Cureus
Part of SPRINGER NATURE

Open Access Case Report

Extensive Linear Morphea Treated With Upadacitinib: A Case Report

Samantha Franco Gonzalez [1, 2], Lucia Achell Nava [1], Genaro Briseño Gascon [1], Cristina Lizbeth [1], Sonia Toussaint Caire [3]

1. Dermatology, Centro Médico Nacional 20 de Noviembre, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Mexico City, MEX 2. Dermatology, Universidad Nacional Autónoma de México (UNAM), Mexico City, MEX 3. Dermatopathology, Hospital General Dr Manuel Gea González, Mexico City, MEX

Corresponding author: Samantha Franco Gonzalez, samanthafrancog@comunidad.unam.mx

Review began 11/11/2026
Review ended 11/24/2026
Published 11/25/2026

© Copyright 2026
Franco Gonzalez et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

DOI: 10.7759/cureus.120219

Abstract

Linear morphea is an inflammatory and fibrosing disorder that can cause tissue damage and functional impairment. Janus kinase (JAK) inhibition may target inflammatory cytokine signaling and profibrotic pathways implicated in its pathogenesis. We present a case of a 35-year-old woman with a seven-month history of progressive linear plaques affecting her right upper extremity. Histopathology confirmed morphea. She began upadacitinib 15 mg once daily as monotherapy. After 10 months, the plaques had softened, pain had improved, and disease severity scores decreased (Modified Localized Scleroderma Skin Severity Index (mLoSSI), 8 to 1; Localized Scleroderma Damage Index (LoSDI), 4 to 1), with no adverse effects reported. This case describes improvement of extensive adult-onset linear morphea during upadacitinib treatment, supporting the potential therapeutic role of JAK1 inhibition in modulating cytokine-driven inflammation and profibrotic signaling. Further studies are needed to establish the efficacy and safety of upadacitinib for morphea.

Categories: Dermatology
Keywords: jak inhibition, linear morphea, th1 inflammation, th2 fibrosis, upadacitinib

Introduction

Morphea, or localized scleroderma, is an uncommon immune-mediated disease in which an early inflammatory phase gives way to sclerosis and, eventually, atrophy of the skin and underlying tissues. Its incidence in adults ranges from 4 to 27 new cases per million people per year, with a clear female predominance [1]. Plaque morphea is the most frequent subtype in adults, whereas the linear variant is mainly a disease of childhood [1]. When linear morphea begins in adulthood, deep tissue involvement can lead to joint contracture, functional limitation, and relapse, particularly when the extremities are affected, although these outcomes have yet to be observed in larger adult-onset cohorts [2].

Methotrexate, usually with a short course of systemic corticosteroids, remains the first-line systemic treatment for linear and deep forms, and mycophenolate mofetil is the main alternative [2]. Responses are variable, and adverse effects, including hematologic and hepatic toxicity with methotrexate and risks of long-term systemic steroid use, limit their use [3]. Beyond these agents, the evidence for other systemic therapies is limited to case reports and case series [4].

The Janus kinase-signal transducer and activator of transcription (JAK-STAT) pathway has emerged as a rational target. It transduces signals from several cytokines involved in morphea, including interferon (IFN)-γ, interleukin (IL)-6, IL-4, IL-7, and IL-13 [5], and it acts downstream of IL-23 and transforming growth factor-β (TGF-β), the central driver of fibroblast activation and collagen deposition [3,6-8]. Upadacitinib is an oral, selective JAK1 inhibitor approved for several immune-mediated diseases [5]. We report an adult woman with extensive linear morphea of the upper limb treated with upadacitinib.

Case Presentation

A 35-year-old woman presented for dermatologic consultation with a cutaneous lesion on the right upper extremity, which appeared seven months prior as a progressive 1.5 cm erythematous-edematous plaque. Clinical evaluation revealed multiple linear plaques on the right arm and forearm, featuring cutaneous atrophy, sclerosis, and light brown hyperpigmentation. These coalesced into larger plaques up to 10 cm with well-defined borders (Figure *1A*) in a subsequent follow-up visit, and baseline scores on the Localized Scleroderma Cutaneous Assessment Tool (LoSCAT), mLoSSI and LoSDI, were assessed at the first consultation in our dermatology department by trainees and dermatology specialists. An elliptical skin biopsy showed fibrosing dermatitis with marked sclerosis in the mid-to-deep reticular dermis and subcutaneous tissue, confirming morphea (Figure *2*). Extensive laboratory workup (blood count, chemistry, liver functions, viral panel, and tuberculosis assay) was unremarkable. Upadacitinib was started at 15 mg once daily as monotherapy due to the benefit of JAK1 inhibition reported previously. After 10 months, the

plaques showed reduced induration: mLoSSI 8 → 1, LoSDI 4 → 1 (Figure *1B*) [9,10]. Clinically, the reduction in the mLoSSI and LoSDI scores was accompanied by softening of the plaques, improvement in pain, and the absence of adverse effects during treatment.

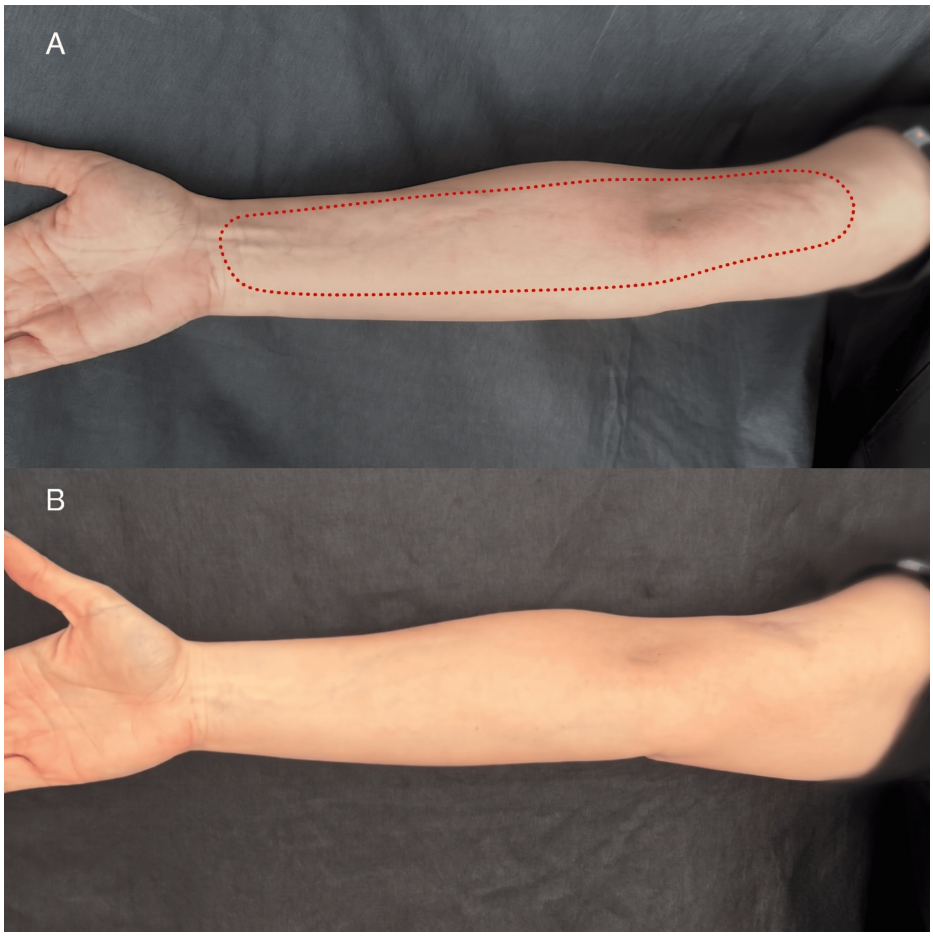


FIGURE 1: Treatment of extensive linear morphea with upadacitinib

Panel A shows extensive dermatosis of the right upper extremity and a proximal biopsy scar. Panel B shows reduced induration of the skin lesion after 10 months of treatment.

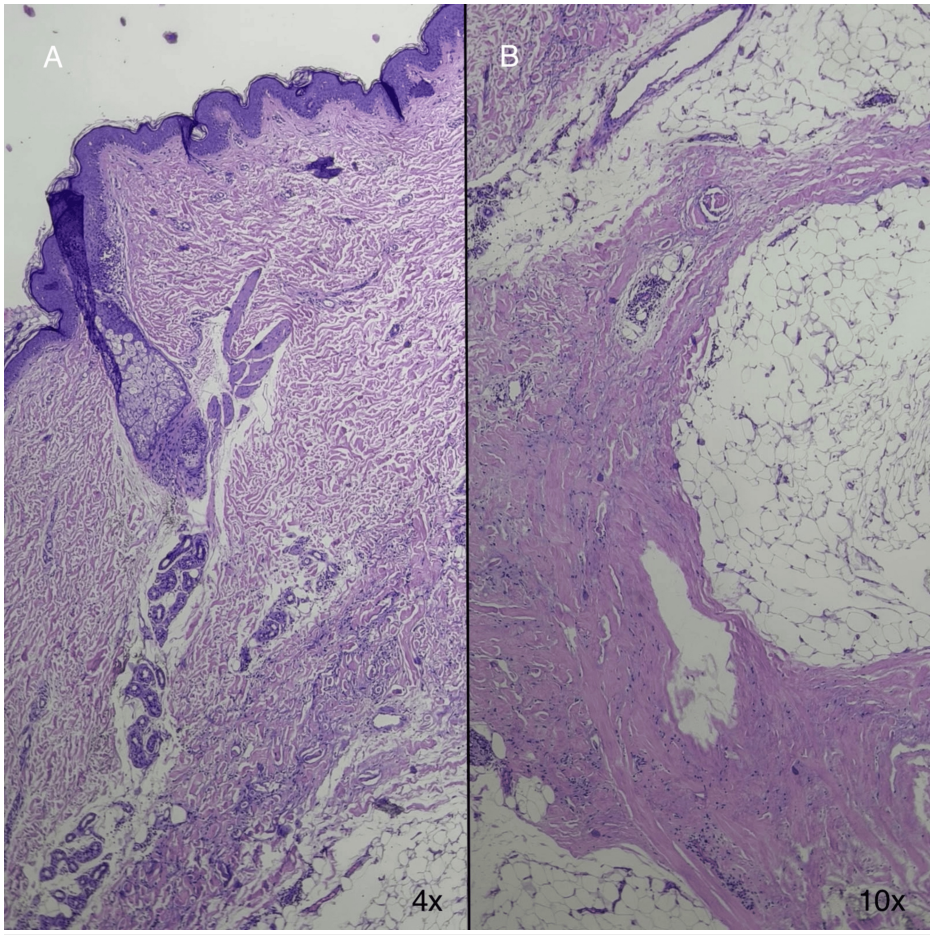


FIGURE 2: Skin biopsy and histopathological findings

Panel A shows hematoxylin and eosin-stained fibrosing dermatitis with marked sclerosis of the mid-to-deep reticular dermis. Adnexal structures are reduced, and eccrine glands appear entrapped and displaced upward. Panel B shows involvement of the subcutaneous tissue, with thickened, sclerotic fibrous septa.

Discussion

This patient showed features that call for systemic treatment according to current recommendations, since linear and deep morphea require prompt systemic therapy [11,12]. Linear morphea of the extremities is also one of the recognized risk factors for relapse, along with delayed treatment [2,13]. Adult-onset linear disease is unusual [12], and most of the published experience with JAK inhibitors in this subtype comes from pediatric cohorts [14,15].

The rationale for JAK inhibition in morphea rests on both its inflammatory and its fibrotic components. Early lesions show a Th1/Th17 profile, with interferon-γ and IL-6, IL-23 signaling [8], while established sclerosis is dominated by Th2 cytokines such as IL-4 and IL-13 and by TGF-β [4,5]. Several of these mediators, including TGF-β, signal through JAK-STAT pathways [6]. Preclinical work has shown that TGF-β activates JAK-STAT3 in dermal fibroblasts and that JAK blockade reduces collagen production in vitro and prevents dermal fibrosis in murine models [3,16]. Damsky et al. also described an interferon-driven JAK-STAT signature in morphea skin and showed that tofacitinib prevented bleomycin-induced fibrosis in mice [17].

The clinical benefit of upadacitinib in morphea likely reflects both the suppression of cytokine-driven inflammation and a direct antifibrotic effect on profibrotic signaling downstream of mediators such as TGF-β [3,16]. If both mechanisms contribute, patients treated during the active, inflammatory phase - as in our case, with a seven-month history and ongoing progression - may be the ones most likely to respond, particularly to the anti-inflammatory component, while established atrophy and dyspigmentation would be expected to change less. Distinguishing the anti-inflammatory from the antifibrotic contribution, and testing whether treatment earlier in the disease course yields greater benefit, would require comparative analysis across phases of disease activity, which a single case cannot provide.

Clinical data on JAK inhibitors in morphea have grown in recent years, although they remain limited to case reports and small series [3]. Tofacitinib is the most frequently reported JAK inhibitor, followed by baricitinib,

with improvement in generalized and deep forms [3]. A systematic review of pediatric morphea identified 16 patients treated with oral or topical JAK inhibitors; 94% improved, although laboratory results were not explicitly reported and mean treatment duration was less than one year, so caution regarding safety is warranted [14]. Experience with upadacitinib is described in more recent reports summarized in Table *1* and is consistent with the response reported with upadacitinib in comparable cases of localized scleroderma [6,18,19]. Maione et al. treated a 77-year-old woman with refractory plaque morphea after a minimal response to UVA1, discontinuation of systemic corticosteroids because of serous chorioretinopathy, withdrawal of methotrexate for adverse effects and inadequate disease control, and insufficient control on mycophenolate mofetil [5]; at three months with JAK inhibition, induration had decreased and ulcerated areas had healed [5]. Cao et al. reported a 53-year-old woman with lichen sclerosus-morphea overlap on the hand who improved within three weeks and showed near resolution at six months [11]. Most relevant to our case, Su et al. described seven children with juvenile localized scleroderma treated with upadacitinib 15 mg daily. Mean mLoSSI fell from 8.2 to 1.8 and mean LoSDI from 12.5 to 3.2 (n=6), and patients with the linear subtype improved noticeably by month 3, earlier than those with plaque or mixed disease [6].

Author, year	Age/sex	Subtype	Prior therapy	Dose	Response	Adverse events
Maione et al., 2025 [5]	77/F	Plaque, bilateral legs	UVA1, systemic corticosteroids, MTX, MMF	15 mg/day	Marked improvement at 3 months; ulcers healed.	No significant blood test changes reported
Cao et al., 2025 [11]	53/F	LS–morphea overlap, hand	Clobetasol 0.05%	15 mg/day	Softening at 3 weeks; near resolution at 6 months	None reported
Su et al., 2026 [6]	7 children (6–17 y)	3 linear, 2 plaque, 2 mixed	Upfront in 6; MTX in 1	15 mg/day	mLoSSI 8.2 → 1.8; LoSDI 12.5 → 3.2 (n = 6)	None reported

TABLE 1: Experience treating different subtypes of morphea with JAK1 selective inhibitors in 3 reports describing clinical outcomes and the safety profile.

Abbreviations: F: female; y: years old; UVA1: UV-A light phototherapy; MTX: methotrexate; MMF: mycophenolate mofetil; mLoSSI: Modified Localized Scleroderma Skin Severity Index; LoSDI: Localized Scleroderma Damage Index; LS: lichen sclerosus; JAK1: Janus kinase.

Upadacitinib has some practical advantages. Its selectivity for JAK1 may spare part of the JAK2-dependent hematopoietic signaling affected by less selective agents; it is taken once daily, clinical outcomes in naive patients are seen in a relatively short period of time, with fewer symptoms and enhancement of quality of life, and also with the same safety profile that has been described in trials in other immune-mediated diseases [20]. The adverse effects of this drug family include herpes zoster and other infections, cytopenias, liver enzyme elevation, and dyslipidemia [4]. Regulatory warnings also cover major cardiovascular events, thrombosis, and malignancy, particularly in older patients and those with cardiovascular risk factors. Our patient was young, had no comorbidities, and had a negative tuberculosis and viral screen, which made her a reasonable candidate. Upadacitinib is approved for other immune-mediated conditions, and its use in morphea remains off-label, supported mainly by case reports [5].

This report has the usual limitations of a single case, and the follow-up length does not allow conclusions about durability. Relapse after discontinuation is a recognized problem in morphea, with the time to first relapse ranging from 20 to 26 months after remission [2]. Spontaneous improvement cannot be fully excluded, although it would be unusual in a lesion that had been progressing for seven months.

Conclusions

This case adds to the small but consistent body of evidence suggesting that upadacitinib can control active linear morphea, here in an adult with extensive involvement of the upper limb. Its selective JAK1 inhibition acts on the inflammatory cytokines that drive early disease, and one hypothetical mechanism, yet to be proven, is that the response reflects control of this early inflammatory activity, possibly together with an effect on profibrotic signaling. Although the present case cannot confirm whether the response is truly greater before fibrosis is established, if it holds, follow-up monitoring should focus on clinical spectra aided by inflammatory biomarkers mixed with clinical measures of fibrosis. Upadacitinib may be a reasonable option when methotrexate is ineffective, poorly tolerated, or contraindicated after careful screening for infection and cardiovascular risk or when the patient's functional capacity is at risk. Prospective studies with validated outcome measures and longer follow-up are needed to define its efficacy, optimal duration, and relapse rate in morphea. Until such data are available, clinicians should document baseline and serial

disease activity with validated scores, such as the mLoSSI and LoSDI, so that treatment responses can be compared across reports.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Samantha Franco Gonzalez, Lucia Achell Nava, Genaro Briseño Gascon, Cristina Lizbeth, Sonia Toussaint Caire

Acquisition, analysis, or interpretation of data: Samantha Franco Gonzalez, Lucia Achell Nava, Genaro Briseño Gascon, Sonia Toussaint Caire

Drafting of the manuscript: Samantha Franco Gonzalez, Lucia Achell Nava, Genaro Briseño Gascon, Sonia Toussaint Caire

Critical review of the manuscript for important intellectual content: Samantha Franco Gonzalez, Lucia Achell Nava, Genaro Briseño Gascon, Cristina Lizbeth, Sonia Toussaint Caire

Supervision: Lucia Achell Nava, Genaro Briseño Gascon, Sonia Toussaint Caire

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Comité de ética del Centro Médico Nacional 20 de Noviembre del Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado issued approval Samantha Franco González 0009-0003-9187-4378. Case illustrations are published with the patients' informed consent and authorization. **AI use statement:** The authors have declared that no AI tools were used during the work or in the drafting of this article. The authors take full responsibility for the work. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Knobler R, Geroldinger-Simić M, Kreuter A, et al.: Consensus statement on the diagnosis and treatment of sclerosing diseases of the skin, part 1: localized scleroderma, systemic sclerosis and overlap syndromes. J Eur Acad Dermatol Venereol. 2024, 38:1251-80. 10.1111/jdv.19912
2. Matucci-Cerinic C, Lipsker D, Malattia C, Martini G: A practical clinical approach to the diagnosis and management of morphea (localized scleroderma). Best Pract Res Clin Rheumatol. 2026, 40:102127. 10.1016/j.berh.2026.102127
3. 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:e15437. 10.1111/dth.15437
4. Teske N, Fett N: Recent advances in treatment of systemic sclerosis and morphea . Am J Clin Dermatol. 2024, 25:213-26. 10.1007/s40257-023-00831-2
5. Maione V, Rovaris S, Romanò C, Bighetti S, Ghini I, Bettolini L: Upadacinib for the treatment of refractory morphea. Australas J Dermatol. 2025, 66:238-9. 10.1111/ajd.14481
6. Su Y, Wang T, Sun J, Li J, Wang X, Sun Y: Treatment of juvenile localized scleroderma with upadacitinib: a case series. J Eur Acad Dermatol Venereol. 2026, 40:e591-4. 10.1111/jdv.70341
7. Wang F, Wang S, Zhang C, et al.: Noncanonical JAK1/STAT3 interactions with TGF-β modulate myofibroblast transdifferentiation and fibrosis. Am J Physiol Lung Cell Mol Physiol. 2022, 323:L698-714. 10.1152/ajplung.00428.2021
8. Bernal-Alferes B, Basilio-Aguilar J, Domínguez-López ML, Romero-López JP: Papel del eje intestino-piel-articulación en enfermedades inmunomediadas. Papel de nuevas terapias con JAKinibs selectivos e inhibidores IL23p19 [Role of the gut-skin-joint axis in immune-mediated diseases. Role of new therapies with selective JAKinibs and IL23p19 inhibitors]. Rev Mex Enferm Inflam Inmunomed. 2021, 1:67-79. 10.24875/imids.m21000012
9. Arkachaisri T, Vilaiyuk S, Torok KS, Medsger TA Jr: Development and initial validation of the localized scleroderma skin damage index and physician global assessment of disease damage: a proof-of-concept study. Rheumatology (Oxford). 2010, 49:373-81. 10.1093/rheumatology/kep361
10. Skrzypek-Salamon A, Lis-Święty A, Ranosz-Janicka I, Brzezińska-Wcisło L: Localized Scleroderma Cutaneous Assessment Tool (LoSCAT) adapted for use in adult patients: report from an initial validation study. Health Qual Life Outcomes. 2018, 16:185. 10.1186/s12955-018-1010-z
11. Cao S, Yang B, Chen S, Liu H, Zhang F: Successful treatment of lichen sclerosus and morphea on the hand with JAK inhibitor upadacitinib. Indian J Dermatol Venereol Leprol. 2025, 1-2. 10.25259/IJDVL_1795_2024

12. Papara C, De Luca DA, Bieber K, Vorobyev A, Ludwig RJ: Morphea: the 2023 update. Front Med (Lausanne). 2023, 10:1108623. 10.3389/fmed.2023.1108623
13. Mertens JS, Seyger MM, Kievit W, et al.: Disease recurrence in localized scleroderma: a retrospective analysis of 344 patients with paediatric- or adult-onset disease. Br J Dermatol. 2015, 172:722-8. 10.1111/bjd.13514
14. Moschella A, DeBiasio C, Liy-Wong C: Janus kinase inhibitors for the treatment of pediatric morphea: a systematic review. Pediatr Dermatol. 2026, 43:654-6. 10.1111/pde.70090
15. Tang JC, Zheng WY, Han GM, Liu SF, Yang B: Successful treatment of paediatric morphea with tofacitinib . Acta Derm Venereol. 2023, 103:adv4805. 10.2340/actadv.v103.4805
16. Wenzel D, Haddadi NS, Afshari K, Richmond JM, Rashighi M: Upcoming treatments for morphea . Immun Inflamm Dis. 2021, 9:1101-45. 10.1002/iid3.475
17. Damsky W, Patel D, Garelli CJ, et al.: JAK inhibition prevents bleomycin-induced fibrosis in mice and is effective in patients with morphea. J Invest Dermatol. 2020, 140:1446-1449.e4. 10.1016/j.jid.2019.12.019
18. Kim SR, Charos A, Damsky W, Heald P, Girardi M, King BA: Treatment of generalized deep morphea and eosinophilic fasciitis with the Janus kinase inhibitor tofacitinib. JAAD Case Rep. 2018, 4:443-5. 10.1016/j.jdcr.2017.12.003
19. Labrandero Hoyos C, Peñuelas Leal R, Echevarría AG, et al.: JAK-STAT pathway is involved in cutaneous sclerosis processes: generalized morphea successfully treated with baricitinib. J Dermatol. 2023, 50:e424-5. 10.1111/1346-8138.16933
20. You H, Xu D, Zhao J, et al.: JAK inhibitors: prospects in connective tissue diseases . Clin Rev Allergy Immunol. 2020, 59:334-51. 10.1007/s12016-020-08786-6