Ixekizumab-treatment-emergent photosensitive cutaneous eruption.

Running title: Ixekizumab photosensitive eruption

Key words: ixekizumab, IL-17A, photosensitive, drug induced lupus erythematosus

Corresponding author: Eleni ANTHONY
Qualifications: MBBS
Email Address: ep_anthony@hotmail.com
Phone: +61 401 368 082
Institutional affiliations: Skin & Cancer Foundation Inc. Carlton, Victoria, Australia

Conflicts of interest: Nil

Author 2: Harini RAJGOPAL BALA
Qualifications: MBBS
Email: harinibala28@gmail.com
Institutional affiliations: 1. Department of Dermatology, St Vincent's Hospital Melbourne, Fitzroy, Australia.
2. Skin & Cancer Foundation Inc. Carlton, Victoria, Australia

Conflicts of interest: Nil

Author 3: Michelle SY GOH
Qualifications: MBBS, BMedSci, FACD
Email: michelle.goh@svha.org.au
Institutional affiliations: 1. Department of Dermatology, St Vincent's Hospital Melbourne, Fitzroy, Australia.
2. Skin & Cancer Foundation Inc. Carlton, Victoria, Australia

Conflicts of interest: Nil

Author 4: Showan BALTA
Qualifications: MBBS
Email: Showan.Balta@svha.org.au

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/ajd.12811](https://doi.org/10.1111/ajd.12811)

This article is protected by copyright. All rights reserved

Institutional affiliations: 1. Department of Anatomical Pathology, St Vincent's Hospital Melbourne, Fitzroy, Australia.

Conflicts of interest: Nil

Author 5: Peter FOLEY

Qualifications: MBBS, BMedSci, FACD

Email: pfoley@skincancer.asn.au

Institutional affiliations: 1. Department of Dermatology, St Vincent's Hospital Melbourne, Fitzroy, Australia.
2. Skin & Cancer Foundation Inc. Carlton, Victoria, Australia.
3. The University of Melbourne, Parkville, Victoria, Australia.

Conflicts of interest: P. Foley has served as a consultant, investigator, speaker and/or advisor for and/or received travel grants from Abbott/AbbVie, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, CeltaSys, Cutanea, Dermira, Galderma, Genentech, GSK/Stiefel, Janssen, LEO Pharma, Lilly, Novartis, Regeneron Pharmaceuticals, Inc., Roche, Sanofi, Schering-Plough/Merck, 3M/iNova/Valeant, Sun Pharma, UCB Pharma, and Wyeth/Pfizer.

Disclosure: Nil. The views expressed in the submitted article are our own and not an official position of the institution.

Source of Support: Nil.

Word count: 510 (excluding references).

Number of Figures: 2.

Article type : Case Letter

Ixekizumab-treatment-emergent photosensitive cutaneous eruption.

A sixty-two-year-old female, who had been commenced on ixekizumab six months prior for chronic plaque psoriasis (CPP), presented in springtime with new-onset, pruritic, symmetric, sharply demarcated, photodistributed erythematous plaques on the lateral arms and dorsal forearms (Fig. 1). The eruption spared her face, neck and chest. She had no history of exposure to new topical contactants, and no prior history of photosensitivity. There were no symptoms of systemic lupus erythematosus. The patient was well-controlled on ixekizumab with a psoriasis assessment severity index (PASI) score of 1.6, from a pre-biologic baseline PASI of 38.1. Prior biologic therapy for her CPP over seven years included etanercept, adalimumab, ustekinumab and secukinumab. There was a suboptimal response to all these therapies. Her other medical comorbidities included Child-Pugh A cirrhosis secondary to a past history of Hepatitis C, hypertension and type two diabetes mellitus. All of her other medications remained unchanged for over five years, and included metformin, glimepiride and perindopril. She had no recent medication changes except for ixekizumab.

Skin biopsies revealed mild to moderate spongiosis with hyperkeratosis, focal parakeratosis, focal interface change with occasional necrotic keratinocytes. There was mild superficial dermal perivascular and interstitial mixed chronic inflammatory infiltrate with lymphocytes, histiocytes, some plasma cells and scattered eosinophils. There was mild upper dermal oedema. There was no significant dermal mucin deposition. (Fig 2). Direct immunofluorescence was negative. The antinuclear nuclear antibody (ANA) was 160 (speckled) and 640 (nucleolar); it was previously negative. Double stranded DNA and extractable nuclear antigen (ENA) screen, including anti-Ro and anti-La, were negative. With clinicopathological correlation, including the drug timeline, we favoured the diagnosis of ixekizumab-induced photosensitive eruption. The diagnosis fell short of cutaneous lupus given the focal and limited interface reaction and the negative direct immunofluorescence.

Given the absence of clinical features of systemic lupus and negative ENA screen, the ANA result was deemed to be of uncertain significance. She was managed with topical betamethasone dipropionate 0.05% ointment daily and strict photoprotection including long-sleeved clothing. At four months' follow-up with continuation of 4-weekly ixekizumab, she was significantly improved by about 75% – there was residual mild patchy erythema and xerosis that was minimally pruritic.

Ixekizumab is a humanised high-affinity monoclonal IgG4 antibody that selectively targets interleukin-17A (IL-17A), and has recently been licensed in the treatment of CPP in Australia. IL-17A plays a key role in regulating both inflammation and neutrophil homeostasis. Common adverse events include *Candida* infections, nasopharyngitis, upper respiratory tract infections, injection site reactions, arthralgia, bronchitis and headaches. Rare adverse events include: neutropaenia (0.6%), malignancies (1.7%), Crohn disease (0.2%), ulcerative colitis (0.2%) and cerebro-cardiovascular events (2.4%).¹

Drug-induced lupus erythematosus (DILE) can be divided into systemic, subacute cutaneous and chronic cutaneous lupus erythematosus.² DILE is reported as a rare side effect of tumour necrosis factor alpha antagonists and other biologics (0.5-1%).^{3,4} There has been one case report of IL-17A inhibitor, secukinumab-induced subacute cutaneous lupus erythematosus.⁵ There have been no reports to date of ixekizumab-induced cutaneous lupus or other photosensitive eruptions. There are no clearly defined mechanisms for the development of DILE. Several hypotheses have been proposed including cytokine shift hypothesis and disruption of apoptotic pathways.²

We report the first case of a photosensitive cutaneous eruption arising in a patient who had commenced ixekizumab six months earlier. Reporting of adverse reactions, particularly with newer biologic agents, is imperative to our understanding of their safety and side effect profile.

References.

1. Blauvelt A, Gooderham M, Iversen L, *et al.* Efficacy and safety of ixekizumab for the treatment of moderate-to-severe plaque psoriasis: results through 108 weeks of randomized, controlled phase 3 clinical trial (UNCOVER-3). *J. Am. Acad. Dermatol.* 2017; **77**: 855-62.
2. Chang C, Gershwin ME. Drug-induced lupus erythematosus: incidence, management and prevention. *Drug Saf.* 2011; **34**: 357-74.

3. Marzano AV, Vezzoli P, Crosti C. Drug-induced lupus: an update on its dermatologic aspects. *Lupus*. 2009; **18**: 935-40.
4. Wetter DA, David MD. Lupus-like syndrome attributable to anti-tumor necrosis factor alpha therapy in 14 patients during an 8-year period at Mayo clinic. *Mayo. Clin. Proc.* 2009; **84**: 979-84.
5. Wehrmann C, Sondermann W, Körber A. Secukinumab-induced subacute-cutaneous lupus erythematosus. *Hautarzt*. 2017. doi: 10.1007/s00105-017-4071-8.

Figure Legends:

Figure 1. Erythematous plaques affecting sun-exposed sites on upper limbs, with proximal sharp demarcation.

Figure 2. Punch biopsy from the left arm. Mild to moderate spongiosis with interface reaction, basal layer vacuolar degeneration and occasional necrotic keratinocyte; superficial dermal perivascular and interstitial mixed chronic inflammatory cell infiltrate including lymphocytes, histiocytes, plasma cells and eosinophils; mild upper dermal oedema (H&E 10 magnification).

ajd_12811_f1.jpg

ajd_12811_f2.jpg

Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:

Anthony, E;Bala, HR;Goh, MSY;Balta, S;Foley, P

Title:

Ixekizumab-treatment-emergent photosensitive cutaneous eruption

Date:

2018-11-01

Citation:

Anthony, E., Bala, H. R., Goh, M. S. Y., Balta, S. & Foley, P. (2018). Ixekizumab-treatment-emergent photosensitive cutaneous eruption. AUSTRALASIAN JOURNAL OF DERMATOLOGY, 59 (4), pp.E284-E286. <https://doi.org/10.1111/ajd.12811>.

Persistent Link:

<http://hdl.handle.net/11343/283918>