Efficacy of Topical Tofacitinib 2% Gel in Chronic Hand Eczema – A Case Series

Dear Editor,

Chronic hand eczema (CHE) is a disabling inflammatory disease of the hands markedly affecting the quality of life. Topical medications like steroids, calcineurin inhibitors, and moisturisers remain the mainstay of therapy. However, there is a continuing search for newer therapies owing to the lack of desired efficacy or side effects to older treatment options. Topical Janus kinase inhibitors (JAKis) like ruxolitinib and delgocitinib have shown efficacy in the treatment of CHE.[1,2] Topical tofacitinib is a JAKi recently marketed in India. Herein, we present eight cases of CHE treated with topical tofacitinib.

There were eight adult patients with CHE (hand eczema lasting more than or equal to 3 months or with at least two episodes per year).[2] The patients were asked to avoid suspected or definite allergens if found positive with any allergen on patch test and were treated with topical tofacitinib after informed consent. A detailed history of the disease's duration associated medical conditions, treatment, and family history was obtained. Topical tofacitinib 2% gel (Tofarus gel ®) was prescribed to all the participants to apply twice daily for 4 weeks. All patients were prescribed levocetirizine at a 5 mg/day dose and a bland moisturizer containing liquid paraffin and white soft paraffin. Hand eczema severity index (HECSI) scoring, and investigator global assessment (IGA) were done at baseline and at 4 weeks. Histopathologic examination was done in cases of doubtful clinical diagnosis. The assessor was blinded. Statistical calculations were done using Microsoft Excel 2021.

The duration of the disease ranged from 3 months to 6 years. The HECSI score ranged from 21 to 121 at the baseline with a mean value of 61.75 ± 32.23. The median HECSI at baseline was 63 with an inter-quartile range (IQR) of 42. At the end of 4 weeks, the mean HECSI score was 44.25 ± 22.7. The median HECSI at the end of 4 weeks was 42 with an IQR of 38. The baseline characteristics with improvement in HECSI and IGA scores are depicted in Table 1. The change in mean HECSI and IGA scores were statistically significant (P = 0.018 and P = 0.00387, respectively). The composite erythema, infiltration, and papulation scores also decreased significantly at 4 weeks (P = 0.017 and 0.015, respectively). Fifty percent of our patients had more than 25% reduction in HECSI. Photographic documentation of improvement in CHE has been shown in Figure 1. Though there was a decrement in the mean score of scales, vesiculation, and edema at 4 weeks, it was not statistically significant. A mild burning sensation was the only side effect observed in one patient.

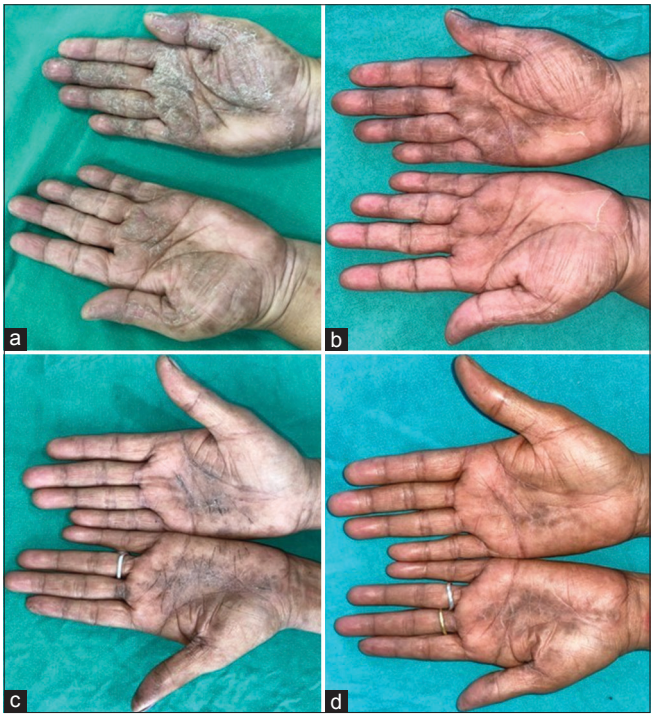

Figure 1: (a-c) Patient 3 and patient 7 with hyperkeratotic eczema at baseline and (b and d) showing their improvement in the disease after 4 weeks of topical tofacitinib treatment, respectively

Biopsy was done in three patients. Histopathology study revealed compact hyperkeratosis, parakeratosis, moderate spongiosis, and lymphocyte exocytosis in the epidermis and perivascular lymphocytic infiltrate in the papillary dermis, suggestive of hand eczema [Figure 2]. Patch test was negative in all the patients.

Topical treatments are preferred in CHE due to the localized nature of the disease and its remitting and relapsing course. Topical corticosteroids, though very effective, are suitable for only short-term remission of disease and are not a sustainable treatment option because of their side effects.[2] JAKi modulates the JAK-STAT pathway, involved in the downstream pathogenesis of Th1 (interferon γ), Th2 (IL-4, IL-13, IL-31, IL-33), and Th22 (IL-22), mediating the pathogenesis of CHE.

Topical delgocitinib, a pan JAKi, has shown promising efficacy and safety in the treatment of CHE over 16 weeks of treatment.[1] Topical deglocitinib at concentrations of 8 mg/g and 20 mg/g showed statistically significant improvement (P < 0.05) in IGA, HECSI, itch and pain numerating rating scales (NRSs), and patient's global assessment (PGA) scores from baseline to 16 weeks.[1] The safety profile of topical deglocitinib has been favorable

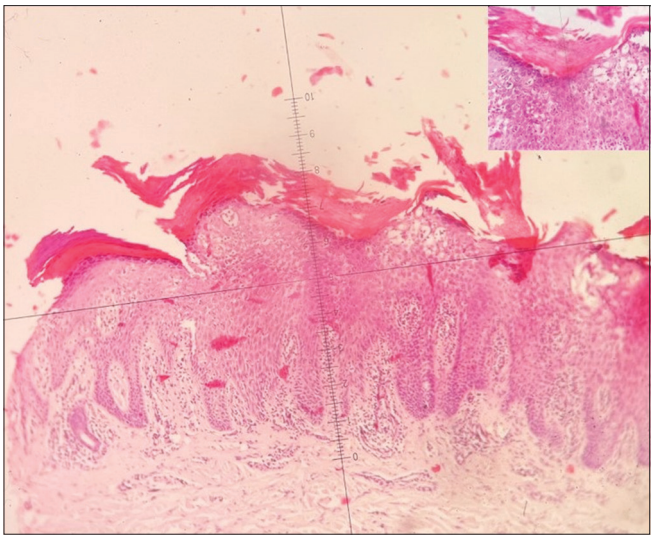

Figure 2: Patient 4 showing compact hyperkeratosis, parakeratosis, moderate spongiosis, and lymphocyte exocytosis in epidermis and perivascular lymphocytic infiltrate in papillary dermis, suggestive of hand eczema (H&E, 100x). The inset shows high-power view demonstrating spongiosis with lymphocytic exocytosis in the epidermis (H&E, 400x)

with only side effects of localized pain and itching not causing any discontinuation in treatment.[1]

A 4-week interim analysis on efficacy of ruxolitinib 1.5% cream in CHE showed a mean reduction in HECSI of 44 ($P < 0.01$) and statistically significant improvement in IGA, itch, and DLQI scores. No treatment-related adverse effects were reported, thus indicating ruxolitinib 1.5% to be a possible effective and safe medication for treatment of moderate to severe CHE.[3]

In the present series of cases, we observed significant improvement in HECSI scores and IGA from baseline after 4 weeks of treatment. The most significant effect of tofacitinib was seen on components of erythema and infiltration in CHE. Our results were similar to those of the study on topical ruxolitinib in CHE treatment at the end of 4 weeks by Smith *et al*.[3] Topical tofacitinib has been used for plaque psoriasis, atopic dermatitis, and alopecia areata.[4,5] We evaluated the efficacy of topical tofacitinib in CHE. This case series gives a preliminary insight into the effects of tofacitinib in hand eczema, making it a potentially safe therapeutic option in CHE management. The short duration of treatment, lack of longer follow-up, and a smaller number of cases are some of the limitations of our case series. A gel formulation of tofacitinib (only available formulation during the observation) was used; however, an ointment would be more appropriate to be used on palms.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The

Table 1: Characteristics of patients with improvement in HECSI and IGA scores after treatment

Case	Age	Gender	Occupation	History of atopy	Duration of disease (in months)	Type of CHE	Baseline HECSI	HECSI after 4 weeks	% HECSI reduction	Baseline IGA score	IGA score after 4 weeks	Biopsy
1	64	Female	Homemaker	Present	24	Hyperkeratotic eczema	62	32	48.4	3	2	Not done
2	35	Male	Industrial worker	Absent	9	Dyshydrosiform eczema	88	76	13.7	4	3	Not done
3	55	Female	Homemaker	Present	6	Hyperkeratotic/psoriasiform eczema	121	68	43.8	4	2	Biopsy proven
4	50	Male	Factory worker	Absent	72	Dyshydrosiform eczema	37	26	29.7	2	1	Biopsy proven
5	70	Female	Homemaker	Absent	24	Chronic insult dermatitis	67	60	10.4	3	1	Not done
6	60	Female	Teacher	Absent	3	Hyperkeratotic	34	26	23.5	2	1	Not done
7	38	Male	Engineer	Absent	6	Hyperkeratotic	64	52	18.8	3	1	Biopsy proven
8	27	Female	Labourer	Absent	3	Hyperkeratotic	21	14	33.3	2	1	Not done

patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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