LICHENOID DRUG ERUPTION ASSOCIATED WITH ANTITUBERCULAR DRUGS: A CASE REPORT

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ABSTRACT

Lichenoid drug eruption, also known as drug-induced lichen planus, is an uncommon cutaneous adverse reaction caused by certain medications. It is characterized by the symmetric appearance of flat-topped, erythematous to violaceous papules resembling idiopathic lichen planus, typically involving the trunk and extremities. The latency period between initiation of the suspected medication and the onset of skin lesions may range from several weeks to over one year, largely depending on the nature of culprit drug, dosage and the patient's individual response. Differentiating lichenoid drug eruption from idiopathic lichen planus can be challenging due to similarities in both clinical and histopathological features. In this study, we present a case of lichenoid drug eruption induced by anti-tuberculosis therapy, one among common triggers presented in clinical practice.

Keywords: *Lichenoid drug eruption, LDE, lichen planus, antituberculosis drugs.*

INTRODUCTION

Lichenoid drug eruption (LDE) is a rare drug-induced reaction which predominantly occurs in older adults, which may be related to accumulative drug exposure with increasing age. The mean age of onset ranges from 44 to 66 years. A wide range of medications have been implicated, including angiotensin-converting enzyme (ACE) inhibitors, thiazide diuretics, antimalarials, beta-blockers, gold salts, penicillamine, tyrosine kinase inhibitors and tumor necrosis TNF-alpha antagonists such as infliximab, adalimumab, and etanercept. Among these, the incidence among patients receiving antituberculosis drugs has been reported to be approximately 10%, with isoniazid and rifampicin being the most common culprits.

Clinically, lichenoid drug eruptions closely resemble idiopathic lichen planus, presenting as flat-topped, violaceous papules and plaques with a symmetric distribution involving both the trunk and extremities. Unlike idiopathic lichen planus, mucosal involvement is typically absent. In addition, photosensitivity may occur in lichenoid drug eruptions, as ultraviolet radiation can induce photochemical reactions that provoke the immune system to recognize the drug or its metabolites as foreign antigens. Given the clinical similarities to idiopathic lichen planus, ancillary investigations are often necessary to aid in making the diagnosis. Dermoscopic examination frequently reveals the absence of Wickham's striae. Histopathology plays a critical role in identifying drug-induced lesions with certain features such as dyskeratosis, necrotic keratinocytes and particularly the presence of eosinophils providing further diagnostic support. In this report, we describe a case of lichenoid drug eruption associated with antituberculosis

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therapy, highlighting the particular clinical course, laboratory findings, and histopathological characteristics.

CASE REPORT

Clinical characteristics

A 70-year-old man presented with a roughly 6-month history of skin lesions. Initially, he developed widespread small, violaceous papules scattered on both forearms, accompanied by extreme pruritus. Over time, the lesions gradually increased in size, with some coalescing into larger plaques. New lesions given similar morphology subsequently appeared on his lower legs, thighs, and abdomen. The patient had not received any prior treatments for his worsening skin condition, and the lesions continued to progress, spreading to multiple body sites.

Upon clinical examination, multiple top-flat papules and plaques with dark violaceous coloration were observed, which symmetrically distributed over the bilateral forearms, lower legs and thighs. Many lesions had merged to form large plaques on the trunk (Figure 1). The patient complained about severe pruritus.

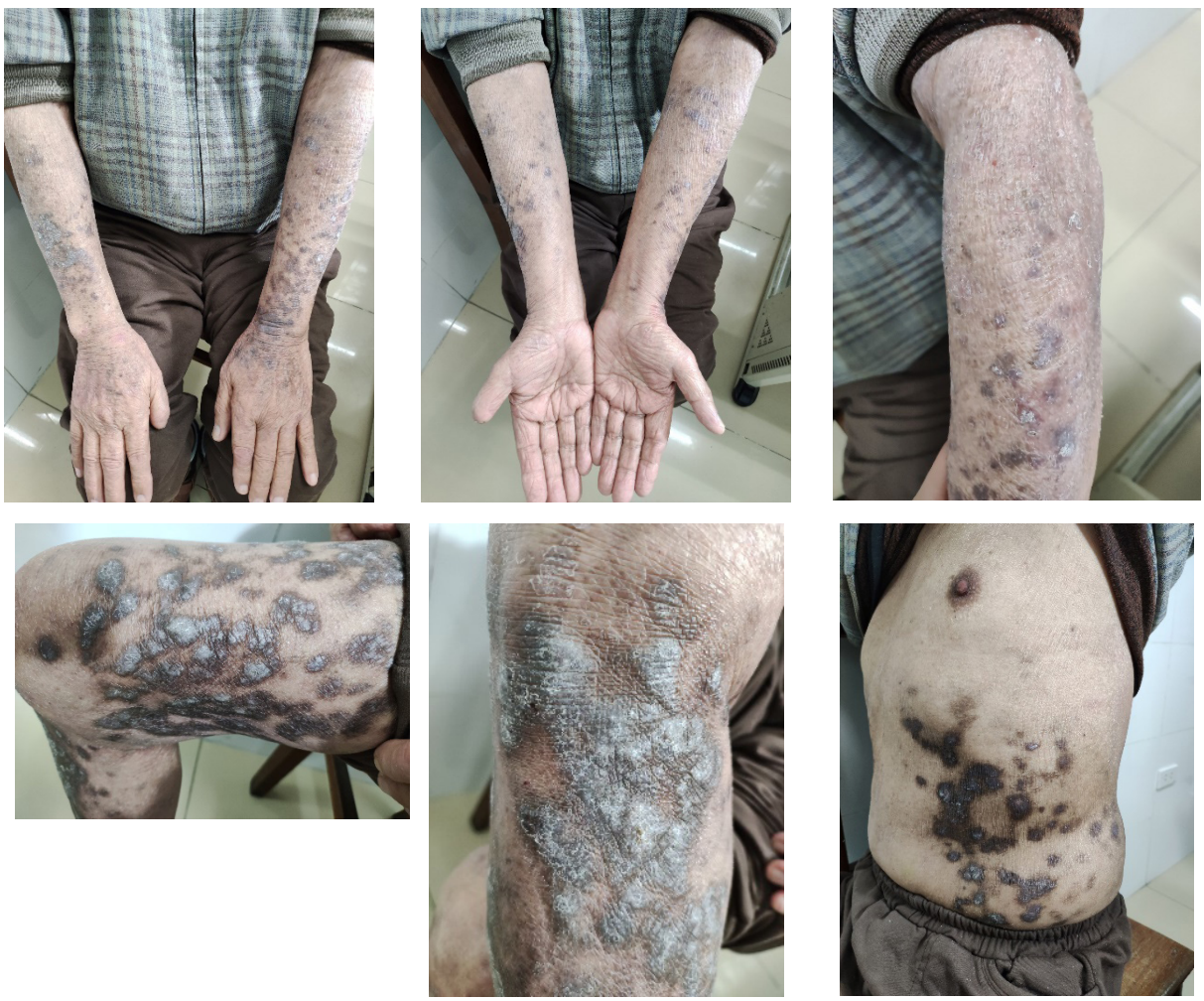

Figure 1. Clinical examination showed shiny violaceous papules and plaques with a symmetric distribution, diffusely involving all four limbs and the trunk

In addition, examinations of other sites, including the scalp, oral mucosa, genital mucosa and nails revealed no detectable lesions (Figure 2).

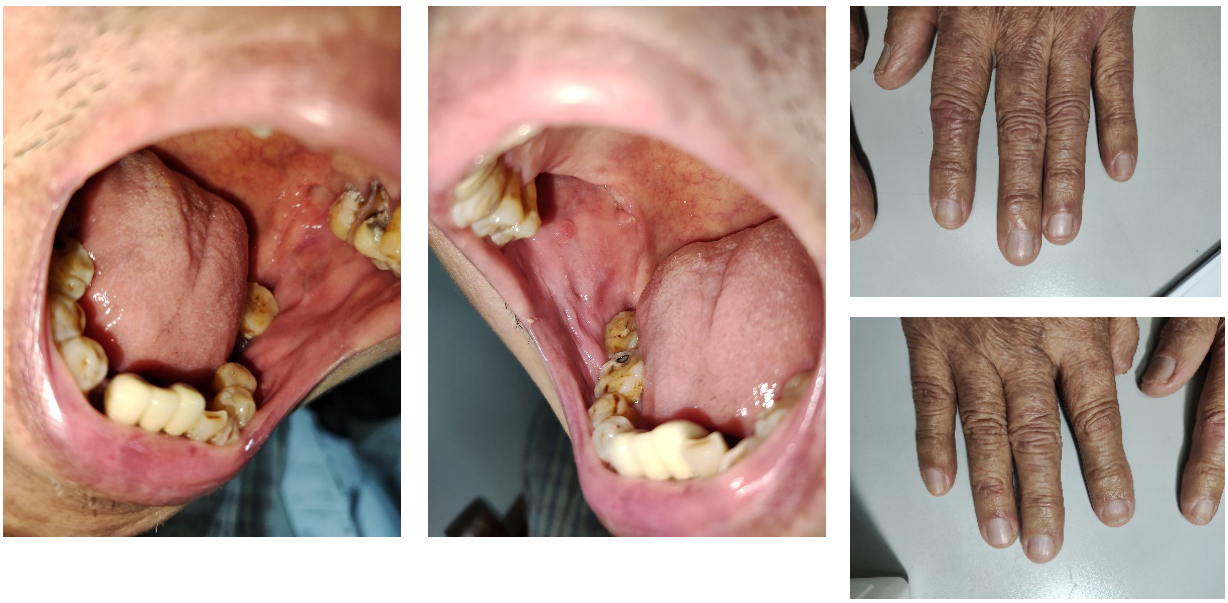

Figure 2. Absence of oral mucosal involvement and nail changes

The patient's medical history revealed a diagnosis of pulmonary tuberculosis, detected following symptoms of fever, fatigue and pleural effusion. He was adhering to the standard regimen of pulmonary tuberculosis, which included isoniazid, rifampicin, and ethambutol. After approximately two months, the patient developed cutaneous lesions with the characteristics described above. No similar condition was reported among family members or close contacts.

Laboratory findings

Dermoscopy of lesions on the hands, legs and abdomen demonstrated bluish-gray dots on a fibrotic background with overlying scales, along with dotted and linear vessels. Histopathological examination of a forearm lesion showed irregular acanthosis, basal layer hyperpigmentation, vacuolar degeneration of the basal membrane and scattered dyskeratotic keratinocytes. The upper dermis revealed pigment incontinence and a band-like lymphohistiocytic infiltrate at the dermoepidermal junction and around blood vessels, with scattered eosinophils (Figure 3).

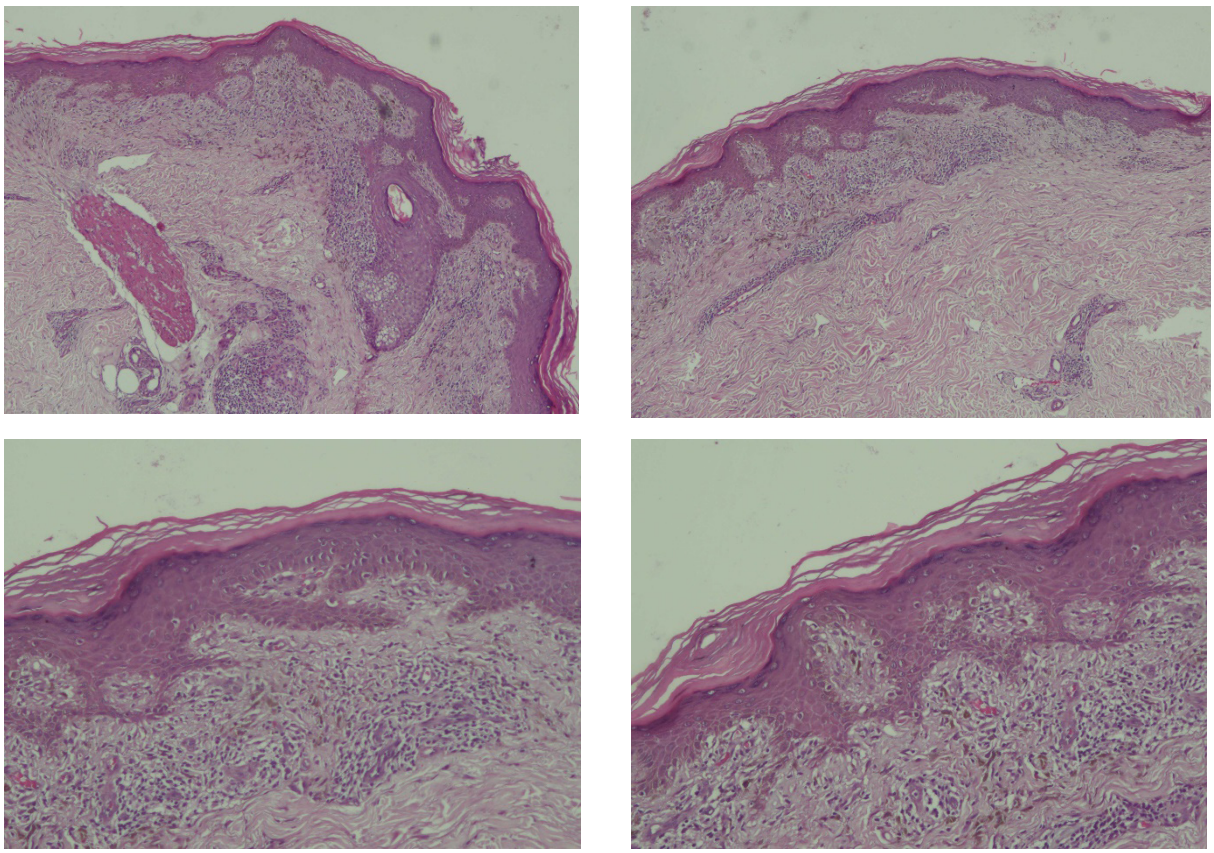

Figure 3. Histopathological features of the skin lesion showed irregular epidermal hyperplasia, basal layer hyperpigmentation, vacuolar degeneration of the basal membrane and scattered dyskeratotic keratinocytes. The dermis exhibits pigment incontinence, a band-like mononuclear infiltrate at the dermal-epidermal junction and around blood vessels with scattered eosinophils

DISCUSSION

Although lichenoid drug eruption can occur at any age, our patient, aged 70 years, fell to a high-risk group due to the increased likelihood of exposure to multiple medications compared with other populations.

The latency period from drug initiation to the onset of LDE can vary from several weeks to one year. Therefore, in many cases, determining the exact causative agent may be challenging and, in some instances, overlooked. In addition to thorough clinical evaluation of lesion morphology, a detailed medication history is of paramount importance in identifying the etiology. In this current case, the patient's cutaneous lesions developed approximately two months after starting antituberculosis therapy. The skin manifestations were relatively typical for lichenoid changes. However, unlike idiopathic lichen planus, lichenoid drug eruptions often occur on the extensor surfaces of the limbs and the dorsal aspects of the hands, with a tendency to symmetrically develop to bilateral upper limbs and widespread extension to the trunk. Thus, in cases with typical lesions, a provisional diagnosis can be made without much difficulty.

To confirm the diagnosis in this patient, we examine dermoscopy and skin biopsy for histopathological examination. Dermoscopy revealed bluish-gray pigmentation with dotted and linear vessels. One notable dermoscopic clue that helps differentiate lichenoid drug eruption from idiopathic lichen planus is the absence of Wickham's striae.

Lichenoid drug eruptions typically involve the dermis and can elicit a type IV hypersensitivity reaction mediated by tumor necrosis factor-alpha (TNF-α), which induces keratinocyte apoptosis via cytotoxic $CD8^+$ T lymphocytes. This inflammatory cascade subsequently affects basal layer melanocytes, leading to excessive melanin production and hyperpigmentation. Histopathological analysis often reveals irregular thickening of the granular layer with basal cell damage, along with alteration or loss of the undulating dermal papillary ridges, producing a "saw-tooth" appearance. In particular, the presence of scattered eosinophils in this case preferally supports a drug-induced hypersensitivity reaction. Therefore, although lichenoid drug eruption can often be diagnosed clinically, in atypical presentations or when obtaining a reliable drug history is challenging, histopathological features substantially contribute to making the diagnosis.

Management of lichenoid drug eruption has remained a challenge. Once the condition is identified, patients are generally advised to discontinue the suspected offending drug and to initiate treatment with high-potency topical corticosteroids, such as fluocinonide or clobetasol. If topical corticosteroids prove ineffective, calcineurin inhibitors may be considered. In cases with widespread or refractory lesions, oral prednisone or systemic retinoids may be required.

In our patient, who was in the final month of antituberculosis therapy, discontinuing the causative drug posed a considerable risk of progessing tuberculosis, particularly drug-resistant tuberculosis. To address this concern, reintroducing medications one at a time can be a feasible approach to help identify the offending agent. Although previous studies have suggested that ethambutol is a more common cause compared to isoniazid or rifampicin, the patient's skin lesions in our cohort gradually improved over time and the hyperpigmentation eventually resolved. Nevertheless, pinpointing the exact causative drug remained challenging. Therefore, given that the patient still had one month of tuberculosis treatment remaining, we opted for strong topical corticosteroids and observed only a modest clinical response after one month. Upon completion of the tuberculosis regimen, the patient will be considered for systemic corticosteroid therapy.

CONCLUSIONS

Lichenoid drug eruption, also referred to as drug-induced lichen planus, is a relatively uncommon clinical entity whose presentation may closely mimic idiopathic lichen planus. Therefore, an accurate diagnosis requires a comprehensive approach, meticulous clinical examination, histopathological evaluation, and a detailed medication history-particularly regarding high-risk drug classes, including antituberculosis agents. The condition often resolves spontaneously within weeks to months after discontinuation of the offending drug. However, in cases where cessation of the medication is not possible or in patients with persistent, extensive lesions that significantly impair quality of life, treatment with potent topical corticosteroids alone or in combination with systemic corticosteroids or retinoids may be warranted, depending on the severity of the disease.

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