Repigmentation in a patient with vitiligo on crisaborole 2% ointment

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INTRODUCTION

Vitiligo is a common condition of autoimmune etiology resulting in skin depigmentation, which often causes psychological distress and reduced quality of life. Treatment options for vitiligo are limited. Phosphodiesterase type 4 (PDE4) is an intracellular enzyme, which is overactive in multiple inflammatory conditions, including vitiligo (Zaky et al, unpublished material). The oral PDE4 inhibitor apremilast is approved for psoriasis, psoriatic arthritis, and Behcet disease.[1] In a recent case series, apremilast demonstrated some improvement in controlling the progression of vitiligo.[2] Crisaborole is a topical PDE4 inhibitor approved for atopic dermatitis in patients aged 3 months or older. We present a patient with vitiligo treated with crisaborole 2% ointment, who demonstrated skin repigmentation and control of depigmentation progression.

CASE REPORT

A 71-year-old male with a history of recalcitrant generalized atopic dermatitis (AD) presented for evaluation and management of vitiligo for many years. The patient was concerned about progressive depigmentation of his forearms and dorsal aspects of his hands. At the time, the patient was transitioning to dupilimab for AD after using various treatments, including topical and oral immunosuppressants.

The patient had used clobetasol propionate 0.05% ointment and tacrolimus 0.1% ointment on the affected areas of AD and vitiligo, without clinical improvement.

The patient was otherwise healthy and denied a family history of vitiligo or other autoimmune conditions. Physical exam revealed scattered eczematous plaques with normal- and de-pigmented macules and patches involving the extremities (Fig 1, *A*) and trunk with a body surface area (BSA) involvement of 10%. Narrow-band ultraviolet B phototherapy was discussed to achieve repigmentation; however, the patient was unable to make frequent trips to the clinic.

Abbreviations used:

AD: atopic dermatitis
PDE4: phosphodiesterase type 4
Th: T-helper

The patient was initiated on a trial of crisaborole 2% ointment twice daily for his eczema and also instructed to use this treatment on his vitiligo. Initial repigmentation of vitiligo was notable after 10 months of crisaborole use. There was also significant improvement of AD through dupilimab in combination with crisaborole. After 22 months, increased repigmentation of the dorsal aspects of the hands was observed (Fig 1, *B*), and progression of depigmented patches was controlled. The patient has tolerated and continued this treatment without adverse effects.

DISCUSSION

Crisaborole is a nonsteroidal topical PDE4 inhibitor approved by the U.S. Food and Drug Administration in December 2016 for the treatment of mild-to-moderate AD. The inhibition of PDE4 blocks the degradation of cyclic adenosine monophosphate (cAMP). The accumulation of intracellular cAMP prevents activation of pro-inflammatory T-helper (Th) 1 and Th17 lymphocytes and increases the expression of anti-inflammatory mediators, such as interleukin 2 and interleukin 10.[3-5] The inflammation and oxidative stress resulting from

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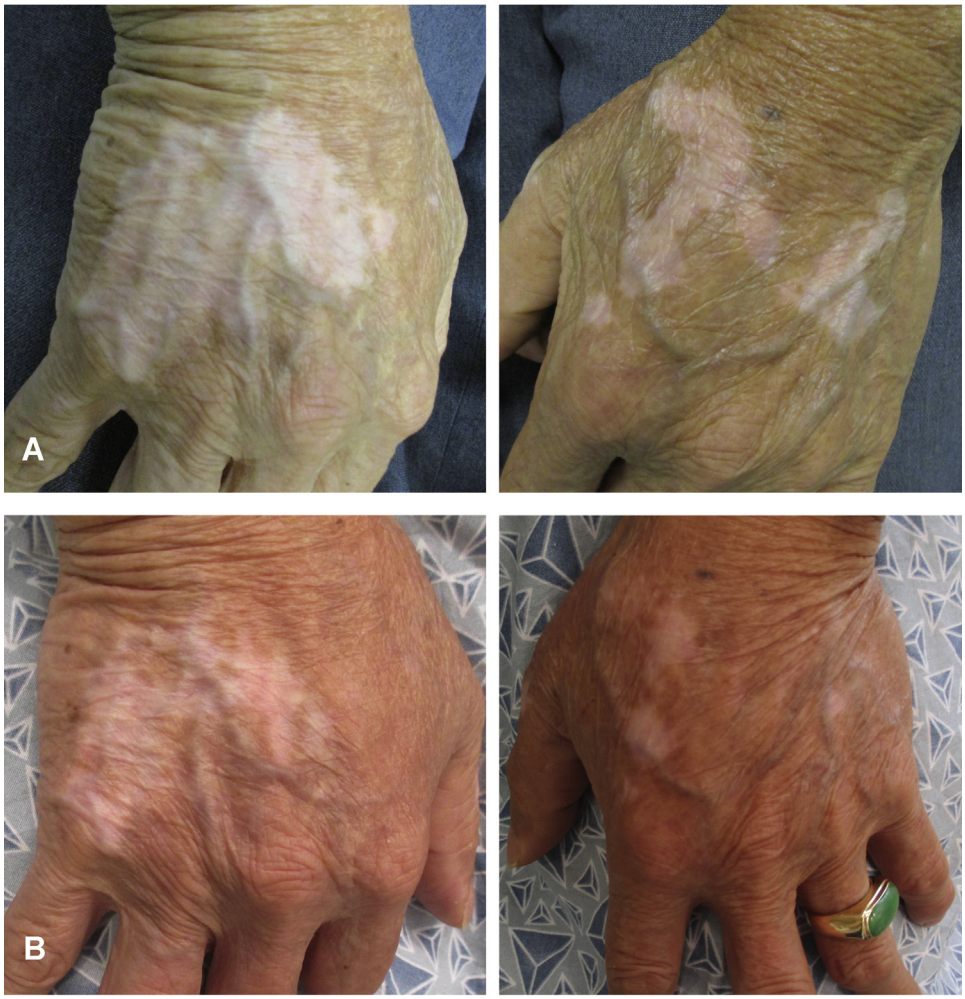

Fig 1. **A**, Vitiligo, before treatment. Depigmented macules and patches on the dorsal aspects of both hands. **B**, Vitiligo, 22 months after treatment with crisaborole 2% ointment. Notable perifollicular repigmentation and control of depigmentation progression of the dorsal aspects of both hands.

the high pro-inflammatory cytokine levels enhance cytotoxicity and impair melanocyte survival. Dupilimab unlikely contributed to the improvement of repigmentation observed in our patient due to its exclusive inhibitory effect on the Th2 pathway.[6]

In a recent abstract presented at the 2020 Vitiligo International Symposium, Zaky et al. demonstrated that the PDE4 enzyme levels were significantly higher in the tissue and serum samples of 20 patients with vitiligo compared with those of age- and sex-matched healthy controls. Thus, PDE4-dependent pathways may play an important role in the pathogenesis of vitiligo. The effects of crisaborole on the immune pathways could therefore explain the pathophysiological and clinical improvement of the vitiliginous lesions. This is supported by the successful use of apremilast in controlling the progression of vitiligo; however, localized application of medication may not have the same efficacy as a systemic agent.[2] In addition, the acral areas are notably challenging to re-pigment.

This case exemplifies that crisaborole may be a potential treatment option for vitiligo. The advantage of using crisaborole include ease of administration with minimal adverse effects.[7] Our patient tolerated this treatment without any adverse effects, such as application site pain. This is an important consideration when patients have minimal BSA involvement of vitiligo or already receive other systemic treatments. Furthermore, it is possible that crisaborole may be more effective when combined with phototherapy, although a recent study found that apremilast combined with narrow-band ultraviolet B was not more effective than narrow-band ultraviolet B alone.[8] Microneedling in combination with topical therapies, such as 5-fluorouracil and corticosteroids, have also

been shown as effective treatments for vitiligo.[9] Further controlled trials are needed to examine the efficacy and safety of crisaborole or other topical PDE4 inhibitors in the treatment of vitiligo.

Conflicts of interest

Dr. Rosmarin has received honoraria as a consultant for AbbVie, Boehringer-Ingelheim, Bristol Meyers Squibb, Celgene, Concert, Dermavant, Dermira, Incyte, Janssen, Kyowa Kirin, Lilly, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharmaceuticals, UCB, VielaBio; has received research support from AbbVie, Amgen, Bristol Meyers Squibb, Celgene, Dermira, Galderma, Incyte, Janssen, Lilly, Merck, Novartis, Pfizer, and Regeneron Pharmaceuticals; and has served as a paid speaker for AbbVie, Amgen, Celgene, Janssen, Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., and Sanofi. All other authors have no conflict of interest to declare.

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