Dermatology Reports
https://www.pagepress.org/journals/index.php/dr/index

eISSN 2036-7406

Please cite this article as:

Paolino G, Di Nicola MR, Mercuri SR, Canti V. Successful use of upadacitinib for the improvement of vitiligo-like and perifollicular dyspigmentation (salt-and-pepper skin) in systemic sclerosis. *Dermatol Rep 2026 [Epub Ahead of Print] doi: 10.4081/dr.2026.10652*

Submitted 16/10/25 - Accepted 31/12/25

Successful use of upadacitinib for the improvement of vitiligo-like and perifollicular dyspigmentation (salt-and-pepper skin) in systemic sclerosis

Giovanni Paolino,[1] Matteo Riccardo Di Nicola,[2] Santo Raffaele Mercuri,[1] Valentina Canti[3]

[1]Unit of Dermatology and Cosmetology, IRCCS San Raffaele Hospital, Milan; [2]Istituto Zooprofilattico Sperimentale del Piemonte, Liguria e Valle d'Aosta, Turin; [3]Department of Internal Medicine and Division of Immunology, Transplantation and Infectious Diseases, IRCCS San Raffaele Hospital, Milan, Italy

Correspondence: Giovanni Paolino, Unit of Dermatology and Cosmetology, IRCCS San Raffaele Hospital, Via Olgettina 60, 20132 Milan, Italy. E-mail: paolino.giovanni@hsr.it. Tel.: +3902/26435770

Key words: upadacitinib; Janus kinase inhibitors; perifollicular depigmentation; repigmentation; systemic sclerosis.

Contributions: Giovanni Paolino: conceptualization, investigation, writing – original draft, writing – review & editing; Matteo Riccardo Di Nicola: writing – original draft, writing – review & editing; Santo Raffaele Mercuri: investigation; Valentina Canti: investigation, writing – review & editing. All authors have read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors have no conflict of interest to declare.

Ethics approval and consent to participate: no ethical committee approval was required for this case report by the Department, because this article does not contain any studies with human participants or animals. Informed consent was obtained from the patient included in this study.

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

Availability of data and materials: the datasets used and/or analyzed during the current study are available upon reasonable request from the corresponding author.

Dear Editor,

Systemic sclerosis (SSc) is an autoimmune connective tissue disease mainly characterized by endothelial dysfunction, aberrant immune activation, and excessive extracellular matrix deposition affecting the skin and visceral organs.[1] SSc exhibits marked clinical heterogeneity, with an estimated prevalence of 7.2-44.3 per 100,000 individuals and a strong female predominance (female-to-male ratio 3:1-8:1).[1,2] Based on the extent of cutaneous involvement, SSc is classified into limited and diffuse forms.[1] The limited subtype typically progresses slowly and affects distal acral areas, whereas the diffuse form is characterized by rapid, widespread proximal and truncal involvement with early internal organ fibrosis.[1,2]

Pigmentary skin alterations are common in SSc and include diffuse hyperpigmentation, vitiligo-like depigmentation, and mixed hyper- and hypopigmented areas, often producing the characteristic "salt-and-pepper" appearance.[1] Although not life-threatening, the diffuse and conspicuous nature of these pigmentary changes often causes relevant cosmetic concern. Thus, targeted dermatologic interventions may improve psychological well-being and support adherence to treatments for associated comorbidities.

A 36-year-old female patient presented with a two-year history of progressively spreading vitiligo-like lesions on the trunk (Figures 1 A, B) associated with Raynaud's phenomenon. The patient also showed areas of hyperpigmentation with a salt-and-pepper appearance. Past medical history included former smoking and allergies to nickel and house dust mites (*Dermatophagoides* spp.). Laboratory investigations revealed positive antinuclear antibodies (ANA 1:1280, centromere pattern), positive anti-topoisomerase I (Scl-70) antibodies, and reduced C3 levels. Pulmonary function tests were within normal limits (forced vital capacity [FVC] 84%, forced expiratory volume in 1 second [FEV1] 88%). Nailfold capillaroscopy showed findings consistent with an active scleroderma pattern, with numerous giant capillaries and microhemorrhages, with focal areas of capillary loss and neoangiogenesis. Cutaneous biopsy of a vitiligo-like depigmented lesion confirmed scleroderma, showing dermal fibrosis with thickened collagen bundles, adnexal atrophy, and a mild perivascular inflammatory infiltrate. The modified Rodnan Skin Score (mRSS) was used to assess cutaneous sclerosis and totaled 18/51, consistent with moderate involvement. To estimate depigmentation extent, we arbitrarily adapted the total Vitiligo Area Scoring Index (T-VASI),[3] which was 29, while the Dermatology Life Quality Index (DLQI) was 21. The patient started hydroxychloroquine 200 mg daily and amlodipine. After 6 months, her general condition stabilized but cutaneous lesions worsened, with a significant psychological impact. For the cutaneous lesions, she had previously used topical clobetasol propionate 0.05% cream, pimecrolimus 1% cream, tacrolimus 0.1% ointment, and

systemic ciclosporin (250 mg/day) without improvement. Accordingly, upadacitinib 30 mg once daily was initiated. Hydroxychloroquine and amlodipine were continued throughout upadacitinib treatment at unchanged doses. After six months of treatment, a decreased incidence of newly developed lenticular vitiligo-like macules was observed, accompanied by enhanced repigmentation. After 12 months, new vitiligo-like areas had ceased to appear, and repigmentation was more evident, with more homogeneous skin color and a reduction in hyperchromic areas and of the salt-and-pepper appearance (Figures 1 C, D). The T-VASI decreased to 14 (−52%, *i.e.*, T-VASI50), the DLQI to 6, and the mRSS to 4. No treatment-emergent adverse events were reported, and the patient expressed satisfaction with the therapeutic response.

To date, only one report has described the use of upadacitinib in SSc, documenting improvement of refractory sclerotic skin involvement without pigmentary changes.[4] Other reports suggest that Janus kinase (JAK) inhibitors, including tofacitinib and baricitinib, may be safe and effective in SSc with cutaneous, vascular, musculoskeletal involvement, and SSc-associated interstitial lung disease.[5-7] However, to the best of our knowledge, no previous reports have addressed vitiligo-like depigmentation in this patient population.

In SSc, pigmentary alterations have been linked to immune-mediated melanocyte damage and microvascular dysfunction, with cytokines such as interferon (IFN)-γ and IFT-γ-induced protein 10 (CXCL10) playing a role in melanocyte loss and the development of vitiligo-like and "salt-and-pepper" depigmentation.[8-10] Upadacitinib is effective for non-segmental vitiligo and, by reducing inflammatory cytokines such as IFN-γ and interleukin (IL)-6, may modulate immune pathways implicated in melanocyte destruction in vitiligo and fibroblast activation in SSc.[8] For this reason and according to the specific mechanism of action, upadacitinib may be considered for vitiligo-like depigmentation in SSc, with the aim of improving both sclerosis-related skin changes and depigmentation, as observed in our patient.

Although the temporal association between upadacitinib initiation and clinical improvement is suggestive, a definitive causal relationship cannot be established. Delayed effects of prior therapies or spontaneous disease stabilization, particularly regarding pigmentary changes, cannot be excluded. However, the patient had shown a two-year progressive course refractory to multiple treatments, with sustained clinical improvement observed only after upadacitinib initiation. Given the patient's young age and the chronic nature of SSc, long-term safety monitoring is particularly relevant. During upadacitinib treatment, regular clinical and laboratory assessments were performed, including surveillance for infections, lipid profile alterations, and thromboembolic risk, with no adverse events observed during follow-up.

While this is a single case, it supports further evaluation of upadacitinib as a therapeutic option under

appropriate clinical supervision. Addressing conspicuous cutaneous manifestations, particularly in young women, as in this case, may also favor long-term adherence.

References

1. Kridin K, Lyakhovitsky K, Tzur-Bitan D, et al. Vitiligo and systemic sclerosis: Are they associated?– Lessons from a population-based study. Aust J Dermatol 2023;64:e65-71.
2. Ingegnoli F, Ughi N, Mihai C. Update on the epidemiology, risk factors, and disease outcomes of systemic sclerosis. Best Pract Res Clin Rheumatol 2018;32:223-40.
3. Kitchen H, Wyrwich KW, Carmichael C, et al. Meaningful Changes in What Matters to Individuals with Vitiligo: Content Validity and Meaningful Change Thresholds of the Vitiligo Area Scoring Index (VASI). Dermatol Ther (Heidelb) 2022;12:1623-37.
4. Sarfaraz S, Chang J, Kirchhof MG. Upadacitinib as a potential management option for diffuse cutaneous systemic sclerosis: A case report. SAGE Open Med Case Rep 2025;13:2050313X251343300.
5. Moriana C, Moulinet T, Jaussaud R, Decker P. JAK inhibitors and systemic sclerosis: A systematic review of the literature. Autoimmun Rev 2022;21:103168.
6. Fiorentini E, Bonomi F, Peretti S, et al. Potential Role of JAK Inhibitors in the Treatment of Systemic Sclerosis-Associated Interstitial Lung Disease: A Narrative Review from Pathogenesis to Real-Life Data. Life 2022;12:2101.
7. McGaugh S, Kallis P, De Benedetto A, Thomas RM. Janus kinase inhibitors for treatment of morphea and systemic sclerosis: A literature review. Dermatol Ther 2022;35:15437.
8. Passeron T, Ezzedine K, Hamzavi I, et al. Once-daily upadacitinib versus placebo in adults with extensive non-segmental vitiligo: a phase 2, multicentre, randomised, double-blind, placebo-controlled, dose-ranging study. eClinicalMedicine 2024;73:102655.
9. Mittal S, Khaitan BK, Ramam M, et al. Pigmentary Changes in Systemic Sclerosis are Associated with More Severe Cutaneous Sclerosis and Severity of Other Systems: A Cross-sectional Study from India. Indian J Dermatol 2024;69:365.
10. Romanowska-Próchnicka K, Dziewit M, Lesiak A, et al. Scleroderma and scleroderma-like syndromes. Front Immunol 2024;15:1351675.

Figure 1. A) Vitiligo-like depigmentation in the chest; **B**) dyschromic hyperpigmentation associated with vitiligo-like depigmentation and perifollicular hypopigmentation; **C**) improvement of the vitiligo-like depigmentation after 12 months of treatment with upadacitinib 30 mg/day; **D**) improvement of the dyschromic hyperpigmentation associated with vitiligo-like depigmentation after 12 months of treatment with upadacitinib 30 mg/day.