Successful Treatment of Erosive Lichen Planus With Tofacitinib: A Case Series and Review of the Literature

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ABSTRACT: Lichen planus (LP) is an inflammatory disease that affects the skin, hair, nails and mucous membranes. Erosive LP is a chronic and difficult-to-treat subtype of lichen planus, characterized by lesions on mucosal surfaces, particularly in the oral and genital areas. The prevalence of erosive LP has not been determined. To date, treatment has consisted of surgical intervention, photodynamic therapy, laser therapy, and systemic or topical drugs, including steroids and immunomodulatory agents. LP usually need longer periods of treatment and are known as precancerous lesions with a 0.4% to 12% conversion rate. In addition, nearly 25% of patients who develop erosive LP of the vulva are resistant to topical corticosteroids, which are the first choice of treatment. This study reports 6 cases with a mean age of 3.33 years, who were diagnosed with erosive LP lesions and previously failed in treatment with local, intralesional, and systemic steroids, and hydroxychloroquine. These patients were then treated with 10 mg of tofacitinib per day. Interestingly, with the new treatment, the patients' mean overall satisfaction score was 9.16 out of 10 (range: 8-10), the mean pain relief score was 9.16 out of 10 (range: 9-10) and patients' symptom improvement also began an average of 1.33 months after starting treatment (range: 1-2.5 months).

KEYWORDS: Lichen planus, erosive lichen planus, oral lichen planus, OLP, tofacitinib, JAK inhibitors

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What's already known about this topic?

Erosive lichen planus (LP), a persistent, inflammatory, and potentially premalignant variant of LP, is characterized by painful lesions on mucosal surfaces, particularly in the oral and vaginal regions.

Erosive LP types require a longer treatment period and are a difficult form of the disease to treat.

What does this study add?

Tofacitinib, a JAK1 and JAK3 inhibitor, could be used as an effective treatment for resistant erosive LP lesions.

Introduction

Lichen planus (LP) is a chronic immunological condition involving 0.5% to 2% of the population, mainly women.[1] The disease affects the skin, hair, nails and mucous membranes, especially the oral cavity and vulva.[2,3] Oral LP (OLP), clinically, can be distinguished by 6 types: reticular, plaque-like, papular, atrophic/erosive, ulcerative, and bullous, and more frequently impacts the gingiva, tongue, and buccal mucosa, symmetrically.[4] While 15% of OLP patients acquire cutaneous lesions, oral lesions can appear in up to 60% of cutaneous LP cases.[4] In addition, 20% of OLP patients also have concurrent vaginal lesions.[4] Erosive LP of the vulva (ELPV) is a form of LP known by painful white reticular plaques, erosive and scarring dermatitits involving the genital mucosa.[2,4]

The etiology of OLP and ELPV is not completely known. According to previous researches, these conditions are due to a localized autoimmune response caused by T-cell malfunction, however it is assumed that Janus kinase–signal transducer and activator of transcription (JAK-STAT)-dependent cytokines like IFN-γ can play a significant role in molecular pathogenesis of this disease.[5] JAKs are one of the therapeutic targets to control overreactive immune responses.[6]

Tofacitinib is a Janus kinase (JAK1 and JAK3) inhibitor, mainly used in moderate to severe rheumatoid arthritis and active ulcerative colitis.[7] Currently, the drug is being widely tested for immune-mediated diseases including psoriasis, alopecia areata, and vitiligo.[8-10] Two large randomized clinical trials have confirmed the efficacy of this drug in patients with moderate-to-severe plaque-type psoriasis,[11,12] some researchers also have reported promising results for controlling resistant LP with tofacitinib.[13-16] JAK inhibitors may control LP through suppressing JAK-STAT signaling in keratinocytes and lymphocytes.[5]

Table 1. Characteristics, treatment approaches and outcomes of patients with oral lichen planus.

PATIENT	AGE	GENDER	DISEASE DURATION (YEARS)	RESPONSE TO TREATMENT TIME (MONTHS)	TOFACITINIB THERAPY DURATION (MONTHS)	PATIENT SATISFACTION (OUT OF 10)	PAIN ALLEVIATION (OUT OF 10)	PREVIOUS TREATMENTS
#1	45	F	2	1	6	10	10	P + HQ
#2	43	M	2	2.5	5	8	9	LS
#3	53	F	4	1	6	9	9	MTX
#4	35	F	8	1.5	6	9	9	P + HQ
#5	44	F	2	1	5	9	9	P
#6	53	F	2	1	4	10	9	LS

Abbreviations: F, female; M, male; P, prednisolone; HQ, hydroxychloroquine; LS, local steroid; MTX, methotrexate.

However, the number of these studies is too small to make any conclusive conclusion. This paper reports 6 patients with erosive oral and genital LP lesions, resistant to the conventional therapies. They received tofacitinib for nearly 6 months and experienced significant improvement in their lesions and expressed high overall satisfaction.

Case Presentations

Six patients are presented in this paper with erosive oral and/or genital LP. Informed consent was taken from patients before starting the treatment. Five of the patients were female and 1 was male. All of the patients were in their 40s to 50s, except patient #4, a 35-year-old woman with a history of LP for 8 years. The mean disease duration was 3.33 years.

In addition to the oral lesions, patient #2, #3, and #4 had genital lesions too. Patient #4 had also gingival lesions.

The mostly previously used drug was corticosteroids. Two patients had used local steroids and 3 patients had used prednisolone 10 to 30 mg/day for 1 to 3 months according to disease severity. Hydroxychloroquine was added to the prednisolone in 2 of the patients.

The lesions were resistant, so tofacitinib was considered as the next treatment approach. After checking complete blood count, comprehensive metabolic panel, and lipid profile, the patients were treated with 5 mg of Rhofanib® (tofacitinib by Nanoalvand Corp, Iran) twice a day. The duration of patients' treatments is demonstrated in Table 1. All patients were treated for about 6 months, except patient #6 (mean: 5.33 months). The average response to treatment time was 2.66 months (Figures 1 and 2).

Visual analog scale (VAS) was used to report the pain alleviation and overall satisfaction of patients after cessation of treatment. As a result, all of the patients experienced alleviation of their symptoms. The range of pain alleviation score was 9 to 10 points on the VAS (mean: 9.16) and the range of overall satisfaction score was also 8 to 10 in VAS (mean: 9.16). No patient had recurrence during a 6 to 12 months of follow up.

Discussion and Review of the Literature

OLP mainly affects the oral cavity, buccal mucosa, gingiva, and the tongue. The most common symptoms are a feeling of burning or pain in the oral cavity, inability to eat certain foods, swelling, irritation, or bleeding of the gingiva and oral mucosa. Despite the skin lesions, OLP is not a self-limiting lesion and requires a longer treatment period. On the other hand, OLP lesions are known to be precancerous, with a conversion rate of 0.4% to 12% to squamous cell carcinoma, making appropriate diagnosis and treatment even more important.[17,18]

Most studies suggest that corticosteroids are the most effective agents for relieving the patient's symptoms. However, the side effects of corticosteroids and immunomodulatory agents are the main concern of researchers.[19] The main immunomodulatory agents are prednisolone, methotrexate, mycophenolate mofetil, cyclosporine, hydroxychloroquine, and rituximab. Currently, there are no reliable randomized clinical trials or systematic reviews to assess the superiority of each drug, and the choice is mainly made by expert opinion.[5]

Tofacitinib, a JAK1/3 inhibitor used mainly in moderate-to-severe rheumatoid arthritis and active ulcerative colitis, is another drug proposed for resistant OLP lesions.[12] In 2016, Vito Di Lernia and Bardazzi pointed out the importance of the IFN-gamma/CXCL10 pathway in the pathogenesis of LP. Since the IFN-gamma/CSCL10 axis is an important factor in the progression of LP lesions, the paper proposed targeting the JAK-STAT pathway as an intermediate factor in IFN-gamma signaling.[20] A summary of previous studies using tofacitinib in patients with different types of LP is shown in Table 2.

Similar to the present study, in a study by Yang et al[16] tofacitinib was prescribed at a dosage of 5 mg twice or 3 times daily for a period of 2 to19 months in 10 patients with lichen planopilaris, and 8 of them experienced significant clinical improvement in their lesion, with no serious adverse effects reported.

Also, a recent study by Damsky et al[5] reported successful treatment of 3 patients with recalcitrant erosive LP through tofacitinib 10 mg per day. Furthermore, another study has suggested this treatment approach for nail LP associated with

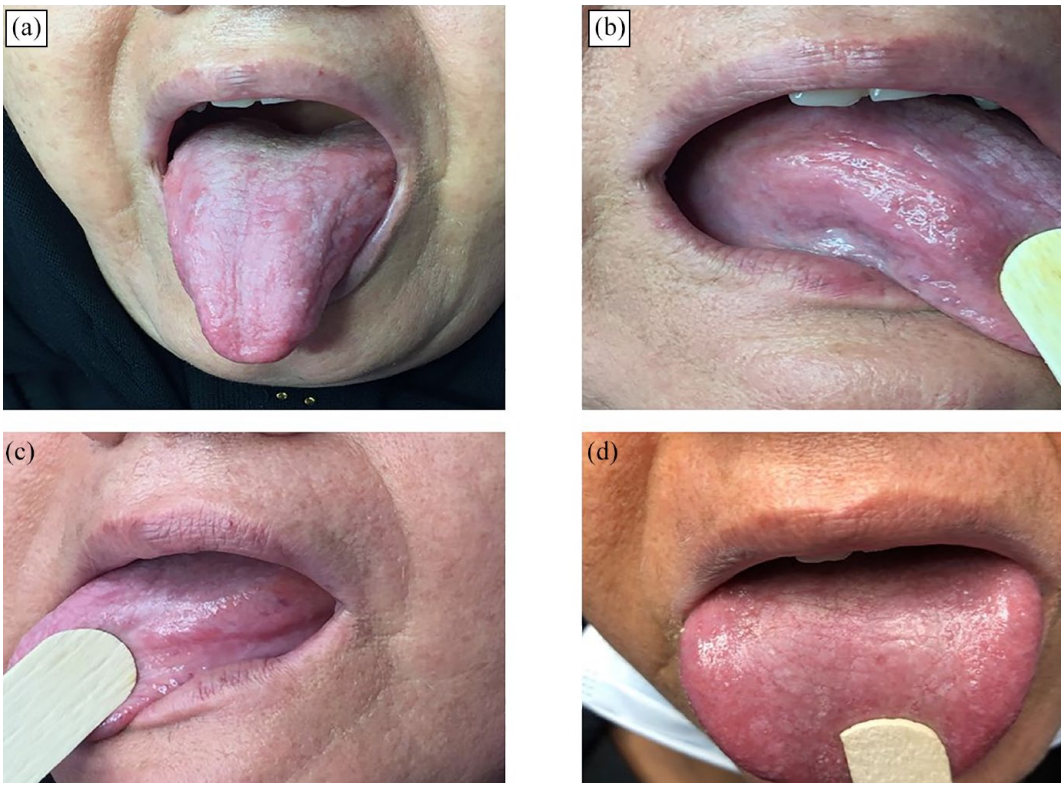

Figure 1. Patient #3, (a,b,c and d): photographs of oral lichen planus lesions in tongue area before treatment, (d): photograph of tongue lesions after receiving daily 10 mg of tofacitinib for 6 months.

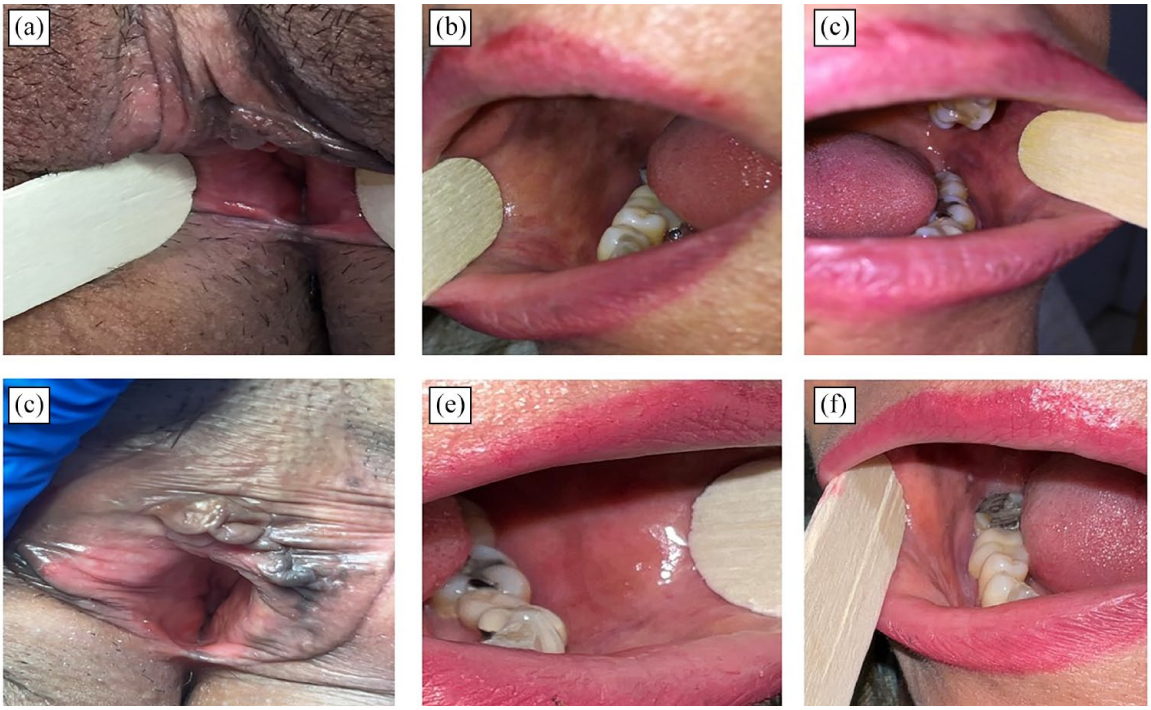

Figure 2. Patient #6, photographs of lichen planus lesion in genital area (a) and buccal mucosa (b and c) before treatment. (d-f): photographs of lesions after receiving daily 10 mg of tofacitinib for 4 months.

alopecia universalis.[13] Batra et al[21] reported a positive clinical response after prescribing tofacitinib and dapsone in 2 patients with lichen planopilaris and frontal fibrosing alopecia who had previously failed treatment several times. In addition, Papp et al[12] reported an improvement of erosive OLP lesions with JAK inhibitor therapy.

This article reports 6 cases with OLP lesions that were resistant to anti-TNF and steroids and had marked clinical

Table 2. Summary of previous studies using tofacitinib for different types of lichen planus.

AUTHORS	YEAR OF PUBLICATION	NUMBER OF PATIENTS	GENDER	AVERAGE AGE	TYPE OF LESIONS	SITE OF LESIONS	TREATMENT TYPE	TREATMENT DURATION	RESULTS	COMPLICATIONS
Yang et al[16]	2018	10	6 F, 4 M	55	Recalcitrant lichen planopilaris	Scalp	Oral tofacitinib 5 mg twice or three times daily	2-19 mo	Clinical improvement in 8 patients	Weight gain
Damsky et al[5]	2020	3	2 F, 1 M	67.33	Recalcitrant erosive lichen planus	Oral, ocular, vaginal, penile, urethra, esophageal	Oral tofacitinib 5 mg twice daily	NS	Clinical improvement in all patients	No adverse effects
Plante et al[14]	2020	9	8 F, 1 M	58.33	Lichen planopilaris with/ without frontal fibrosing alopecia	Scalp	Topical in 3 patients (2% cream twice daily), oral in 5 patients (5mg twice or three times daily), both types in one patient	Topical: 1-17 mo	Clinical improvement in all patients in long-term (better in oral type) Oral: 4-15mo	NS
Seiringer et al[15]	2020	1	M	51	Hypertrophic lichen planus	Extremities	Oral tofacitinib 5 mg twice daily	20 wk	Improvement in Dermatology Life Quality Index and pruritus	No adverse effects
Batra et al[21]	2020	1	M	27	irreversible lichen planopilaris and frontal fibrosing alopecia	Scalp	oral tofacitinib 5mg twice a day	4 mo	Reduced itching, visibility of scalp and regrowth of hair	NS
Diab et al[22]	2022	1	F	60	irreversible lichen planopilaris	cheeks, forehead, and hairline	oral tofacitinib (dose not specified)	NS	Gradual improvement	NS
Kooybaran et al[23]	2022	1	F	77	Resistant severe lichen planus	Oral, esophageal, vaginal, scalp	oral tofacitinib 5mg twice daily then tapered to 5 mg/day	7.5 mo	Cessation of oropharyngeal and esophageal pain, improvement in oral mucosa erosions	NS

Abbreviations: F, female; M, male; NS, not specified.

improvement after treatment with tofacitinib (Rhofanib®). Controlled clinical trials are needed to more accurately evaluate these results and to more accurately assess the side effects of the drug with long-term use. However, the JAK inhibitors can be considered potentially effective drugs for the treatment of resistant OLP lesions.

Conclusion

This study reports the clinical efficacy of tofacitinib in relieving symptoms of resistant erosive OLP lesions and improving patient satisfaction. Further studies are needed to evaluate the drug with a larger sample size and to investigate its efficacy in controlling patients' signs and symptoms and its potential long-term side effects.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

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Informed Consent

Informed consent was obtained from the patients for participating in the study and the right of subjects were protected.

Consent for Publication

Written informed consent was obtained from the patients for publication of their anonymized information and any accompanying images.

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