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Journal

Dermatology Online Journal, 30(3)

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Publication Date

2024

DOI

10.5070/D330363864

Recalcitrant multi-variant lichen planus successfully treated with oral baricitinib and topical ruxolitinib cream

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Abstract

Lichen planus is a chronic auto-inflammatory disease that primarily affects mucocutaneous regions. There are many variants of lichen planus including cutaneous, oral, nail, follicular, and erosive forms. Without any disease-specific treatment options, multi-variant lichen planus can be a challenging disease to manage. We present a 61-year-old woman with multivariant lichen planus that was refractory to numerous systemic and topical therapies. Subsequently, her cutaneous and vulvovaginal lesions improved with the use of oral baricitinib and the erosive oral lesions improved with topical ruxolitinib.

Keywords: baricitinib, Janus kinase, lichen planus, ruxolitinib

Introduction

Lichen planus is a chronic inflammatory disease commonly characterized by pruritic, well-demarcated, violaceous papules and plaques occurring on the skin and mucous membranes [1]. Up to 5% of the general adult population is affected by lichen planus, with up to 77% of patients having oral involvement [2]. Oral lichen planus affects the buccal mucosa, gingiva, and tongue. Erosive or atrophic variants may present with burning and pain which may restrict food intake and further impact quality of life (QoL). Other variants include vulvovaginal, esophageal, and follicular forms such as lichen planopilaris of the scalp [3].

Currently, there are no disease-specific therapies for lichen planus. The primary goals of therapy include symptomatic management and monitoring for dysplastic changes [4]. First-line treatments include topical corticosteroids, topical calcineurin inhibitors, retinoids, and phototherapy [4]. Recalcitrant cases may require management with systemic agents. Although not FDA-approved for use in lichen planus, Janus kinase inhibitors have demonstrated efficacy in cutaneous lichen planus, lichen planopilaris, and erosive oral lichen planus [5]. We report a patient with recalcitrant cutaneous and vulvovaginal lichen planus treated with oral baricitinib, as well as erosive oral lichen planus successfully treated with topical ruxolitinib cream, both of which are selective JAK1/2 inhibitors.

Case Synopsis

A 61-year-old woman presented to our clinic with a history of biopsy-proven lichen planus involving the mouth, body, and genitalia, which was refractory to multiple treatments. For approximately one year, she had been experiencing flares of painful, pruritic plaques bilaterally on her forearms (**Figure 1A**, **B**) and lower legs (**Figure 1C**) with overlying erosions, crusting, and thickened scale. Furthermore, she presented with erosions on oral and vaginal mucosa, severely impacting her quality of life and ability to eat (**Figure 1D**). Past treatments included trials of clobetasol 0.05% ointment, triamcinolone 0.1% ointment, multiple courses of oral prednisone, oral mycophenolate, betamethasone 0.05% ointment,

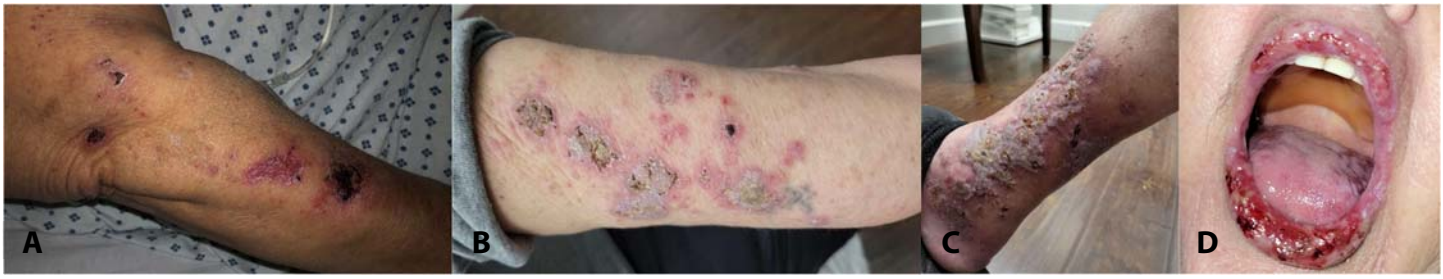

Figure 1. *Clinical images showing cutaneous lichen planus over the **A)** right arm, **B)** left arm, **C)** right lower leg, and **D)** erosive oral lichen planus over the oral mucosa prior to any JAK inhibitor treatment.*

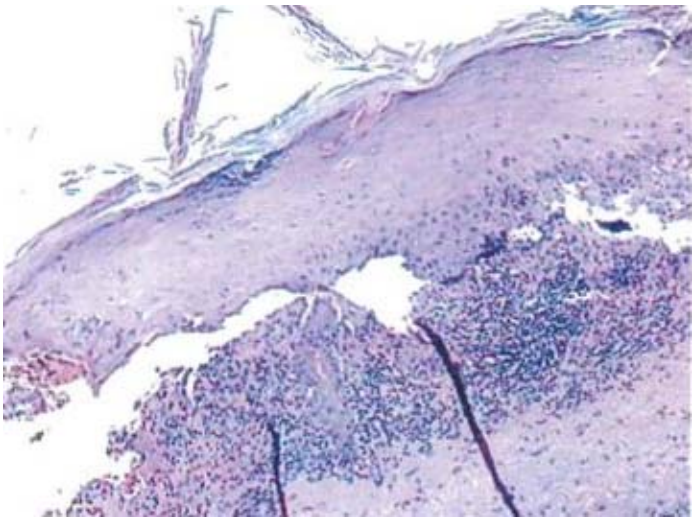

Figure 2. *Histological images of left forearm demonstrating lichenoid dermatitis.*

intramuscular triamcinolone injections, and adalimumab, all of which led to minimal improvement. She could not tolerate hydroxychloroquine owing to intense nausea. Medical history was notable for hypertension, chronic obstructive pulmonary disease on supplemental oxygen, seasonal allergies, resolved hepatitis C, and a remote history of intravenous drug use over 10 years ago. Two punch biopsies were performed of the left forearm which demonstrated lichenoid dermatitis and negative direct immunofluorescence (**Figure 2**).

Prior to treatment and throughout the follow-up period, laboratory tests including complete blood counts, liver function tests, lipid panels, serum vitamin D, vitamin B12, zinc, copper, and ceruloplasmin did not exhibit any abnormal values. Human immunodeficiency virus testing was negative. Hepatitis C RNA-PCR testing was negative, ruling out an active hepatitis C infection.

Given her lack of responses to other agents and continued severe disease, the patient was started on baricitinib at a dose of 2mg by mouth once daily. Concurrent treatments included topical corticosteroids and prednisone tapers as needed for flares. After 1.5 months, she reported significant improvement of her forearms (**Figure 3A**), lower legs (**Figure 3B**, **C**), and vaginal lesions. However, she was still experiencing oral flares (**Figure 3D**).

After four months, the dose of baricitinib was increased to 4mg by mouth once daily. Three months later, the patient was still having frequent, albeit less severe, flares of her erosive oral lesions,

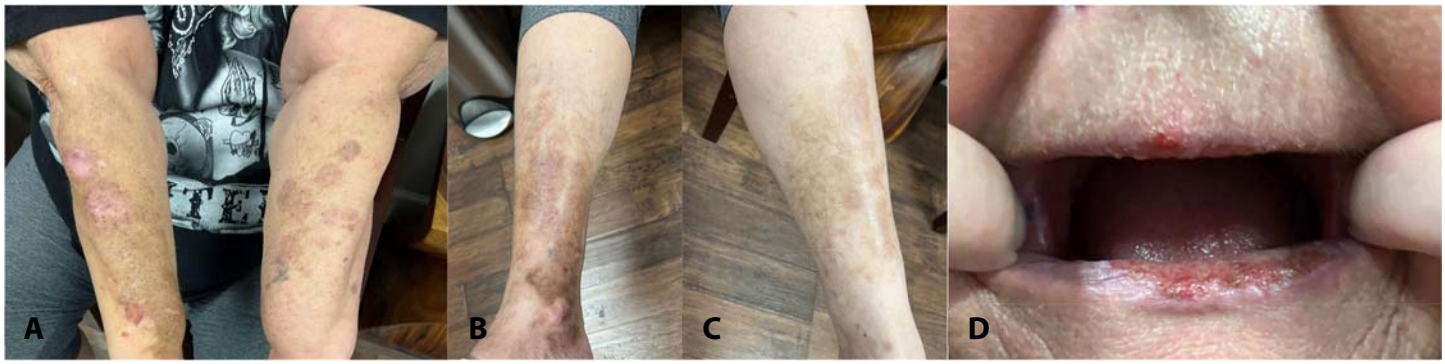

Figure 3. *Clinical images showing improvement of cutaneous lichen planus over the **A)** bilateral arms, **B)** right lower leg, and **C)** left lower leg after 1.5 months of treatment with 2mg oral baricitinib once daily. **D)** There were still active erosive lesions on the oral mucosa.*

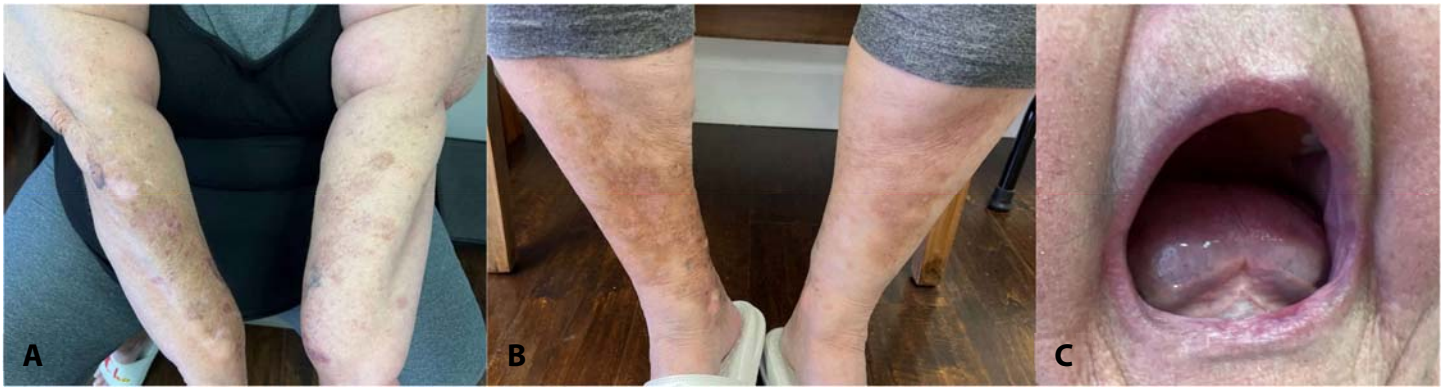

Figure 4. *Clinical images showing sustained improvement of cutaneous lichen planus over the **A)** bilateral arms, and **B)** bilateral lower legs after four months of treatment with 4mg oral baricitinib once daily. **C)** Treatment with ruxolitinib 1.5% cream for one month led to the clearance of erosive lesions on the oral mucosa.*

despite the increased dose of baricitinib and trials of multiple topical corticosteroids.

Subsequently, the patient was started on topical ruxolitinib 1.5% cream twice daily to the affected oral mucosa in addition to the baricitinib. Within one month of starting the ruxolitinib cream, her forearms (**Figure 4A**) and legs (**Figure 4B**) had sustained significant improvement. Furthermore, her oral mucosa was clear (**Figure 4C**), and the patient was able to eat regularly again.

When the patient ran out of ruxolitinib cream for three weeks, her oral lesions returned. However, restarting the ruxolitinib cream cleared the lesions.

Currently, the patient's disease remains well-controlled and off all other immunosuppressants and is controlled on oral baricitinib 4mg and topical ruxolitinib 1.5% cream twice daily. She does not note any side effects to date.

Case Discussion

Lichen planus is a chronic inflammatory condition associated with impaired quality of life. Risk factors for developing lichen planus include trauma, drugs, allergens, other autoimmune diseases, and hepatitis C [5]. Although it is unclear what may have contributed to our patient's disease, it is possible that her lichen planus was related to her history of hepatitis C or intravenous drug use. Following histopathological confirmation of her lichen planus, our patient failed many first-line therapies including systemic and topical agents.

There are no disease-specific treatments for lichen planus, so when it is recalcitrant to first-line therapies, finding the right therapeutic regimen can be a challenge. It is theorized that the pathogenesis of lichen planus is a consequence of autoimmune cytotoxic CD8+ T-cell responses against basal keratinocytes located in the epidermis [6]. Moreover, CD8+ T cell cytotoxicity is mediated via JAK2 signaling [6].

Thus, JAK inhibitors have shown therapeutic efficacy in immune-mediated diseases such as lichen planus. For example, topical ruxolitinib, a JAK1/2 inhibitor, has been shown to block interferon gamma signaling and downregulate STAT1 in cutaneous lichen planus, thereby improving disease severity [7].

A systematic review of JAK inhibitors for all variants of lichen planus found that patients on baricitinib (JAK1/2 inhibitor) achieved the highest rate of complete disease resolution (25%), followed by tofacitinib (JAK1/2/3 inhibitor), ruxolitinib (JAK1/2 inhibitor), and upadacitinib (JAK1 inhibitor), [5]. **Table 1** demonstrates the fold selectivity of these medications for the Janus kinase receptors [8-10].

Our patient had significant improvement of her cutaneous and vulvovaginal lesions with baricitinib therapy but continued to have flares of her erosive oral lichen planus despite increasing the dose from 2mg to 4mg daily. Although our patient did not report any side effects before or after the dosing change, adverse effects reported from JAK inhibitor usage include infectious events, embolism and thrombosis, and malignancy [11]. Higher dosing of

Table 1. *Relative fold selectivity of the Janus kinase receptors for baricitinib, ruxolitinib, tofacitinib, and upadacitinib [8-10].*

	Fold selectivity*			
JAKi	**JAK1**	**JAK2**	**JAK3**	**TYK2**
Baricitinib [8-10]	1.0	1.5	196.8	15.3
Ruxolitinib [8]	1.0	1.3	81.2	5.0
Tofacitinib [8,9]	1.0	2.0	1.0	42.0
Upadacitinib [8-10]	1.0	2.6	49.0	99.8

**JAK inhibitory activity (IC_{50}) was measured in μM. The numbers in the table represent the minimum possible fold selectivity.*

baricitinib seems to increase the risk of viral infections [11]. Lower dosing and scheduled laboratory monitoring may decrease the risk of adverse effects associated with JAK inhibitor use.

For cases of multi-variant lichen planus such as in our patient with cutaneous, vulvovaginal, and erosive oral lichen planus, a step-up approach to therapy may be necessary to achieve patient goals and minimize the use of other immunosuppressive therapies. In the case of our patient who failed a variety of topical corticosteroids and prednisone tapers to mitigate oral flare-ups while on baricitinib, adding a topical JAK inhibitor such as ruxolitinib cream was our next step. Although several case reports have demonstrated that oral JAK inhibitors can treat erosive oral lichen planus [12-14], our case demonstrates the novel use of addition of a topical JAK inhibitor to treat oral lichen planus refractory to oral baricitinib. Overall, the inhibition of inflammatory cytokine pathways by baricitinib and ruxolitinib likely contributed to the improvements in disease as seen in our patient.

Conclusion

Our case report expands on the utility of JAK inhibitors for the management of refractory lichen planus and variants of lichen planus, such as erosive oral lichen planus. Although the exact mechanism of action by which JAK inhibitors mitigate lichen planus remains unclear, our novel approach of combining oral baricitinib with topical ruxolitinib demonstrates a unique combination therapy to manage a challenging disease variant of lichen planus.

Potential conflicts of interest

RKS serves as a scientific advisor for LearnHealth, Arbonne, and Codex Labs and has served as a consultant or speaker for Burt's Bees, Novozymes, Biogena, Novartis, Sanofi, Bristol Myers Squibb, Pfizer, Nutrafol, Galderma, Novartis, Abbvie, Leo, UCB, Sun and Regeneron Pharmaceuticals. Remaining authors declare no conflicts of interest.

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