SHORT COMMUNICATION



# Teriflunomide-induced Palmoplantar Lichenoid Eruption: A Case Report

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Teriflunomide is frequently administered as a disease-modifying agent for the treatment of relapsing types of multiple sclerosis (MS). Teriflunomide functions by inhibiting dihydroorotate dehydrogenase (DHODH), an enzyme integral to *de novo* pyrimidine synthesis. It suppresses the proliferation of activated lymphocytes and curtails the expansion of activated T and B cells, which initiate the inflammatory cascade within the central nervous system (1). Lichenoid drug eruption (LDE) represents an uncommon type of cutaneous lichenoid reaction triggered by various medications. Clinically and histopathologically, LDE closely mirrors lichen planus (LP), making differential diagnosis challenging. Like LP, LDE infrequently affects the palms and soles, with only isolated cases reported in the literature (2). Herein, we present a lichenoid drug eruption induced by teriflunomide that solely affects the palms and soles.

## CASE REPORT

A 43-year-old man with MS presented with a pruritic eruption on the palms and soles that was not accompanied by systemic symptoms. He had no prior history of dermatological disorders, including the absence of previous similar eruptions, and his family history was unremarkable. Two months ago, the recent modification to his medication regimen was the initiation of teriflunomide for MS. These skin lesions appeared within the first month of treatment. Dermatological examination revealed numerous scaly, hyperkeratotic, violaceous papules and plaques on both hypothenar eminences, mid-palms, and the internal arch of the plantar areas (**Fig. 1**). The oral mucosa, hair, nails, and other skin surfaces were normal. Standard laboratory testing was routine, including blood chemical analysis, urine analysis, and complete blood count. The results of serological testing for syphilis, autoimmune antibodies, and the hepatitis B and C viruses were negative. Examination with potassium hydroxide (10% KOH) and the mycologic cultures of scrapings from palmar/plantar lesions also yielded negative results. Histopathological examination showed hypergranulosis, irregular acanthosis with a saw-tooth-like appearance, apoptotic basal keratinocytes, and band-like mononuclear cell infiltration with rare eosinophils involving the dermo–epidermal junction (**Fig.**

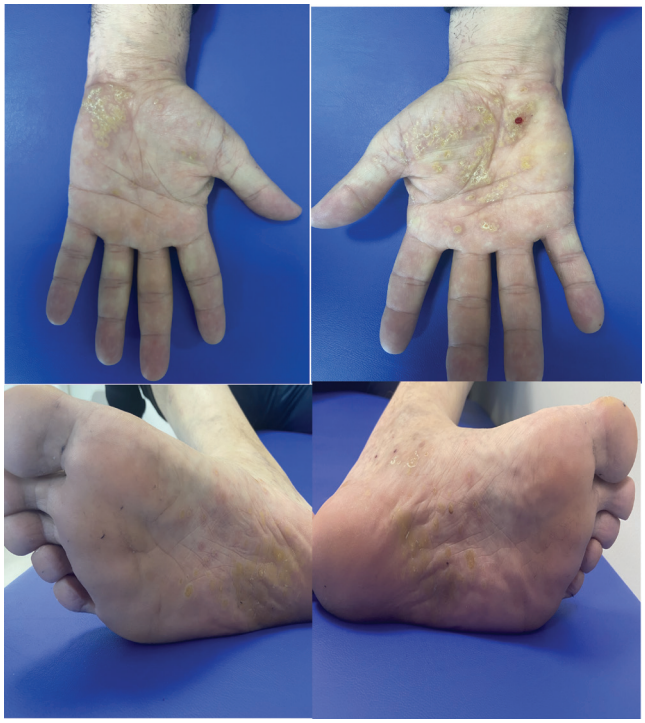

**Fig. 1. Numerous scaly, violaceous papules and hyperkeratotic plaques on both hypothenar eminences, mid-palms, and the internal arch of the plantar areas.** Permission given by patient to publish these photos.

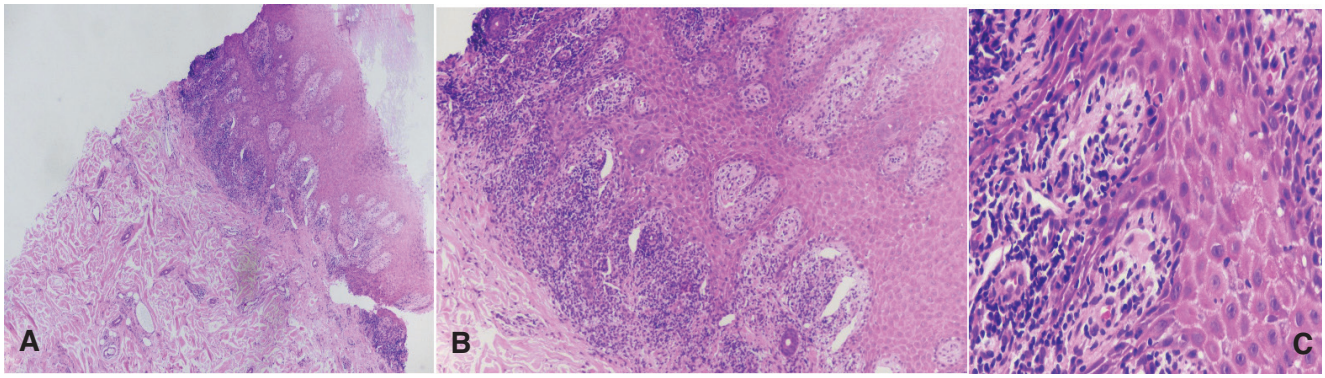


**Fig. 2. Histopathological findings.** (A) Hypergranulosis and irregular acanthosis with a saw-tooth-like appearance (H&E, x10). (B) Band-like mononuclear cell infiltration with rare eosinophils involving the dermo–epidermal junction (H&E, x100). (C) Apoptotic basal keratinocytes with rare eosinophils (H&E, x200).

**2**). The dermatological and histopathological findings concurred with a teriflunomide-induced lichenoid drug eruption diagnosis. Following the discontinuation of teriflunomide treatment, the patient received a daily dose of 25 mg of oral acitretin and applied a topical moisturizing emollient. After 2 months, all the acral lesions were cleared entirely, although the palms and soles retained residual hyperpigmentation. After 3 months, the patient stopped using acitretin and had no lesions at the 6-month follow-up.

## DISCUSSION

LDE is marked by the chronic activation of CD8+ cytotoxic T lymphocytes targeting epidermal cells. These lymphocytes can trigger apoptosis in basal keratinocytes and secrete various cytokines, elevating the expression of class II major histocompatibility complex molecules and facilitating antigen presentation to $CD4^+$ T cells (1, 2). The drugs most frequently associated with these reactions include gold salts, penicillamine, beta-blockers, antihypertensives, thiazide diuretics, antimalarials, nonsteroidal anti-inflammatory drugs, several antibiotics, and antitubercular medications (1, 3). Only 1 case report triggered by teriflunomide has been reported in the literature (1).

Frequent adverse effects associated with teriflunomide include but are not limited to the following: gastrointestinal disturbances (e.g., diarrhoea and nausea), headache, hypertension, cardiovascular mortality, thrombocytopenia, interstitial lung disease, opportunistic infections (caused by immunosuppression), and peripheral neuropathy (1, 4). Alopecia and hair thinning are common adverse effects of teriflunomide from a dermatological standpoint. Furthermore, several case reports have reported additional cutaneous adverse reactions associated with teriflunomide. These include psoriasiform eruptions, bullous pemphigoid, toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, and nail loss (4, 5).

The lesions are often purple, flat, and polygonal, resembling classic lichen planus. However, LDE shows significant polymorphism, with more scaly lichenoid, psoriasiform, and eczematiform lesions resolving with more residual hyperpigmentation and no Wickham striae. These lesions are typically more widespread, with symmetrical distribution over the trunk and limbs, and are more commonly found in photo-distributed areas with infrequent mucosal involvement (2, 3). In our case, the lesions were primarily hyperkeratotic and atypically located on the palms and soles. Eosinophils, localized parakeratosis, perivascular dermal infiltrates, and deeper lymphocytic infiltrate involvement are histological indicators of LDE. However, histopathologically, it is not possible to consistently distinguish between LDE and idiopathic LP. An indication of an LDE is the spontaneous resolution of symptoms within weeks to months after the offending drug is discontinued, as well as a history of drug use.

Topical corticosteroids are considered the first-line treatment for LDE, along with cessation of the causative drug. Additionally, oral corticosteroids, oral antihistamines, and topical calcineurin inhibitors have been reported as beneficial. For patients who do not respond to corticosteroid treatment, experience a relapse after therapy, or have contraindications to corticosteroids, acitretin may be considered as a potential second-line therapy (4, 5). In our patient, acitretin was selected as the initial treatment due to the hyperkeratotic nature of the lesions on the palms and soles.

In conclusion, individuals undergoing treatment with teriflunomide commonly present with dermatological manifestations, predominantly characterized by hair thinning. However, the occurrence of LDE linked to teriflunomide, like that described in our case, has also been reported. Neurologists must acknowledge the crucial importance of identifying this possible adverse reaction associated with teriflunomide, the medication may require to be stopped in individuals with MS.

## REFERENCES

1. Agharbi FZ, Aasfara J, Oqbani K, Slamti K, Chiheb S. Lichenoid drug eruption induced by teriflunomide. Ann Indian Acad Neurol 2023; 26: 275–277. https://doi.org/10.4103/aian.aian_27_23
2. Paolino G, Rongioletti F. Palmoplantar lichenoid drug eruptionfollowing the administration of Pfizer-BioNTech COVID-19 vaccine. JAAD Case Rep 2022; 21: 182–184. https://doi.org/10.1016/j.jdcr.2022.01.014
3. Musicante M, Goenaga-Vázquez Y, Klimas N. Lichenoid drug eruption induced by erenumab. JAAD Case Rep 2023; 32: 26–28. https://doi.org/10.1016/j.jdcr.2022.11.018
4. Khurana D, Kaur G, Kumaran MS, Choudhary R, Ashraf R, Thakur V. Teriflunomide-induced drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome. Clin Exp Dermatol 2021; 46: 166–169. https://doi.org/10.1111/ced.14339
5. Arslan D, Aksakal AB, Erdem Ö, Tuncer MA. A case of drug-induced bullous pemphigoid associated with teriflunomide: a patient with relapsing multiple sclerosis. Mult Scler Relat Disord 2020; 43: 102157. https://doi.org/10.1016/j.msard.2020.102157