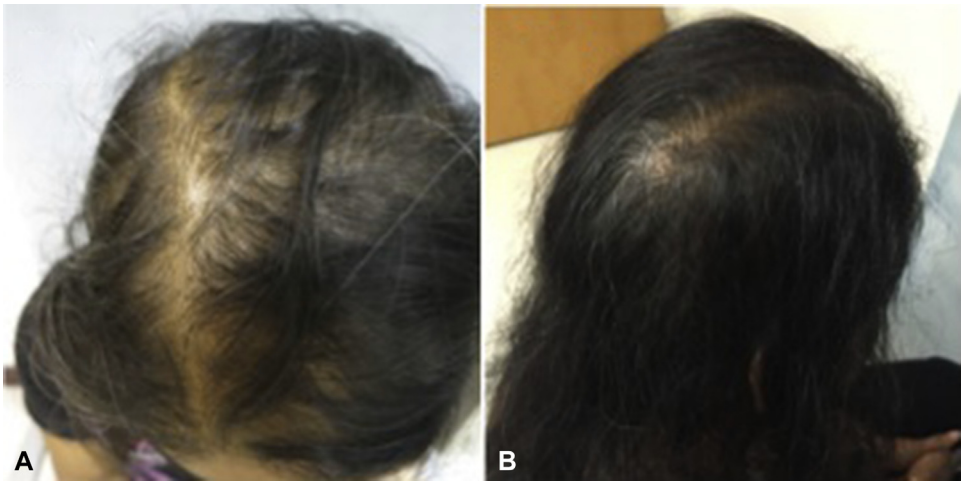

Fig 2. Patient at week 0 of ustekinumab therapy with visible scattered alopecia patches and markedly decreased overall hair density (**A**) compared to week 20 (**B**) of ustekinumab therapy with visible regrowth and increased hair density.

scalp (Fig 1). The vitiligo on her face and neck also improved. At week 20, hair density had visibly increased and repigmented macules were noted around the hair follicles in previously depigmented patches (Fig 2). The patient tolerated ustekinumab without adverse effects, and laboratory monitoring revealed no abnormalities.

DISCUSSION

Over the last few years, the number of therapeutic options for the treatment of plaque psoriasis has increased dramatically. Secondary to discoveries in the immunopathogenesis of the disease, different molecular targets, including tumor necrosis factor—alpha, ILs-12 and -23, IL-17, and others, have paved the way for targeted biologic therapies. On the contrary, vitiligo and AA have seen little success thus far in efficacious therapeutic options. Classically, these 2 entities have been treated with topical, intralesional, or systemic steroids. Recently, however, advances toward the development of biologic therapies for these 2 autoimmune diseases have been made.

The Janus kinase (JAK) pathway has been explored as a potential target for treatment of both vitiligo and AA. In several case reports, 1 open-label study, and 1 retrospective study, JAK inhibitors were shown to be effective for inducing hair regrowth in patients with AA. The efficacy of JAK inhibitors for AA is currently being investigated in clinical trials.

Similarly, JAK inhibitors show promise for the treatment of vitiligo.[3] In a recently published report, a vitiligo patient quickly improved after receiving ruxolitinib, a drug that inhibits JAKs, which are important for immune cell signaling. The patient's facial pigmentation improved from <1% to >50% in just 4 to 5 months.[4]

While the pathogenesis of vitiligo and AA is not straightforward and likely involves a combination of genetic susceptibility and environmental factors, it is evident that proinflammatory cytokines play a role and can perhaps be targeted with the same therapies that have seen great success in psoriasis. The role of IL-23 in the immunopathogenesis of autoimmune disorders is complex. Genomic association studies have shown ILs-12 and -23 to be implicated in the pathway responsible for psoriasis; therefore, the 2 have been targets for drug development. These studies resulted in the discovery of ustekinumab, an IL-12/23 antagonist that has proven to be highly efficacious in treating plaque psoriasis. IL-23 is the cytokine responsible for proliferation and survival of T_H17 cells, which represent an important T-cell subset in autoimmune disease beyond psoriasis. These disorders include Crohn's disease, vitiligo, and AA.[5-7]

As expected, our patient's psoriatic lesions responded dramatically to ustekinumab. However, marked improvement was also noted in her vitiligo and AA. It is the striking increase in hair density and notable repigmentation that suggest IL-12/23 blockade is a promising therapeutic strategy for patients with these autoimmune conditions as well as psoriasis. It should be noted that the complex pathophysiology of these conditions means that ustekinumab may not have such robust response in all patients with vitiligo and AA. Two published studies had conflicting results on ustekinumab effectiveness in vitiligo and AA.[8,9] However, the success seen in this patient with concomitant psoriasis, vitiligo, and AA should prompt consideration of ustekinumab in those for whom vitiligo and AA have proven refractory to other available treatments. Additional prospective studies will be required to determine the long-term safety and efficacy of ustekinumab in these populations.

REFERENCES

1. Park K, Jang WS, Son IP, et al. Combination therapy with cyclosporine and psoralen plus ultraviolet a in the patients with severe alopecia areata: a retrospective study with a self-controlled design. *Ann Dermatol*. 2013;25:12-16.
2. Guttman-Yassky E, Ungar B, Noda S, et al. Extensive alopecia areata is reversed by IL-12/IL-23p40 cytokine antagonism. *J Allergy Clin Immunol*. 2016;137:301-304.
3. Samadi A, Ahmad Nasrollahi S, Hashemi A, Nassiri-Kashani M, Firooz A. Janus kinase (JAK) inhibitors for the treatment of skin and hair disorders: a review of the literature. *J Dermatolog Treat*. 2017:1-11. http://dx.doi.org/10.1080/09546634.2016.1277179 [Epub ahead of print].
4. Harris J, Rashighi M, Nguyen N, et al. Rapid skin repigmentation on oral ruxolitinib in a patient with coexistent vitiligo and alopecia areata (AA). *J Am Acad Dermatol*. 2016;74:370-371.
5. Stockinger B, Veldhoen M. Differentiation and function of Th17 T cells. *Curr Opin Immunol*. 2007;19:281.
6. Blauvelt A. T-helper 17 cells in psoriatic plaques and additional genetic links between IL-23 and psoriasis. *J Invest Dermatol*. 2008;128:1064.
7. Tesmer LA, Lundy SK, Sarkar S, Fox DA. Th17 cells in human disease. *Immunol Rev*. 2008;223:87.
8. Méry-Bossard L, Bagny K, Chaby G, et al. New-onset vitiligo and progression of pre-existing vitiligo during treatment with biological agents in chronic inflammatory disease. *J Eur Acad Dermatol Venerol*. 2017;31:181-186.
9. Slowińska M, Kardynal A, Warszawik O, Czuwara J, Rudnicka L. Alopecia areata developing parallel to improvement of psoriasis during ustekinumab therapy. *J Dermatol Case Rep*. 2010;4:15-17.