Letter to the Editor

The first case of adalimumab-induced hypertrophic lichen planus

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Sir,

Tumor necrosis factor (TNF) alpha inhibitors are new therapeutics used to treat a range of rheumatological diseases refractory to conventional drugs. Several anti-TNF-α side effects have been described, especially cutaneous manifestations [1]. A number of so-called lichenoid eruptions have been reported in three different clinical patterns: lichen planus-like (LP-like), non-specific maculopapular eruption, and psoriasis-like. These cases are unified by a common lichenoid histology [2]. However, hypertrophic LP has never been reported in association with anti-TNF-α therapy.

A healthy 68-year-old male had suffered from arthropathic psoriasis for twenty-six years. His medical history involved multiple cutaneous psoriatic lesions almost on the entire body (body surface affected (BSA) = 60%), which had been resistant to topical treatment. The patient was treated with methotrexate. Three years later, we noted a slight improvement in both cutaneous (BSA = 40%) and arthropathic symptoms. We opted for one injection of adalimumab weekly. We noted rapid clinical improvement (BSA = 2%) and relieving of arthropathic symptoms. However, several months later, the patient presented himself with purplish nodular lesions on both forearms (Fig. 1). We noted neither mucosal involvement nor hair or nail lesions. A histopathological examination confirmed the diagnosis of hypertrophic LP (Fig. 2). Based on the clinical history and the histopathological findings, the diagnosis of adalimumab-induced hypertrophic LP was established. Adalimumab could not be stopped. The hypertrophic LP was treated with a topical corticosteroid with a slight improvement.

TNF is a pro-inflammatory cytokine produced by a wide variety of cell types, including keratinocytes, that plays a complex role in innate immunity and host defense, particularly against mycobacterial infections, and that may both enhance and suppress adaptive immunity. The main anti-TNF-α drugs (adalimumab, etanercept, and infliximab) have all been shown to be very effective in treating psoriasis [3].

Our patient presented an unusual side effect of adalimumab. A temporal association and a histopathological examination of our patient strongly suggested a causative relationship between the TNF blockage and the onset of the cutaneous lesions. With the Naranjo algorithm, a causality score of 6 was obtained and the case was categorized as a probable reaction to adalimumab.

Lichenoid eruptions induced by TNF-α inhibitors have, for the first time, been described by Vergara et al. in 2002 [4]. Since then, multiple cases of lichenoid eruption, including cutaneous and oral LP, lichen planopilaris, maculopapular eruption, and psoriasis-like LP, have been reported [1,2,4,7]. Only twenty cases of LP induced by TNF-α inhibitors have been described [1,2,4]. The three main TNF-α inhibitors (infliximab, etanercept, and adalimumab) were incriminated [5]. Some mechanisms have been suggested to explain the occurrence of lichenoid eruption due to TNF-α inhibitors therapy. In fact, the suppression of TNF may lead to the development

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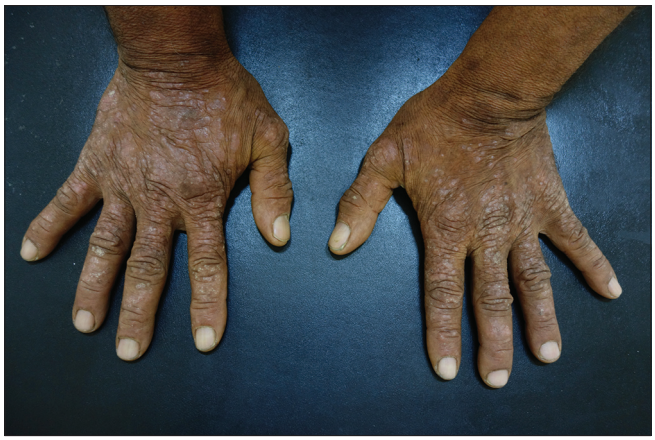

Figure 1: Hypertrophic cutaneous lichen planus with a nodular, polygonal, flat-topped, purplish plaque on both hands.

of opposing inflammatory cytokines, which may activate T cells and dendritic cells leading to lichenoid eruption [6].

Our patient presented hypertrophic LP, which is a particular clinical and histological form of LP. To the best of our knowledge, no case of hypertrophic LP induced by an anti-TNF-α drug has been reported [1,2,4]. Only one case of hypertrophic LP induced by anti-interleukin 17 (secukinumab) has been reported [7].

In conclusion, we witnessed the first case of hypertrophic LP induced by an anti-TNF-α drug. Physicians should be aware of this rare side effect. In fact, patients with cutaneous hypertrophic LP are prone to skin cancer. Therefore, we believe it to be worthwhile to monitor patients who use anti-TNF-α drugs for psoriasis against hypertrophic LP.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

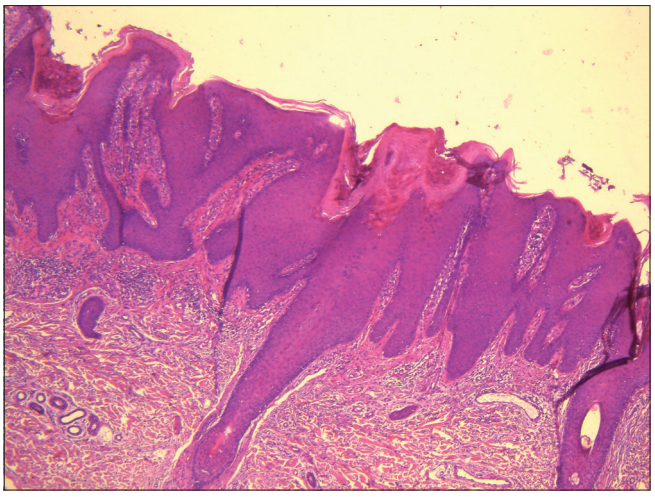

Figure 2: A thin, acanthotic epidermis with orthohyperkeratosis and wedge-shaped hypergranulosis with some necrotic keratinocytes associated with a dermal inflammatory lichenoid infiltrate and lymphocytes exocytosis in the basal layers of the epidermis (H&E, 40×).

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