SKIN

BRIEF ARTICLE

JAK of All Trades: A Case Series of Oral Janus Kinase Inhibitors for Treatment of Lichen Planus

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ABSTRACT

Lichen planus (LP) presents as pruritic, polygonal papules and plaques on skin or lacy-reticulated striae and papules on mucosal surfaces. Severity ranges from mild to severe, with recalcitrant cases being particularly difficult to treat with standard therapies. There is a need for more effective and targeted therapies to manage this often-chronic disease and improve quality of life. Prior translational studies of LP have proposed pathophysiology involving a predominantly interferon-mediated inflammatory response, and case reports successfully using Janus kinase (JAK) inhibitor therapies provide early validation. This case series presents four patients treated with JAK inhibitors who noticed a significant improvement in their cutaneous and/or oral LP on therapy.

INTRODUCTION

Lichen planus (LP) is an inflammatory condition commonly characterized by pruritic, polygonal papules and plaques on skin or lacy-reticulated striae and papules on mucosal surfaces.[1] The prevalence of cutaneous and oral LP are respectively 0.2-1% and 1-4%.[2] LP most commonly affects women between 30 to 60 years old but can affect all ages and races.[1,2] The exact cause is not fully known but may be due to an insult causing chronic T-cell activation in the upper dermis, leading to persistent lichenoid inflammation of basal epidermal cells.[1,2] Topical and intralesional corticosteroids remain a dissatisfactory gold-standard therapy, with unpredictable responses when using common off-label treatments, including acitretin, prednisone, methotrexate, ultraviolet light, metronidazole, and cyclosporine. Prior translational studies have proposed LP having a predominant interferon (INF)-mediated inflammatory response,[2,3] with case reports successfully using Janus kinase (JAK) inhibitor therapies providing early validation. It is theorized keratinocytes primed with INF-γ are more susceptible to T-cell-mediated cytotoxicity.[3] INF-γ sends signals via JAK/signal transducer and activator of transcription (STAT) pathways which, when inactivated, make INF-γ-primed keratinocytes less susceptible to T-cell mediated cytotoxicity.[3] Findings like this have led to increased usage of JAK inhibitors in the treatment of LP. The four cases discussed herein further support the use of JAK inhibitors in patients with LP (**Table 1**).

Table 1. Summary of Cases

	Type of LP	JAK Inhibitor	JAK Target	Time Until Improvement	Side Effects
Case 1	Cutaneous and Oral	Baricitinib 4 mg daily	JAK1 and JAK2	No new lesions at 1 month. No active lesions at 2 months.	Mild acne
Case 2	Cutaneous	Upadacitinib 15 mg every other day for 2 months then daily	JAK1	Improvement in pruritus at 2 weeks with every other day dosing. No new or active lesions at 1 month of daily dosing.	None
Case 3	Oral	Upadacitinib 15 mg daily	JAK1	No new or active lesions at 45 days.	None
Case 4	Cutaneous and Oral	Abrocitinib 100 mg daily	JAK1	No new or active lesions at one month.	Mild fatigue

CASE SERIES

Case 1

Patient 1 was a 68-year-old female who presented with months of a pruritic rash on her trunk and extremities with associated oral involvement (Figure 1a). Biopsies demonstrated lichenoid interface dermatitis, consistent with the clinical diagnosis of LP. While she noted decreased pruritus and decreased oral severity on three months of acitretin 25 mg and topical corticosteroids, the disease persisted, and hydroxychloroquine 400 mg was added. She noticed improvement at four months but experienced mild hair thinning and headaches. These side effects as well as cost limitations led to discontinuation of both therapies after 10 months of use. She was subsequently started on metronidazole 500 mg and twice weekly narrowband ultraviolet B (nbUVB) phototherapy resulting in temporary resolution of LP. She remained symptom-free for three years but had severe recurrence involving the groin, back, and all four extremities and began a trial of baricitinib 4 mg daily. After two months, she achieved significant improvement on baricitinib with no new cutaneous lesions (Figure 1b). Baricitinib was tapered to 2 mg daily for two months, followed by a trial off of the

medication. However, she experienced a flare of her groin lesions and restarted baricitinib. Mild acne was the only noted adverse effect.

Case 2

A 53-year-old female with history of atopic dermatitis presented with a few weeks of a pruritic rash on her lower extremities and back (Figure 2a). Histological analysis showed lichenoid interface dermatitis consistent with the clinical impression of LP. Initially, she was treated with two months of topical clobetasol and twice weekly nbUVB therapy, but new lesions continued to develop. Secondary to cost restrictions, she started mycophenolate mofetil 500 mg twice daily for one month without improvement. She stated she was miserable and was having difficulty sleeping due to constant scratching and was subsequently given a starter pack of upadacitinib 15 mg daily and a two-week prednisone taper. Two weeks later, she noticed significant improvement in pruritus only, and thus was prescribed hydroxychloroquine 200 mg twice daily. She took upadacitinib every other day for two months to lengthen the duration of treatment on the starter pack while obtaining insurance. After a month of daily upadacitinib, there was clinical improvement in her rash (Figure 2b). Upadacitinib was increased back to once daily after she obtained insurance, and she also continued twice daily hydroxychloroquine 200 mg and topical clobetasol ointment. The following month, her pruritus had nearly resolved, and she denied new lesions or side effects.

Case 3

A 77-year-old female with history of psoriasis on risankizumab presented with painful oral lesions and pain with eating that began during a COVID-19 infection one year prior. Physical exam showed gingival erosions and white patches on the buccal mucosa. Biopsy showed squamous mucosa with nonspecific chronic inflammation. She was diagnosed with LP based on clinical criteria and started on oral dexamethasone and clobetasol ointment with minimal improvement. Several months later, she noted worsening discomfort of oral lesions with new genital involvement and began a trial of upadacitinib 15 mg daily. She had marked improvement on JAK inhibitor therapy without side effects during her follow-ups over the next four months.

Case 4

Patient 4 was a 75-year-old male with biopsy-confirmed cutaneous and oral LP, treated with rounds of acitretin and topical steroids over nine years with intermittent resolution. Due to dry lips and muscle aches with acitretin, was started abrocitinib 100 mg daily to control his LP and comorbid atopic dermatitis. One month later, he had no active LP lesions and significantly improved atopic dermatitis. The only side effect noted with abrocitinib was mild fatigue.

DISCUSSION

JAK1 plays a role in T-cell development and JAK2 responds to INF-1, INF-2, and INF-γ to promote an inflammatory response.[4] JAK inhibitors are thought to treat LP by making keratinocytes less susceptible to INF-mediated apoptosis via cytotoxic T-cells.[2] While multi-JAK inhibitors such as baricitinib and tofacitinib are available, their broader activity implies a greater side effect profile, leading to increased preference for more selective JAK1 inhibitors like upadacitinib and abrocitinib. Currently, JAK inhibitors have no label indication for LP, but there is burgeoning support of it being safe and effective. A 2023 systematic review demonstrated complete resolution with baracitinib in 25% (4/16) of patients and

partial resolution in 31.3% (5/16) of patients, while upadacitinib resolved LP in 100% (2/2) of patients.[5] A phase II study employing topical ruxolitinib displayed a significant decrease in lesion count at 4-weeks.[6] None of the patients discussed in our case series experienced adverse events, and all four patients experienced at least partial remission with oral JAK inhibitor therapy; specifically, Patients 2 and 4 experienced complete resolution, and Patients 1 and 3 had partial resolution.

CONCLUSION

LP is a debilitating dermatologic condition due to its recalcitrant behavior with historically limited treatment options. JAK/STAT pathways play a role in the destruction of keratinocytes in LP, making JAK inhibitors seemingly effective in treating LP. Additional clinical trials to elucidate JAK inhibitors' role in treating cutaneous and oral LP are needed to further evaluate its efficacy and safety. In line with the existing literature to-date, these favorable responses exhibited in our four patients highlight how JAK inhibitors should be considered when treating patients with recalcitrant LP.

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