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Case Report

Refractory Lichen Amyloidosis Successfully Treated with Upadacitinib: A Case Report and Literature Review

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Abstract

Lichen amyloidosis (LA) is characterized by keratinocyte-derived amyloid deposition in the superficial dermis. LA predominantly affects the shins and extensor surfaces, and is frequently associated with severe, treatment-resistant pruritus, significantly impairing quality of life. Current therapeutic options often provide limited and inconsistent benefits. We report the case of a 63-year-old man with long-standing, refractory LA, unresponsive to multiple systemic and topical therapies, who was successfully treated with upadacitinib. The patient experienced rapid and sustained improvement, achieving almost complete resolution of pruritus and marked clinical improvement of skin lesions, with no relapse at 6-month follow-up. This case supports the potential role of selective JAK1 inhibition in the management of refractory LA and highlights the importance of targeting neuroimmune pathways involved in chronic pruritus. A review of the current literature on similar cases is also provided.

Keywords: Lichen amyloidosis; Pruritus; JAK inhibitors; Upadacitinib; Treatment

Introduction

Lichen amyloidosis (LA) is a chronic skin-limited form of amyloidosis where abnormal protein, called amyloid, is deposited in the upper dermis without internal organ involvement. Clinically, LA presents with intensely pruritic, hyperkeratotic papules predominantly on the shins or extensor sites [1]. Chronic pruritus is the main clinical feature and significantly impairs quality of life. Conventional therapies, including topical corticosteroids, systemic immunosuppressants, and retinoids, often provide incomplete or unsustained responses [2,3]. Recent insights into the role of cytokine signaling in pruritic skin disorders have opened new therapeutic options [4]. Among them, Janus kinase (JAK) inhibitors, particularly those targeting JAK1, have shown strong efficacy in treating pruritic dermatosis, such as atopic dermatitis [5]. Herein, we report a case of LA refractory to standard treatments, successfully managed with upadacitinib.

Case Presentation

A 63-year-old man was referred to our outpatient clinic in 2020 with long-standing LA histologically confirmed by the presence of amyloid deposits in papillary dermis positive on Congo red staining. Physical examination revealed bilateral multiple coalescing hyperpigmented and lichenified papules, with excoriations, located on the pretibial areas (Figure 1A). The patient reported severe, persistent pruritus for several years. Pruritus Numeric Rating Scale (NRS) score was 10/10, significantly impairing sleep and daily activities (Dermatology Life Quality Index (DLQI) score was 21/30). In the past, the patient had received a variety of systemic and topical treatments, including topical and

systemic corticosteroids, acitretin, cyclosporine, pentoxifylline, methotrexate, and dupilumab, with no sustained benefit. A transient response was observed with topical dimethyl sulfoxide solution and topical tacrolimus.

Given multiple therapeutic failures and debilitating pruritus [6,7], treatment with upadacitinib 30 mg/day was initiated. Baseline laboratory investigations, including complete blood count, liver function tests, lipid profile, and screening for viral hepatitis and tuberculosis, were unremarkable. Within four weeks, the patient reported dramatic improvement in pruritus, with a NRS score of 2/10 and DLQI of 8/30. After two months, pruritus had further improved, with an NRS score of 1/10 and DLQI of 6/30. The patient showed an almost complete resolution of pruritus, with no recurrence at 6-month follow-up. Additionally, marked flattening of the lesions and a reduction in pigmentation were observed (Figure 1B). No laboratory abnormalities or treatment adverse events were observed during follow-up.

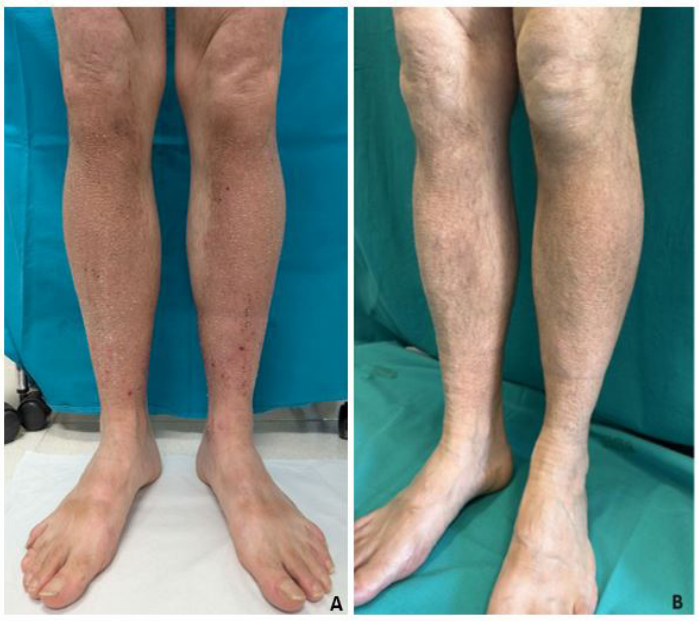

Figure 1: A) Baseline clinical presentation showing bilateral coalescing hyperpigmented and lichenified papules with excoriations on the pretibial areas. **B)** Marked clinical improvement after 6 months of treatment with upadacitinib, with flattening of the papules and reduction in hyperpigmentation.

Discussion

LA remains a therapeutically challenging condition, primarily due to the persistence of severe pruritus and its self-perpetuating itch–scratch cycle, which contributes to ongoing keratinocyte damage and amyloid deposition. Despite the availability of multiple topical, systemic, and procedural interventions, treatment responses are often inconsistent and incomplete, highlighting the absence of a standardized, evidence-based therapeutic approach [3]. Increasing evidence suggests that chronic pruritus in LA is not merely a secondary symptom but a central pathogenic driver, sustained by complex immune interactions [4,8]. In particular, T helper 2 (Th2) cytokines including interleukin (IL)-4, IL-13, and IL-31 play a pivotal role in modulating both cutaneous inflammation and neuronal itch signaling. IL-31 has emerged as a key mediator of pruritus through its direct action on sensory neurons, while IL-4 and IL-13 contribute to neuronal sensitization and amplification of itch perception, in several disorders including LA [9]. JAK inhibitors, such as abrocitinib and upadacitinib, are oral small molecules that provide a broader suppression of cytokine signaling via the JAK-STAT pathway, supporting their use as a mechanism-based therapeutic approach in chronic pruritic disorders [5].

Upadacitinib, a selective JAK1 inhibitor, has demonstrated rapid and sustained antipruritic effects in atopic dermatitis, largely attributable to its dual action on immune and neuronal pathways. By inhibiting JAK1-dependent signaling, upadacitinib modulates the activity of multiple pruritogenic cytokines while simultaneously attenuating neuronal hypersensitivity. This dual mechanism is particularly relevant in LA, where chronic scratching not only exacerbates inflammation but also perpetuates amyloid deposition derived from keratinocyte degeneration.

To date, the evidence supporting the use of JAK inhibitors in LA remains limited to a small number of case reports and short case series. A non-systematic literature search was conducted in PubMed and Embase using the terms '*lichen amyloidosis*' AND '*JAK inhibitors*' (including upadacitinib, abrocitinib, baricitinib, and tofacitinib). Only English-language reports describing clinical outcomes were included. Given the limited number of available studies, a qualitative synthesis was performed (Table 1). Overall, 46 patients treated with JAK inhibitors were identified in the literature, including abrocitinib, baricitinib, tofacitinib, and upadacitinib [6,10-16]. Across these reports, a consistent and rapid reduction in pruritus has been observed, often accompanied by partial improvement of cutaneous lesions. However, complete clinical remission has been rarely documented. Notably, previously reported cases treated with upadacitinib have shown variable responses, with differences in dosing (15 mg/day vs 30 mg/day) and clinical outcomes, suggesting that factors such as disease chronicity, baseline severity, and individual susceptibility may influence therapeutic response more than dosage alone [6, 15].

Study	No. of patients	Drug	Dose (mg/day)	Age/sex	Comorbidities	Pruritus outcome (Scale)	Skin outcome (Scale)	DLQI outcome
Tsai et al.	1	Abrocitinib	200	44/F	Atopic dermatitis	Partial improvement	3 to 1 (IGA)	n.a.
Zhang W et al.	2	Abrocitinib Abrocitinib	100 100	29/F 31/M	Neurodermatitis n.a.	7 to 1 (VAS) 5 to 2 (VAS)	5 to 4 (IGA) 5 to 4 (IGA)	n.a.
Zhang Y et al.	1	Abrocitinib	100	32/M	Atopic dermatitis	10 to 1 (NRS)	Significant improvement	n.a.
Xia D et al.	1	Baricitinib	4	46/M	Atopic dermatitis	6 to 1 (VAS)	Improvement	n.a.
Ziebart RL et al.	1	Upadacitinib	15	28/F	n.a.	Resolution	Resolution	n.a.
Solimani F et al.	1	Upadacitinib	30	41/M	n.a.	9 to 3 (VAS)	Improvement	26 to 8
Zou P et al.	15	Tofacitinib	5	Mean 50.3/ 10M-5F	n.a.	6.9 to 0.4 (pNRS)	13.3 to 4.9 (LS)	11.8 to 2.6
Wang QX et al.	24	Tofacitinib	10	Mean 49/ 16M-8F	n.a.	8 to 1 (ppNRS)	3 to 2 (IGA)	n.a.
Our case	1	Upadacitinib	30	63/M	n.a.	10 to 1 (NRS)	Improvement	21 to 6

DLQI: Dermatology Life Quality Index. IGA: Investigator Global Assessment. LS: Lesion Severity. n.a.: not available. pNRS: pruritus Numerical Rating Scale. ppNRS: peak pruritus Numerical Rating Scale. VAS: Visual Analogue Scale.

Table 1: Patient demographic, clinical characteristics and outcomes.

In this context, our case is noteworthy for the rapid and sustained improvement of pruritus in a patient with long-standing, treatment-refractory disease, previously unresponsive to multiple systemic immunomodulatory agents, including dupilumab [11, 17]. The marked improvement in both patient-reported outcomes (NRS and DLQI) and clinical appearance further supports the potential of JAK1 inhibition to effectively disrupt the itch scratch cycle and modify disease perpetuation [18]. Importantly, the absence of relapse at 6-month follow-up suggests a durable response, although longer observation is required to confirm sustained remission.

The discrepancy between the rapid resolution of pruritus and the more gradual improvement of cutaneous lesions observed in our patient aligns with previous reports and may reflect the distinct kinetics of pruritus modulation versus structural skin remodeling. This observation reinforces the concept that targeting pruritus is a critical therapeutic objective in LA, not only for symptomatic relief but also for interrupting the pathogenic cycle driving disease persistence [18].

This report has limitations inherent to its design, including single-patient observation, the lack of standardized lesion scoring, and the relatively short follow-up period. Furthermore, the off-label use of upadacitinib warrants careful consideration of long-term safety, particularly in older patients.

In conclusion, our findings support the emerging role of selective JAK1 inhibition as a promising therapeutic strategy in refractory LA. By targeting key neuroimmune pathways involved in chronic pruritus, upadacitinib may offer a mechanism-based approach capable of achieving meaningful and sustained clinical benefit. Although limited to low-level evidence, the consistency of antipruritic response across different JAK inhibitors suggests a class effect targeting shared neuroimmune pathways. Larger, controlled studies are needed to better define its efficacy, optimal dosing, and long-term safety profile in this setting.

Acknowledgments

A.D. and M.M. conceived the report. A.D., G.P., N.B., and S.V. collected clinical data. A.D. and M.M. drafted the manuscript. G.G. critically revised the manuscript. All authors reviewed and approved the final version of the manuscript.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying clinical images.

Conflict of Interest

G. Girolomoni has received personal fees from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Leo Pharma, Merck Serono, Novartis, Pfizer, Pierre Fabre, Samsung Bioepis, and Sanofi. The other authors declare no conflicts of interest.

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