Journal of Clinical & Experimental Dermatology Research

Doolan et al., J Clin Exp Dermatol Res 2017, 9:1
DOI: 10.4172/2155-9554.1000437

Case Report Open Access

Cutaneous Lichen Planus Induced by Secukinumab

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Received date: November 20, 2017; **Accepted date:** December 05, 2017; **Published date:** December 08, 2017

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Abstract

Lichen planus (LP) is a chronic mucocutaneous disease, characterised by an inflammatory immune response with sub-epithelial infiltration of T lymphocytes causing basal epithelial cell damage. Secukinumab is a monoclonal antibody that blocks IL-17A; which is the primary cytokine of Th17 cells involved in the aetiology of inflammatory skin diseases such as psoriasis. Secukinumab has been linked to induction of oral LP, but never directly to cutaneous LP. We report the first case of drug-induced cutaneous LP in the setting of secukinumab for treatment of chronic plaque psoriasis. A 56-year-old man with chronic plaque psoriasis presented with a 2-month history of violaceous and pruritic, thickened plaques on his bilateral lower limbs and buttocks in the setting of secukinumab use for psoriasis. Histological analysis showed a band-like lymphocyte inflammatory infiltrate just beneath the epithelium and was consistent with cutaneous LP. He was treated with topical betamethasone dipropionate cream with moderate effect. Initial laboratory tests including hepatitis and inflammatory screens were within normal limits. We hypothesise that this causal association may be due to a microbial trigger, activating a T-cell mediated immunologic response in CD8+ T-cells and dendritic cells, causing activation of type I interferons and an inflammatory skin response consistent with LP. Clinicians should monitor patients for mucosal and cutaneous LP when using secukinumab or other biologic modulators of IL-17 for extended periods with psoriasis.

Keywords: Lichen planus; Drug eruption; Secukinumab; Cutaneous; Psoriasis

Introduction

Lichen planus (LP) is a relatively common, chronic mucocutaneous disease, characterised by an inflammatory immune response causing sub-epithelial infiltration of T lymphocytes (T cells) and basal epithelial cell damage [1]. Although the exact pathogenesis of LP is unknown, it can involve the oral and genital mucosal surfaces, skin, hair and nails. Risk factors include; hepatitis C infection, autoimmune disease, internal malignancies, dyslipidaemia, graft-versushost disease and medications such as beta-blockers, anti-malarials, thiazide diuretics and metals [2]. Secukinumab is a monoclonal human immunoglobulin antibody that specifically blocks pro-inflammatory interleukin (IL)-17A; a key cytokine produced by Th17 cells which has been implicated in the aetiology of autoimmune inflammatory skin diseases such as psoriasis [1]. Secukinumab has recently been associated with cutaneous LP, post-development of oral LP during administration of infliximab (tumour necrosis factor-α antagonist) [3]. It has also been linked to induction of oral LP, but never directly to cutaneous LP [4]. Herein, we report the first case of direct drug-induced cutaneous LP in the setting of secukinumab for treatment of chronic plaque psoriasis.

Case Presentation

A 56-year-old man of Indian descent diagnosed with chronic plaque psoriasis presented to the outpatient dermatology clinic with a 2-month history of violaceous and pruritic plaques to his bilateral lower limbs and buttocks. This was in the setting of 6-months of treatment with monthly subcutaneous injections of 300 mg of secukinumab for chronic plaque psoriasis. After administration of secukinumab, his psoriasis symptoms improved significantly, but after 6-months of treatment he noticed thickened plaques developing on his ankles bilaterally (Figure 1). These plaques extended proximally, involving his posterior thighs and buttocks, but sparing other sites. Significant past medical history included hypertension and latent tuberculosis that was treated 2 years prior with a 10-month course of isoniazid. His only other medication was valsartan (angiotensin II receptor antagonist), which was commenced 36-months prior to secukinumab. There had been no previous injury to the skin, stressors, recent travel or new medications commenced.

When he initially commenced secukinumab, he had failed treatment with methotrexate, acitretin and narrow band ultraviolet B phototherapy and had severe chronic plaque psoriasis, with a psoriasis area of severity index (PASI) score of 29.0. On physical examination, large cutaneous, violaceous plaques were noted, with Wickham striae. There was no mucosal or nail involvement. Initial laboratory results including full blood count, inflammatory markers, hepatitis screen, extractable nuclear antigens and antinuclear and double stranded DNA antibodies were all within normal limits. Histopathology was consistent with LP. Analysis showed a band-like lymphocytic inflammatory infiltrate just beneath the epithelium with basal epithelial apoptosis, hypergranulosis, focal hyperkeratosis and saw-tooth acanthosis (Figures 2A and 2B). Due to the remarkable improvement in this man's psoriasis (PASI score 0), the patient opted to continue secukinumab administration and his cutaneous LP was treated with topical betamethasone dipropionate cream (0.05%) with moderate effect.

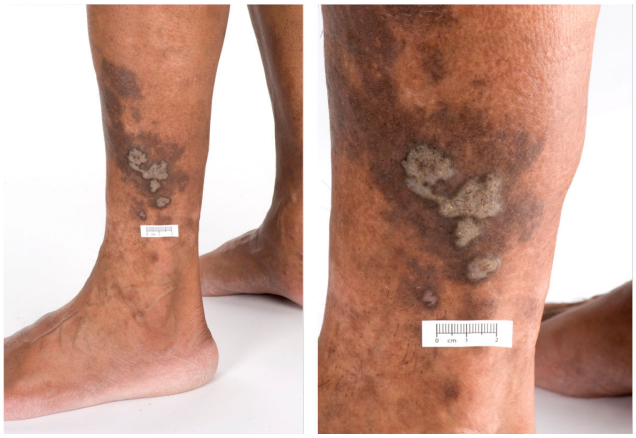

Figure 1: Hypertrophic cutaneous lichen planus with violaceous, polygonal, flat-topped papules and plaques. Post-inflammatory hyperpigmentation can be seen over the distal lower limbs.

Discussion

In this case, the development of cutaneous LP was related to administration of secukinumab for psoriasis. Although the actual pathological relationship between cutaneous LP and secukinumab remains unknown, we hypothesise that this causal association may be due to a microbial trigger and activation of type I interferons (IFNs), in the setting of dysfunctional regulatory T-cells (Tregs) commonly observed in psoriasis. It is well documented that IL-17 plays an important role in innate immunity, by inducing expression of antimicrobial peptides and chemokines in epithelial cells and fibroblasts [5]. IL-17 also guards against fungal, viral and gram-positive extracellular bacteria such as *Staphylococcus aureus* mucocutaneous infections [5]. Thus, IL-17 neutralisation may increase the likelihood of a pathogenic infection, and activation of innate immunity. Berg & Forman have supported the role of auto-reactive cytotoxic (CD8+) T-cells and the subsequent upregulation of myeloid dendritic cells in innate immunity [6]. This leads to induction of precursor cytokines such as IFNs, causing an inflammatory skin response as seen in LP [6]. This is supported by De Vries et al., who found dramatic increases in plasmacytoid dendritic cells and upregulation of IFNs in cutaneous and oral lesions of LP [7]. Our finding of predominantly CD8+ T-cells in the inflammatory infiltrate (Figure 2C) was reinforced by Rana et al., who noted a significant prevalence of CD8+ T-cells in the inflammatory dermo-epidermal infiltrate of 20 cases with cutaneous LP [8].

In addition to CD8+ T-cells, we also found a clear presence of forkhead box P3 (Foxp3) expressing Tregs (Figure 2D). Tregs are canonically associated with immune modulation to ensure self-tolerance and suppression of the auto immune response, by regulation of immune mediated Th cells and CD8+ T-cells. However, such IL-17 producing Tregs as are seen in psoriasis are known to be lacking the normal suppressive capacities of Tregs and it is this loss of immune suppression that is thought to be the primary driver of pathogenic T-cell proliferation [9]. Shen et al. found a substantially increased expression of Foxp3+ and IL-17 in LP lesions, including oral and cutaneous variants, suggesting a similar pathogenic role for Tregs in LP as in psoriasis [10].

Thus, IL-17 inhibition may have contributed to activation of new or repressed pathogenic microorganisms and triggered a T-cell mediated immunologic response in CD8+ T-cells and dendritic cells. This response is potentially exacerbated by a lack of proper regulation due to a dysfunctional, non-suppressive Tregs phenotype, ultimately resulting in development of cutaneous LP. In conclusion, we experienced a novel case of cutaneous LP related to secukinumab administration for severe chronic plaque psoriasis. Clinicians should monitor patients for mucosal and cutaneous LP when using secukinumab or other biologic modulators of IL-17 for psoriasis.

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