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Title:

Successful treatment of recalcitrant lichen planus pemphigoides with tildrakizumab

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Main text:

Lichen planus pemphigoides is an acquired immunobullous dermatosis with clinical, histological and immunological features of both lichen planus and bullous pemphigoid.¹ We report a case of recalcitrant lichen planus pemphigoides treated successfully with tildrakizumab, a humanized monoclonal antibody to interleukin-23.

A 35-year-old man presented with a 15-year history of pruritic lichenoid papules and plaques. He reported tense blisters intermittently developing on both pre-existing lichenoid lesions as well as normal skin. Examination revealed multiple plaques of varying size with erythematous to violaceous borders and overlying scale across his limbs and trunk (Fig. 1a). Erosions from prior blistering were scattered within and adjacent to the lesions. His face, scalp, mouth and genital areas were spared. Previous treatment with topical and oral corticosteroids, psoralen and ultraviolet A (PUVA) therapy, as well as azathioprine and methotrexate, were ineffective and did not halt the appearance of new lesions. He was otherwise well and was not currently taking any medications. A biopsy from lesional skin on the left lower leg demonstrated hypergranulosis and hyperkeratosis with focal mild parakeratosis and a moderate lymphocytic infiltrate (Fig. 2). Deeper levels revealed partial separation of the epidermis from dermis. Direct immunofluorescence (DIF) staining of perilesional skin was weakly positive for linear C3 deposition along the base of the epidermis; IgG and IgM were negative. The clinical, histological and immunofluorescence findings were consistent with a diagnosis of lichen planus pemphigoides.

In view of the fact that lichen planus pemphigoides shares features with lichen planus (LP) and a separate patient at our centre demonstrated clinical improvement of their oral LP after therapy with tildrakizumab,² we chose to use tildrakizumab for our patients lichen planus pemphigoides. After screening investigations, including QuantiFERON-TB Gold, were negative, treatment was commenced with tildrakizumab, 100 mg, injected subcutaneously and repeated at weeks 4 and 16. After one dose of tildrakizumab there was noted subjective reduction in itch. After three doses there was significant improvement with near complete clinical resolution of lichen planus pemphigoides lesions (Fig. 1b). The response was sustained at week 20.

Lichen planus pemphigoides is rare, with only a few cases reported in the literature.^{1,3} Lichen planus pemphigoides was previously been regarded as either a clinical variant of bullous pemphigoid (BP) or as the coexistence of LP and BP, however it is now considered to be a distinct clinical entity.^{1,3} Diagnosis can be confirmed by the appearance of bullae arising on both LP lesions and uninvolved skin; histopathological findings of LP and a subepidermal bulla; and DIF showing linear deposits of C3 and/or IgG along the basement membrane zone.^{1,3} Indirect immunofluorescence assay (IFA) or enzyme-linked immunosorbent assay (ELISA) can also be used to detect circulating anti-BP180 autoantibodies. Treatment of lichen planus pemphigoides is challenging. Systemic corticosteroids, dapsone, and acitretin have been used with varying degrees of success.^{1,3} Systemic corticosteroids remain the mainstay of therapy despite their unfavourable side effect profile.^{1,3} The pathogenesis of lichen planus pemphigoides, LP and BP are not yet fully understood.^{1,3,4,5} However, lesional skin in both LP and BP has been shown to overexpress interleukin-23 (IL-23),^{4,5} and successful treatment of oral LP with an IL-23 inhibitor has been published.² In addition there is a single published case report of lichen planus pemphigoides having been successfully treated with ustekinumab an IL-12 and IL-23 blocker.⁶

Our patients' lichen planus pemphigoides improved after the first dose of tildrakizumab and had nearly cleared after the 3rd dose. The tildrakizumab was well-tolerated. This case report further supports the potential role of IL-23 in in the pathogenesis of lichen planus pemphigoides.

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Figure legends:

Figure 1: Clinical images (a) Before treatment with tildrakizumab: erythematous to violaceous plaques over the abdomen and anterior thigh, and (b) After treatment with tildrakizumab: resolution of lesions with some residual post inflammatory hyperpigmentation.

Figure 2: Histopathological images (a) low power (hematoxylin and eosin stain, x 40) image showing a lichenoid, chronic inflammatory infiltrate in the superficial dermis, and (b) higher magnification (hematoxylin and eosin stain, x 200) image showing scattered apoptotic keratinocytes with interspersed exocytotic lymphocytes within the epidermis. The lichenoid inflammatory infiltrate principally consists of a mixture of lymphocytes and histiocytes with occasional melanophages and occasional scattered pigment incontinence.

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