SHORT COMMUNICATION

Efficacy of Oral Alitretinoin in Treatment of Mycosis Fungoides Palmaris et Plantaris

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Mycosis fungoides palmaris et plantaris (MFPP) is a subtype of mycosis fungoides (MF) characterized by hyperkeratotic psoriasiform patches or plaques on the palms and soles (1). Treatment for early-stage MF typically involves skin-directed therapies (SDTs), such as phototherapy and topical agents. However, phototherapy is very time-consuming, and the efficacy of SDTs can be limited in MFPP due to the curved/hidden nature of the affected skin surfaces and the specific location where thick stratum corneum can reduce the absorption of topical agents. Oral bexarotene, the only approved retinoid for the treatment of cutaneous T-cell lymphomas (CTCLs), has a high frequency of adverse effects and is unavailable in certain countries, including Korea. Oral alitretinoin, approved for chronic recalcitrant hand eczema with positive outcomes and minimal side-effects, (2, 3) has shown promising results in the treatment of MF (4–6), as well as in MFPP (7).

MATERIALS AND METHODS

In all patients, the diagnosis was established by a combination of clinical presentation, histopathology, and immunohistochemistry based on the diagnostic algorithm for early-stage MF (8). Patients with equivocal cases of MFPP, in which palmoplantar eczema cannot be completely ruled out histologically; for example, in cases where atypical lymphocytes are observed but prominent spongiosis is also present, were excluded. Patients who received any type of concomitant topical treatment were also excluded. The efficacy of the treatment at week 12 was assessed by reviewing clinical photographs and medical records, using Physician's Global Assessment (PGA) and the modified total lesion symptom score (mTLSS) (2, 3). Instead of area-based assessment tools, such as severity-weighted assessment tool (SWAT) (9), mTLSS was used because it enables a comprehensive assessment of detailed features (erythema, scaling, fissured, etc.) of localized lesions in MFPP. Assessments were performed weekly for the first 12 weeks and then at monthly intervals in stable cases.

RESULTS AND DISCUSSION

Clinical data are summarized in **Table I**. The mean age at diagnosis was 52.4 years. Eight patients (57.1%) were women, and 6 (42.9%) were men. The mean disease duration was 45.1 months. Assessing the baseline PGA grade, 5 (35.7%) were assessed as severe, and 9 (64.3%) as moderate, and the mean baseline mTLSS score for all patients was 9.5. All patients were in stage IA and received oral alitretinoin monotherapy (30 mg) for at least 12 weeks. None of the patients received any other systemic treatments before using alitretinoin. After 12 weeks of treatment, 9 out of 14 patients (64.3%) achieved a clinical response, as determined by a PGA of "clear" or "almost clear". The mean time to clinical response was 10.3 weeks. At 12 weeks of treatment, the mTLSS reduced from 9.5 to 2.9, representing a 69.5% reduction. The follow-up data are shown in Table SI. During the mean follow-up period of 33.1 months, 5 out of 9 patients (55.6%) who achieved a clinical response experienced relapse after discontinuing alitretinoin, with a mean relapse time of 19.8 months. Four of the 5 relapsed cases restarted alitretinoin, and all showed improvement. The mean total treatment duration was 48.6 weeks. In patient 8, who achieved a partial response, a follow-up biopsy was performed after 12 weeks of treatment, revealing the disappearance of epidermotropism and scant dermal lymphocytic infiltrate (Fig. S1). Regarding safety, alitretinoin was generally well-tolerated, showing minimal side-effects, such as headache (35.7%) and hypertriglyceridaemia (28.6%). Other reported side-effects included mucocutaneous dryness (21.4%) and facial flushing (7.1%). No severe adverse events or marked laboratory abnormalities were observed.

Retinoids are synthetic derivatives of vitamin A that bind to intracellular retinoic acid receptors A (RAR) and/or retinoid X receptors (RXR). Among retinoids, alitretinoin (9-cis-retinoic acid) is an endogenous pan-agonist that binds to both RARs and RXRs with high affinity

Table I. Treatment and efficacy assessment during 12 weeks of oral alitretinoin

Pat. No.	Age (years)/ Sex	Duration (months)	Stage	PGA grade baseline	mTLSS score baseline	PGA grade at week 12	mTLSS score at week 12	Time to response within 12 weeks
1	62/M	12	IA	Moderate	8	Almost clear	3	12 weeks
2	58/M	7	IA	Moderate	8	Clear	1	5 weeks
3	50/F	12	IA	Moderate	8	Clear	0	10 weeks
4	63/F	12	IA	Moderate	7	Moderate	6	NA
5	52/M	12	IA	Severe	13	Almost clear	2	10 weeks
6	59/F	36	IA	Moderate	10	Clear	1	12 weeks
7	52/F	12	IA	Moderate	9	Almost clear	3	12 weeks
8	17/M	168	IA	Severe	14	Moderate	9	NA
9	48/F	60	IA	Moderate	6	Clear	1	12 weeks
10	54/F	36	IA	Moderate	9	Clear	1	8 weeks
11	67/M	36	IA	Severe	12	Clear	1	12 weeks
12	45/M	180	IA	Severe	10	Mild	4	NA
13	31/F	12	IA	Moderate	7	Mild	4	NA
14	76/F	36	IA	Severe	12	Mild	5	NA

NA: not applicable; mTLSS: modified total lesion symptom score; PGA: Physician`s Global Assessment.

(10), while other retinoids are limited in their binding to either RARs (isotretinoin, acitretin) or RXRs (bexarotene). The use of retinoids for the treatment of CTCLs is well established. In previous retrospective studies investigating alitretinoin treatment in CTCLs, response rates were reported to be favourable, and side-effects were minimal (4–6). Overall, alitretinoin demonstrated efficacy in treating MFPP, as it exhibited a significant improvement in disease severity (**Fig. 1**). However, relapse following alitretinoin discontinuation was common, highlighting the need for prolonged maintenance therapy or timely re-administration based on short-term follow-up. As alitretinoin shows a favourable response in MFPP as well as in chronic recalcitrant hand eczema (2, 3), it could be a good option in cases where the diagnosis is equivocal between MFPP and palmoplantar eczema.

In conclusion, alitretinoin demonstrates rapid clinical improvement and appears to be an effective and safe option for MFPP. Further studies with larger sample sizes and more extended follow-up periods are needed to confirm these findings and optimize the treatment approach for MFPP.

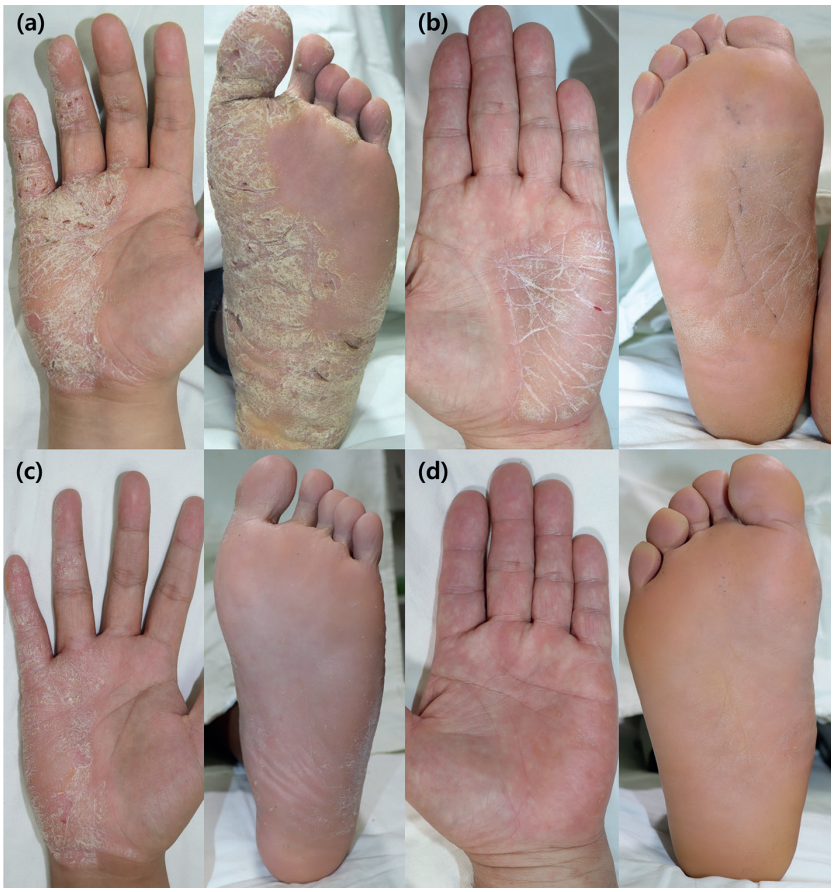

Fig. 1. (a, b) Erythematous to brownish hyperkeratotic, fissured, or desquamated patches and plaques on the palms and soles. (Patient numbers 8, 11) (c, d) After 12 weeks of oral alitretinoin treatment, the skin lesions were almost completely improved. (Patient numbers 8, 11).

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The authors have no conflicts of interest to declare.

REFERENCES

1. Kim ST, Jeon YS, Sim HJ, Kim SH, Kim YK, Suh KS, et al. Clinicopathologic features and T-cell receptor gene rearrangement findings of mycosis fungoides palmaris et plantaris. J Am Acad Dermatol 2006; 54: 466–471.
2. Dirschka T, Reich K, Bissonnette R, Maares J, Brown T, Diepgen TL. An open-label study assessing the safety and efficacy of alitretinoin in patients with severe chronic hand eczema unresponsive to topical corticosteroids. Clin Exp Dermatol 2011; 36: 149–154.
3. Ruzicka T, Lynde CW, Jemec GB, Diepgen T, Berth-Jones J, Coenraads PJ, et al. Efficacy and safety of oral alitretinoin (9-cis retinoic acid) in patients with severe chronic hand eczema refractory to topical corticosteroids: results of a randomized, double-blind, placebo-controlled, multicentre trial. Br J Dermatol 2008; 158: 808–817.
4. Kapser C, Herzinger T, Ruzicka T, Flaig M, Molin S. Treatment of cutaneous T-cell lymphoma with oral alitretinoin. J Eur Acad Dermatol Venereol 2015; 29: 783–788.
5. Alhusayen R, Vu TT, Almuhanna N, Wohlmuth-Wieser I, Hardin J, Hughes JM, et al. Evaluation of alitretinoin for the treatment of mycosis fungoides and Sézary syndrome. Dermatology 2021; 237: 479–485.
6. Kaemmerer T, Stadler PC, Helene Frommherz L, Guertler A, Einar French L, Reinholz M. Alitretinoin in the treatment of cutaneous T-cell lymphoma. Cancer Med. 2021; 10: 7071–7078.
7. Miernik B, Schmidt V, Technau-Hafsi K, Kern JS, Meiss F. Alitretinoin in the treatment of palmoplantar mycosis fungoides: a new and promising therapeutic approach. Clin Exp Dermatol 2015; 40: 445–447.
8. Pimpinelli N, Olsen EA, Santucci M, Vonderheid E, Haeffner AC, Stevens S, et al. Defining early mycosis fungoides. J Am Acad Dermatol 2005; 53: 1053–1063.
9. Stevens SR, Ke MS, Parry EJ, Mark J, Cooper KD. Quantifying skin disease burden in mycosis fungoides-type cutaneous T-cell lymphomas: the severity-weighted assessment tool (SWAT). Arch Dermatol 2002; 138: 42–48.
10. Cheng C, Michaels J, Scheinfeld N. Alitretinoin: a comprehensive review. Expert Opin Investig Drugs 2008; 17: 437–443.