

CAS CLINIQUE / CASE REPORT

ADALIMUMAB-INDUCED LICHENOID DRUG ERUPTION

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ABSTRACT • Tumor necrosis factor (TNF)- α inhibitors are being widely and increasingly used for the management of a spectrum of rheumatologic diseases that are refractory to conventional disease modifying anti-rheumatic drugs. Various cutaneous side effects have been reported after treatment with TNF- α inhibitors. We present a case report of a 26-year-old male patient who developed a lichenoid drug eruption few months after the initiation of adalimumab for the management of Crohn's disease. We also highlight the clinical and histopathologic differences between lichenoid drug eruptions and idiopathic lichen planus.

Keywords : adalimumab, drug reaction, lichenoid, anti-TNF- α , Crohn's disease

INTRODUCTION

Tumor necrosis factor (TNF)- α inhibitors are being widely used for the management of a spectrum of rheumatologic diseases. TNF- α inhibitors have been reported to cause a wide range of cutaneous drug eruptions. The most common being urticaria, rash, stomatitis, and injection-site reactions [1-4]. More severe side effects such as erythema multiform, discoid and subacute cutaneous lupus erythematosus, atopic dermatitis, necrotizing vasculitis, and bullous skin lesions have also been reported [5]. We report a rare case of lichenoid drug eruption secondary to adalimumab.

CASE DESCRIPTION

A 26-year-old Caucasian male patient, known to have Crohn's disease, presented to our clinic for evaluation of mildly pruritic skin lesions of three months duration.

Nine months prior to presentation, the patient was started on 40 mg adalimumab, a fully humanized anti-TNF- α monoclonal antibody, one subcutaneous injection every two weeks for the management of Crohn's disease. The patient denied the use of any other medication. Six months after starting adalimumab, the patient started noticing the appearance of skin lesions over the

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RÉSUMÉ • Les inhibiteurs du facteur de nécrose tumorale alpha sont largement utilisés dans le traitement d'un large spectre de maladies rhumatologiques réfractaires aux agents conventionnels anti-rhumatismaux modificateurs de la maladie. Divers effets secondaires cutanés ont été rapportés après traitement par les inhibiteurs du facteur de nécrose tumorale alpha. Nous présentons le cas d'un jeune homme de 26 ans qui a développé une éruption médicamenteuse lichénoïde peu après le début de l'adalimumab pour le traitement de la maladie de Crohn. Ce travail met en relief les effets secondaires cutanés de l'adalimumab. De plus, il relève les différences cliniques et histopathologiques entre les éruptions médicamenteuses lichénoïdes et le lichen plan idiopathique.

forehead, right temporal area, forearms, and dorsum of the hands. Upon questioning, the patient reported no fever, myalgia, arthralgia, abdominal pain, nor throat pain prior to the onset of the cutaneous lesions. Adalimumab was suspended.

Three months after the onset of skin lesions, the patient presented to our clinic for evaluation. Examination of the skin revealed multiple annular, hyperpigmented, centrally atrophic lesions, localized over the anterior scalp, forehead, and right temple with no associated alopecia. Flat topped, polygonal, papular and annular, erythematous-to-violaceous lesions localized on the dorsal aspect of both forearms and hands were noted (Fig. 1). Koebner phenomenon was present secondary to itching over the right forearm. Patient had no nail or mucosal lesions. Two skin biopsies were taken from the forearm and dorsal hand lesions for histopathologic evaluation. Histopathologic findings included irregular epidermal acanthosis, compact orthokeratosis, hypergranulosis, and scattered necrotic keratinocytes. A superficial dermal perivascular lichenoid lymphocytic infiltrate with few eosinophils, encroaching upon the dermo-epidermal junction with vacuolar alteration was noted (Fig. 2). There was no histologic features suggestive of cutaneous lupus. These findings were compatible with lichenoid drug eruption.

Knowing that the patient was only taking adalimumab prior to the appearance of these skin lesions, a causal correlation between adalimumab administration and the appearance of the lichenoid lesions was assumed.

Patient was put on oral prednisone at a dose of 1 mg/kg per day tapered over 12 weeks, desloratadine per os, and clobetasol propionate cream.

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FIGURE 1. (a) Annular, hyperpigmented, centrally atrophic lesions over the forehead, and right temporal area. (b-c). Multiple polygonal, flat topped, papular/annular, erythematous-to-violaceous lesions over both forearms and hands.

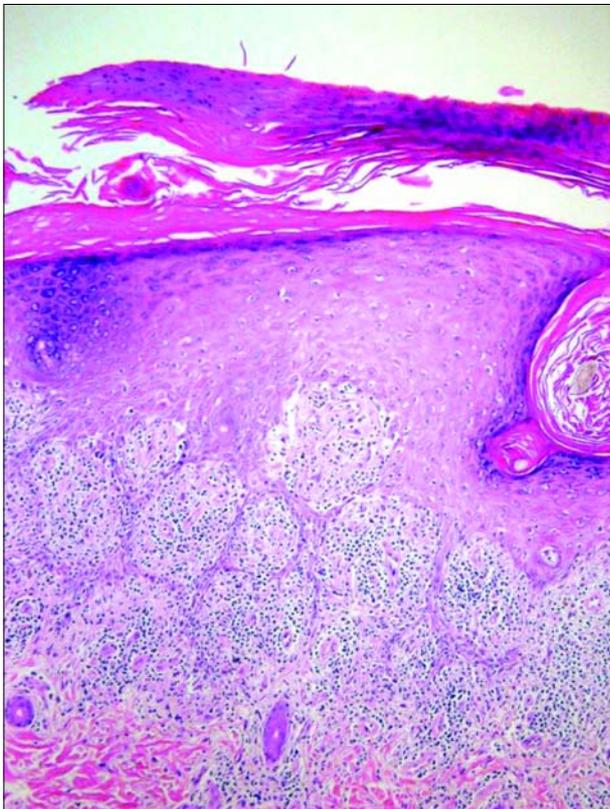


FIGURE 2. Presence of prominent parakeratosis, hypergranulosis, band-like dermal lichenoid lymphocytic infiltrate, and scattered necrotic keratinocytes (hematoxylin and eosin x100).

DISCUSSION

TNF- α inhibitors have been previously described in the literature as a treatment modality for many cutaneous inflammatory diseases, including lichen planus [6-7]. Despite being effective in treating immuno-mediated conditions, TNF- α inhibitors have been associated with the induction of autoimmune cutaneous phenomena due to an uncontrolled production of interferon- α by plasmacytoid dendritic cells [8-9]. Adalimumab has been implicated in many cases of drug-induced lichen planus. One report described the occurrence of a mucosal lichenoid drug eruption one month after the initiation of adalimumab for treatment of psoriasis [10]. Asarch *et al.* also reported a case of mucocutaneous lichen planus-like lesions 16 months after initiating adalimumab for the treatment of psoriasis [11]. Another report by Flendrie *et al.* described the occurrence of a lichen-planus like eruption sparing the mucous membranes, three weeks after the initiation of adalimumab for treatment of rheumatoid arthritis [5].

Differentiating between lichenoid drug eruption and idiopathic lichen planus can be evident clinically and on histopathology. Lesions in lichenoid drug eruption are more generalized, photo distributed, and spare the classic sites of idiopathic lichen planus, mainly the mucous membranes [12]. Wickham's striae that are frequently

TABLE I
CLINICAL AND HISTOPATHOLOGIC DIFFERENCES BETWEEN DRUG-INDUCED AND IDIOPATHIC LICHEN PLANUS (LP)

	DRUG-INDUCED LICHEN PLANUS	IDIOPATHIC LICHEN PLANUS
Distribution	Generalized, sparing the classic sites of idiopathic LP	Wrists, flexor forearms, sacral area, lower legs, genitalia
Mucous membrane involvement	Often spared	Often involved
Wickham's striae	Absent	Present
Photodistribution	Frequent	Unusual
Morphology	Ecematous, psoriasiform	Shiny, flat-topped, polygonal, violaceous papules
Histology	Presence of parakeratosis	Absence of parakeratosis

present in idiopathic lichen planus are absent in lichenoid drug eruption. Lesions in idiopathic lichen planus appear to be shiny, flat-topped, polygonal, and violaceous. The main difference on histopathology is the presence of parakeratosis in lichenoid drug-induced eruptions which is absent in cutaneous idiopathic lichen planus. Varying degrees of eosinophilic and/or plasma cell infiltrates may also be present in lichenoid drug eruption (Table I) [12]. The main diagnostic clinical feature is the disappearance of the lesions after the cessation of the culprit drug [10]. Our patient had mild improvement after three months of cessation of adalimumab. In a review article by Asarch *et al.* seven out of the nine patients who stopped the TNF- α inhibitor after the appearance of the lichenoid drug eruption had complete recovery. The remaining two patients had mild-to-moderate improvement [11].

In conclusion, lichenoid drug eruption and idiopathic lichen planus have different clinical and histopathological features. In the majority of the cases, lesions clear after stopping the culprit drug. However, the diagnosis of TNF- α inhibitors induced lichenoid drug eruption should not be ruled out in the presence of other clinical and histopathological features, even if the lesions do not disappear few months after stopping the anti-TNF therapy.

REFERENCES

- Maini R, St Clair EW, Breedveld F *et al.* Infliximab (chimeric anti-tumor necrosis factor alpha monoclonal antibody) versus placebo in rheumatoid arthritis patients receiving concomitant methotrexate: a randomised phase III trial. ATTRACT Study Group. *Lancet* 1999; 354: 1932-9.
- Weinblatt ME, Keystone EC, Furst DE *et al.* Adalimumab, a fully human anti-tumor necrosis factor alpha monoclonal antibody, for the treatment of rheumatoid arthritis in patients taking concomitant methotrexate: the ARMADA trial. *Arthritis Rheum* 2003; 48: 35-45.
- Keystone EC, Kavanaugh AF, Sharp JT *et al.* Radiographic, clinical, and functional outcomes of treatment with adalimumab (a human anti-tumor necrosis factor monoclonal antibody) in patients with active rheumatoid arthritis receiving concomitant methotrexate therapy: a randomized, placebo-controlled, 52-week trial. *Arthritis Rheum* 2004; 50: 1400-11.
- Moreland LW, Schiff MH, Baumgartner SW *et al.* Etanercept therapy in rheumatoid arthritis. A randomized, controlled trial. *Ann Intern Med* 1999; 130: 478-86.
- Flendrie M, Vissers WH, Creemers MC *et al.* Dermatological conditions during TNF-alpha-blocking therapy in patients with rheumatoid arthritis: a prospective study. *Arthritis Res Ther* 2005; 7: R666-76.
- Yarom N. Etanercept for the management of oral lichen planus. *Am J Clin Dermatol* 2007; 8: 121.
- Chao TJ. Adalimumab in the management of cutaneous and oral lichen planus. *Cutis* 2009; 84: 352-8.
- Pontikaki I, Shahi E, Frasin LA *et al.* Skin manifestations induced by TNF-alpha inhibitors in juvenile idiopathic arthritis. *Clin Rev Allergy Immunol* 2012; 42 (2): 131-4.
- Holló P, Szakonyi J, Kiss D *et al.* Successful treatment of lichen planus with adalimumab. *Acta Derm Venereol* 2012; 92 (4): 385-6.
- De Simone C, Caldarola G, D'Agostino M *et al.* Lichenoid reaction induced by Adalimumab. *J Eur Acad Dermatol Venereol* 2008; 22: 626-7.
- Asarch A, Gottlieb AB, Lee J *et al.* Lichen planus-like eruptions: an emerging side effect of tumor necrosis factor-alpha antagonists. *J Am Acad Dermatol* 2009; 61: 104-11. Review.
- Bolognia JL, Jorizzo JL, Rapini RP. Lichen Planus and Lichenoid Dermatoses. In: *Dermatology*, 2nd ed., Elsevier Inc, 2008: 167-170.