Case Report

Lichenoid Drug Eruption Induced by Teriflunomide

Fatima-Zahra Agharbi, Jehanne Aasfara[1], Kenza Oqbani[2], Khalqui Slamti, Soumiya Chiheb

Departments of Dermatology, [1]Neurology and [2]Pathology, Sheikh Khalifa Hospital, Faculty of Medicine, Mohamed VI University of Health Sciences, Casablanca, Morocco

Abstract

Lichenoid drug eruptions are a type of skin reaction that is caused by medication and mimics idiopathic lichen planus. Various medications have been known to cause lichenoid drug eruptions, such as antibiotics, anti-convulsants, anti-diabetics, anti-malarials, anti-tubercular drugs, anti-hypertensives, psychiatric drugs, chemotherapeutic agents, diuretics, heavy metals, and non-steroidal anti-inflammatory drugs. Various cutaneous side effects have been reported in association with teriflunomide. We present the case of a patient who developed a lichenoid eruption because of teriflunomide. The dermatologists and neurologists should be aware of these skin side effects.

Keywords: Aubagio, lichenoid eruption, teriflunomide

Introduction

Teriflunomide, the active metabolite of leflunomide, is a recent treatment for relapsing remitting multiple sclerosis.[1] There are some reported skin changes associated with teriflunomide.[2-8] Here, we report a first case of lichenoid drug eruption in a 34-year-old man which developed 1 month after teriflunomide initiation for treated multiple sclerosis with complete resolution after 6 weeks of drug withdrawal.

Observation

A 34-year-old man with multiple sclerosis presented with generalized itchy scaly rash of 1 month duration. These skin lesions appeared 1 month after starting teriflunomide (Aubagio®) for multiple sclerosis. Dermatological examination of the patient revealed a diffuse lichenoid eruption made of purple-colored papules without typical wickham striae involving the trunk and extremities [Figure 1]. No significant nail changes or mucosal involvement was identified. Pathology showed a band-like lymphocytic infiltrate with basal keratinocyte vacuolization and hyperkeratosis orthokeratosis [Figure 2]. This clinical and histopathological finding was consistent with a lichen planus or a drug-induced lichenoid reaction. Teriflunomide was the only drug implicated in the absence of other drug use. Improvement of the lesions after its withdrawal confirmed the diagnosis of lichenoid reaction. Remission was complete after 6 weeks.

Discussion

Teriflunomide is the second oral agent approved by the United States Food and Drug Administration and European Medicines Agency for maintenance therapy of relapsing remitting multiple sclerosis.[1] Its mechanism of action is via reversible inhibition of the mitochondrial enzyme dihydroorotate dehydrogenase (DHODH), a key enzyme of the pyrimidine de novo synthesis in rapidly dividing cells, mainly lymphocytes.[1,2] Teriflunomide limits the proliferation of activated T- and B-cells which are thought to contribute to the damaging inflammatory processes associated with multiple sclerosis within the central nervous system.[1]

Common side effects of this drug include diarrhea, nausea, headache, elevated transaminase levels, hypertension, cardiovascular death, thrombocytopenia, interstitial lung disease, opportunistic infections because of the immuno-suppression and peripheral neuropathy. Regarding skin side effects, teriflunomide usually is reported to induce hair thinning and loss of hair.[1,7] There are also a few case reports about other cutaneous adverse effects of teriflunomide, such as psoriasiform eruption, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, nail loss, and bullous pemphigoid.[2-8]

Lichenoid drug reaction (LDR) is a cutaneous drug reaction that mimics lichen planus. These reactions can occur months or years after taking a medication. The underlying basis for

Address for correspondence: Prof. Fatima-Zahra Agharbi, Service de Dermatologie, Hôpital Universitaire Cheikh Khalifa, Faculté de Médecine, Université Mohamed VI des Sciences de la Santé, Casablanca, Maroc.
E-mail: aghmarifz@gmail.com

Submitted: 11-Jan-2023 **Revised:** 12-Feb-2023 **Accepted:** 20-Feb-2023
Published: 15-Jun-2023

DOI: 10.4103/aian.aian_27_23

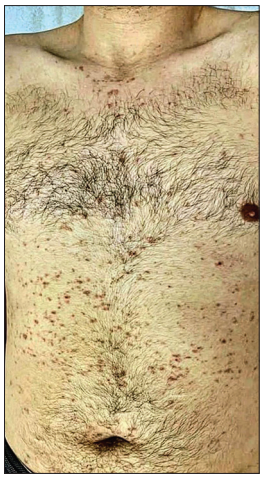

Figure 1: Lichenoid drug eruption of trunk

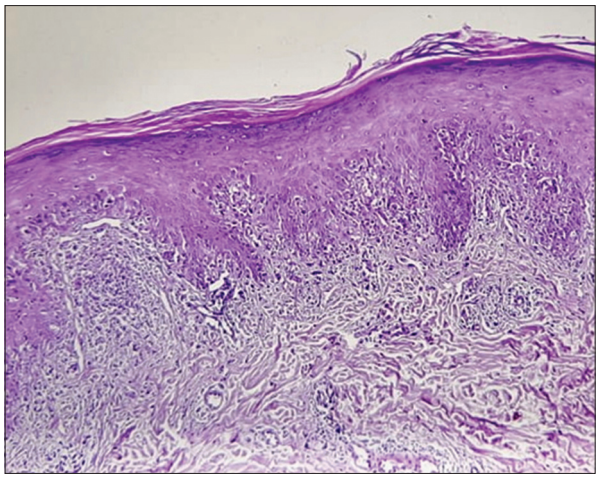

Figure 2: Band-like lymphocytic infiltrate with basal keratinocyte vacuolization and hyperkeratosis orthokeratosis

this delay remains unclear but is likely to be influenced by many variables, including dose, medication class, drug–drug interactions, and other host factors.[9] The lesions are typically purple, flat, and polygonal in shape and look like classic lichen planus. However, LDRs are characterized by a marked polymorphism including lichenoid, psoriasiform, and eczematiform lesions with the absence of Wickham striae. They tend to be more disseminated with symmetrical distribution on the trunk and limbs. In addition, they are more commonly present in photo-distributed areas and rarely involve the mucosa.[9-12] Some histologic findings are indicative of drug-induced lichenoid eruption, such as the presence of eosinophils, focal parakeratosis, and perivascular dermal infiltrates and deep involvement of the lymphocytic infiltrate; however, histology alone cannot be reliably used to distinguish between drug-induced and idiopathic lichen planus.[11]

A history of drug intake and spontaneous resolution which occurs within weeks to months after stopping the offending drug is considered indicative of an LDR.[12]

The medications known to be frequently associated with LDRs are gold salts, penicillamine, anti-malarial drugs, thiazide diuretics, and β-blockers. Other drugs that have been relatively frequently associated with lichenoid eruption include non-steroidal anti-inflammatory drugs, hypolipidemic agents, phenothiazine, and several antibiotics.[12] To the best of our knowledge, lichenoid drug eruption has never been reported in association with teriflunomide treatment. However, there are rare cases reports of lichenoid drug eruption induced by his precursor leflunomide.[13]

LDRs are classified as type IV delayed hypersensitivity; however, the physiological mechanism by which drugs can induce lichenoid reactions remains unclear.[14] It seems to be that drug molecules bind to epidermal proteins and render the epidermis antigenic by acting as haptens stimuli. CD8+ cytotoxic T-cells may secrete TGF, which triggers keratinocyte apoptosis.[13,14]

In the present case, the diagnosis of LDR is made based on the temporal relationship between lesion onset and exposure to the suspected causative agent, resolution of symptoms upon discontinuing the causative agent, and clinical and histopathologic features.

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 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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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