Morphea-like lesions after treatment with ustekinumab

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To the Editor:

Ustekinumab is a monoclonal antibody approved by the FDA for the treatment of moderate-to-severe plaque psoriasis. Rarely in psoriasis patients treated with ustekinumab, cases of morphea or localized scleroderma have been reported [1-3]. Herein, we present a patient who received ustekinumab treatment for psoriasis with resolution but exhibited subsequent development of sclerotic nodules consistent with morphea.

A 44-year-old man with a 12-year history of plaque psoriasis and psoriatic arthritis (PsA) and a 7-year history of morphea localized to the skin was referred to dermatology clinic. Three years prior to presentation, the patient received ustekinumab for psoriasis treatment. After 11 months of treatment, his psoriatic lesions resolved; however, subcutaneous nodules with overlying hyperpigmentation on his forearms and a new sclerotic plaque on his left cheek were observed. Biopsy of a sclerotic nodule was consistent with morphea. He was transitioned off ustekinumab and the sclerotic nodules and plaques resolved.

The patient presented to our institution off all systemic medication with worsening joint pain, erythematous plaques with superimposed scale on his hands and right leg, and hyperpigmented indurated plaques on his back and right shoulder (**Figure 1**). Increased sclerosis of the deep dermis and subcutaneous septa with lack of inflammatory infiltrate were observed on internal review of his previous biopsy (**Figure 2**). He was started on deucravacitinib, and, after two months of treatment, his psoriasis clinically improved and his morphea remained stable.

Psoriasis is a disease of the innate and adaptive immune system primarily mediated by proinflammatory cytokines interleukin IL12 and IL23. IL12 and IL23 stimulate naive T cell differentiation

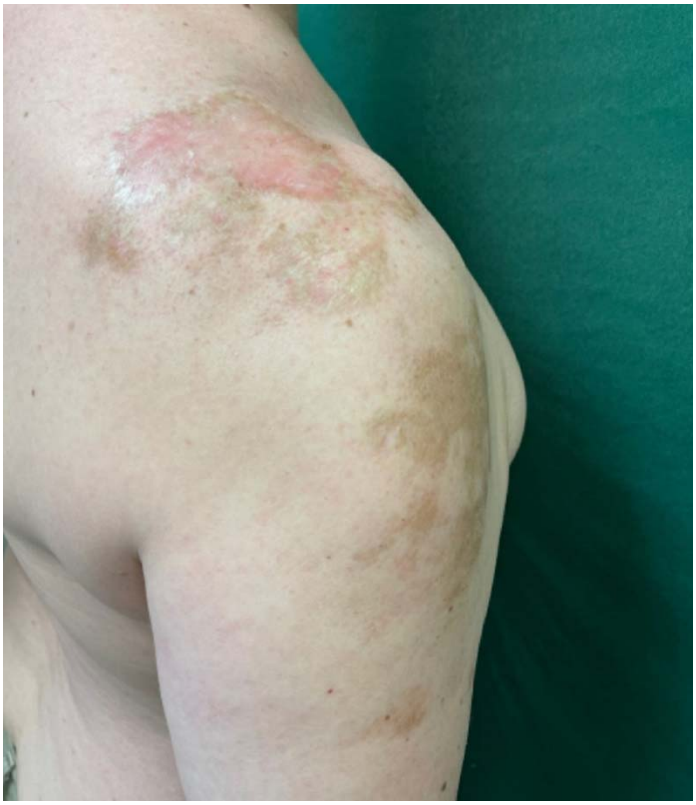

Figure 1. *Hyperpigmented indurated plaques on right shoulder.*

into type 1 T helper cells (Th1) and Th17 cells, respectively. Th1 and Th17 stimulate cells of the immune system to secrete additional inflammatory substances, tumor necrosis factor, and interferon, responsible for psoriatic disease. Treatment ranges from topical corticosteroids and light therapy to immunomodulatory biologics. Ustekinumab is a monoclonal antibody against the p40 subunit shared by both IL12 and IL23 and it is indicated for the treatment of moderate-to-severe psoriasis. Cases of ustekinumab-induced morphea are rare but have occurred in patients with and without history of sclerotic disease [1-3].

Morphea, or localized scleroderma, is a fibrosing autoimmune disease limited to the skin, subcutaneous tissue, and, rarely, the underlying bone. The disease mechanism is not fully known but likely related to the profibrotic activity of Th2 cells [4]. Given the negative feedback loop between Th2 and Th1 cells, ustekinumab-induced morphea may be impacted by suppression of Th1 by ustekinumab, with subsequent increased numbers of Th2 cells [1]. However, patients with both morphea and psoriasis are documented in the literature, and psoriasis is the most common autoimmune disease associated with morphea [4].

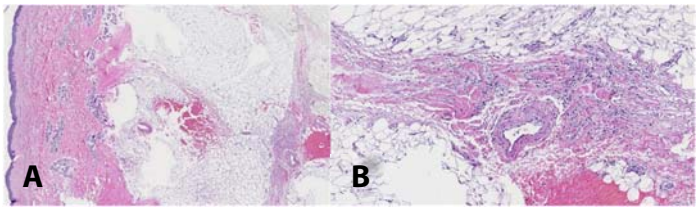

Figure 2. *H&E histopathology.* ***A)*** *Sclerosis of the deep dermis and subcutaneous septa, 2×.* ***B)*** *Thickening of the subcutaneous septa with sclerosis and focal lymphoplasmacytic inflammatory infiltrate, 10×.*

Deucravacitinib is an inhibitor of tyrosine kinase 2, a member of the Janus kinase family. There is a lack of literature on deucravacitinib use in patients with morphea. Although other Janus kinase inhibitors may be beneficial for morphea patients [5], the effects of inhibiting the tyrosine kinase 2 pathway are unclear. A longer therapy window is probably needed to determine our patient's response to deucravacitinib.

The relationship between psoriasis, morphea, and ustekinumab-induced morphea is complex and lack of literature on the interplay of disease may complicate management in patients with comorbid disease. Herein, we present a psoriasis patient with comorbid morphea who developed worsening sclerotic lesions in response to ustekinumab treatment and whose lesions resolved once the medication was stopped. Selecting systemic therapeutics with specific targets may be of benefit in psoriasis patients at risk of comorbid disease.

Potential conflicts of interest

Steve Feldman has received research, speaking and/or consulting support from AbbVie, Accordant, Almirall, Alvotech, Amgen, Arcutis, Arena, Argenx, Biocon, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly and Company, Eurofins, Forte, Galderma, Helsinn, Janssen, Leo Pharma, Micreos, Mylan, Novartis, Ono, Ortho Dermatology, Pfizer, Regeneron, Samsung, Sanofi, Sun Pharma, UCB, Verrica, Voluntis, and vTv Therapeutics. He is founder and part owner of Causa Research and holds stock in Sensal Health. The remaining authors have no conflicts to disclose.

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