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Targeting JAK/STAT signaling: ruxolitinib cream in the management of concurrent vitiligo and discoid lupus erythematosus

Andrea Bassi,¹ Vincenzo Piccolo,² Grazia Gallippi,³ Giuseppe Argenziano,² Michela Magnano,⁴ Carlo Mazzatenta¹

¹Unit of Dermatology, Azienda USL Toscana Nord Ovest, Lucca; ²Dermatology Unit, University of Campania, Naples; ³Pathology Unit, Monterosso Specialist Outpatient Clinic, Azienda USL Toscana Nord Ovest, Lucca; ⁴Unit of Dermatology, Versilia Hospital, Azienda USL Toscana Nord Ovest, Lucca, Italy

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Correspondence: Andrea Bassi, Unit of Dermatology, Azienda USL Toscana Nord Ovest, Lucca, Italy.
E-mail: bassiderma@gmail.com. Tel.: 0039 3389340371

Dear Editor,

A 50-year-old Caucasian male presented with a 30-year history of facial vitiligo, primarily affecting the chin and the perioral and periorbital regions (Figures 1A and 2A). He had undergone multiple treatments over the years, including targeted phototherapy, topical corticosteroids, and calcineurin inhibitors, with limited success. Additionally, he reported an 8-month history of moderately itchy small erythematous, scaly plaques bilaterally distributed on both eyelids, only treated with medium-potency steroids with little

improvement (Figure 1A). Histopathologic examination of an eyelid papule revealed hyperkeratosis and basal layer vacuolization of the epidermis, with superficial and mid-reticular dermal interstitial and periannexal lymphocytic infiltrates. Alcian blue staining revealed periannexal and occasional interstitial mucin deposits. These findings were consistent with discoid lupus erythematosus (DLE) (Figure 1E). The patient was treated with hydroxychloroquine (200 mg twice daily, then tapered to a single dose) for 4 months with a poor therapeutic response.

Given the concurrent presentation of vitiligo and DLE and the



Figure 1. Initial lesions of vitiligo and DLE on the periorbital area (A); improvement after therapy with single details (B-D) and histopathological examination (E).

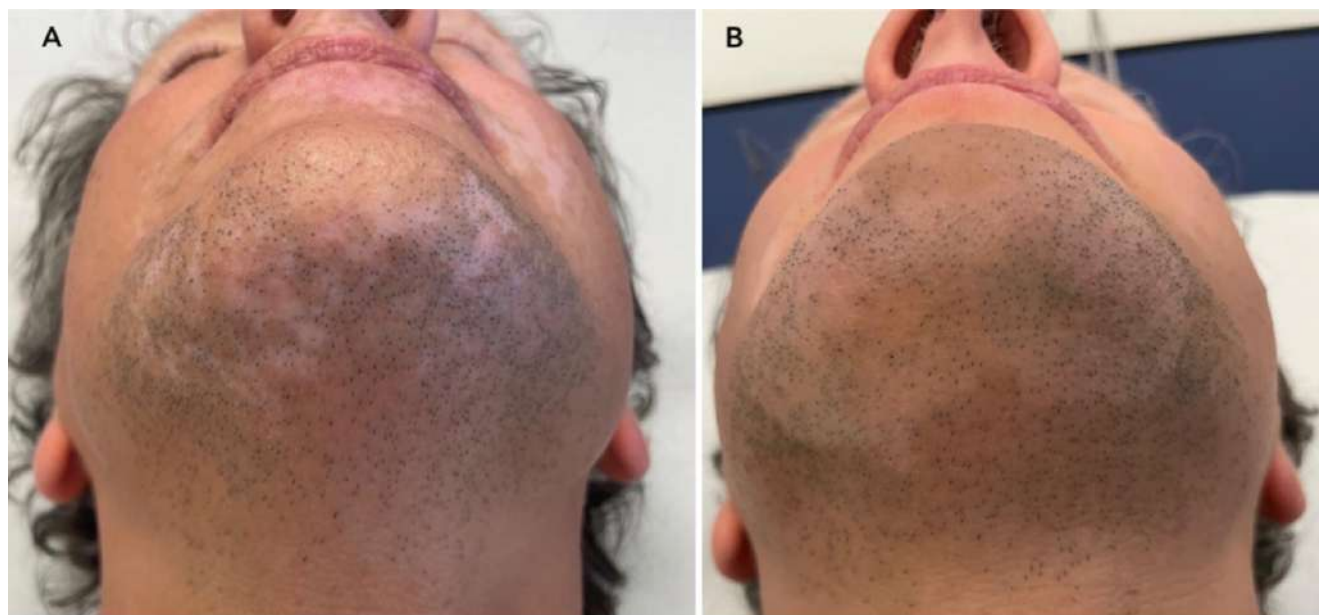


Figure 2. Initial lesions on the chin (A) and improvement after therapy with ruxolitinib (B).

potential for Janus kinase (JAK) inhibition to target both conditions, the patient was started on topical ruxolitinib 1.5% cream with instructions to apply a thin layer twice daily. After six months, partial repigmentation of vitiligo lesions was observed in the chin and periorbital regions, with the emergence of new hyperpigmented spots. Notably, the hyperkeratotic DLE lesions had completely resolved, with no residual erythema or scaling (Figures 1 B-D, and 2B). The patient is still on topical ruxolitinib treatment without relapse or reported adverse effects.

This case highlights the effectiveness of topical ruxolitinib in treating both long-standing facial vitiligo and concurrent DLE. Ruxolitinib cream is a selective JAK1/2 inhibitor approved by the European Medicines Agency (EMA) for the topical treatment of non-segmental vitiligo.¹ Its efficacy in DLE was recently demonstrated in an open-label study involving 10 patients, where it led to a significant improvement in lupus lesions within two weeks, as assessed by the Cutaneous Lupus Erythematosus Disease Area and Severity Index.² The JAK-signal transducers and activators of transcription (STAT) pathway plays a central role in the pathogenesis of both vitiligo and DLE.³ In vitiligo, JAK inhibition blocks interferon-gamma and other pro-inflammatory cytokines, thereby promoting melanocyte survival and proliferation.⁴⁻⁶ In DLE, JAK inhibition downregulates key inflammatory mediators, including interleukin (IL)-12, IL-23, and interferon- α , reducing inflammation and lesion severity.^{7,8} A recent study in a murine model demonstrated elevated phosphorylated JAK1 expression in DLE lesions within both the epidermis and dermis, with notable improvement following topical JAK inhibition.⁹

The occurrence of DLE in a previously vitiliginous area raises an interesting hypothesis linked to the concept of the “immunocompromised district”.¹⁰ This theory suggests that localized immune dysregulation, influenced by cytokine and neuropeptide imbalances, may predispose an area affected by one disease (e.g., vitiligo) to the development of another immune-

mediated disorder (e.g., DLE). The observed repigmentation in vitiligo after 6 months of ruxolitinib treatment is consistent with previous studies demonstrating its ability to restore melanocyte function.¹ The complete resolution of the DLE lesions further supports the therapeutic potential of JAK inhibition for this condition.

Topical ruxolitinib offers clear advantages over systemic therapies, including targeted delivery to the affected areas and a reduced risk of systemic side effects, making it particularly suitable for patients with limited disease involvement, such as facial vitiligo and eyelid DLE. The dual improvement in vitiligo and DLE suggests a promising role for JAK inhibitors in the management of overlapping immune-mediated skin disorders. Further research is warranted to fully elucidate the therapeutic benefits of JAK inhibition in this context.

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Consent for publication: the patient gave his written consent to use his personal data for the publication of this case report and any accompanying images.

Availability of data and materials: all data underlying the findings are fully available.

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