Accepted: 9 December 2018

DOI: 10.1111/phpp.12446

WILEY Photodermatology, Photoimmunology & Photomedicine

Treatment of erlotinib-induced acneiform eruption with chromophore gel-assisted phototherapy

To the Editor,

A 49-year-old female presented with an acneiform eruption induced by erlotinib. She had been diagnosed with stage IV (T1N3M1) EGFR-mutant adenocarcinoma of the lung and commenced on erlotinib 150 mg daily. Within 3 days, she developed an acneiform eruption prompting empiric treatment with topical hydrocortisone and systemic doxycycline 100 mg daily. The acneiform eruption progressed with evolution to widespread pustules and papules with proud erythema involving the entire face with minor extension to the scalp, décolletage and back (Figure 1). Treatment was escalated to daily washes with benzoyl peroxide and transition to topical methylprednisolone aceponate and minocycline 100 mg daily, met with modest response (Figure S1). The patient was demonstrating a reduction in tumour burden on erlotinib but significant cutaneous toxicity recalcitrant to standard therapy. Given the significant burden on her quality of life (QOL), it was decided to continue erlotinib but trial adjuvant chromophore gel-assisted phototherapy (CGAP). The patient received twelve treatment sessions over six weeks involving application of a 2 mm layer of the photoconverter chromophore gel (Kleresca® treatment) followed by irradiation with a multi-LED lamp (447 nm) (Kleresca®, Balerup, Denmark). Within three weeks of treatment, the acneiform eruption was arrested and topical treatment was withdrawn one week after. The patient completed a further three weeks of CGAP as per standard protocol and maintained on minocycline 50 mg daily thereafter. The severity of her acneiform eruption decreased from an Investigator's Global Assessment (IGA) of 5 to 0. Scoring of the patient-reported outcomes of the Acne Quality of Life Index decreased from 78 to 23 and increased on the Acne-specific Quality of Life Questionnaire (Acne-QOL) from 49 to 109 demonstrating marked improvement in quality of life.[1,2] She continues treatment with erlotinib maintaining tumour arrest without any active cutaneous toxicity, only post-inflammatory erythema, hyperpigmentation and ice-pick scarring as sequelae of the initial acneiform eruption (Figure 2).

Cutaneous toxicities are the most common side effects associated with targeted therapies in oncology. For the tyrosine kinase inhibitor erlotinib, these include acneiform eruption, xeroderma, pruritus and paronychia.[3] Dermatological pathologies exert unique detrimental influence on QOL, and in some instances, cutaneous toxicities may be severe enough to warrant interruption of oncological treatment. For the acneiform eruption of the EGFR inhibitors, management options include topical corticosteroids, topical retinoids, systemic tetracyclines, isotretinoin and prednisolone. However, for patients with severe acneiform eruption and contraindications to systemic therapies (such as in the setting of hepatic

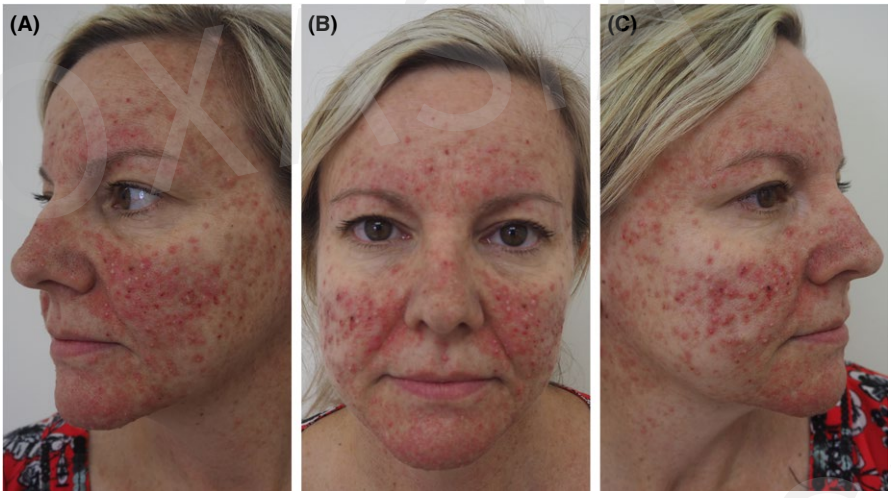

FIGURE 1 Acneiform eruption induced by erlotinib as treatment of EGFR-mutant adenocarcinoma of the lung. A, left face B, central face C, right face

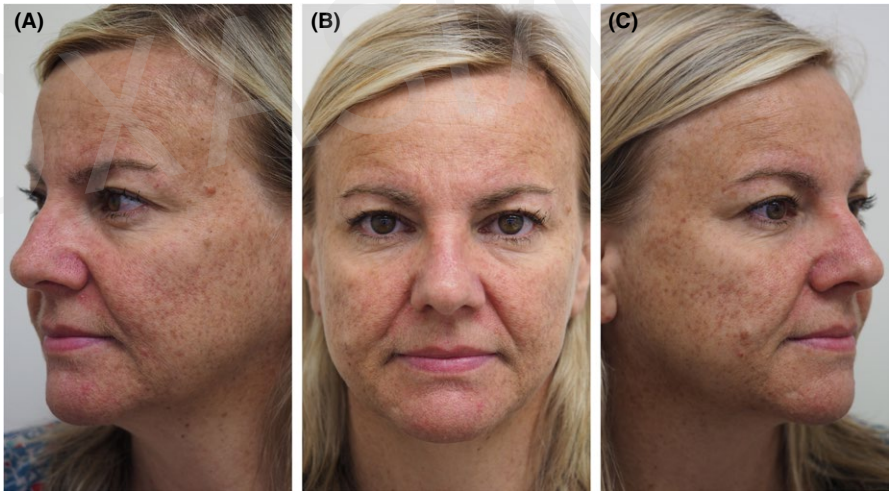

FIGURE 2 Resolution of acneiform eruption with chromophore gel-activated phototherapy leaving residual hyperpigmented and atrophic scarring. A, left face B, central face C, right face

metastases with liver function perturbation as in our case), treatment poses more of a challenge.

CGAP is a new therapeutic modality in acne.[4,5] The topical gel contains target chromophores which upon irradiation by the light emitting diode lamp emit electromagnetic radiation in the visible spectrum. The precise mechanism of action is yet to be elucidated but one hypothesis is that this photodynamic reaction excites endogenous porphyrins which generate reactive oxygen species leading to reduction in the size of sebaceous glands. There is emerging evidence for the effectiveness of CGAP in acne as well as other dermatological conditions with adnexal pathology such as rosacea.[6] CGAP is non-invasive, in-office intervention with no known systemic side effects.

The case presented herein suggests that there may be some promise in CGAP as management of acneiform eruptions induced by EFGR inhibitors. At the same time, methodologically, as a single case report, the placebo effect cannot be diminished, nor the possibility of a delayed response to tetracycline therapy or spontaneous remission. Further, in terms of outcome measures, the IGA is a subjective score which was evaluated by a single non-blinded assessor, and the patient reported outcome measures employed have been validated in acne but not acneiform eruptions. Nonetheless, the remarkable response our patient demonstrated suggests that this might be a therapeutic avenue that warrants further investigation through study with more scientifically robust methodology.

ACKNOWLEDGEMENTS

We are grateful to Sydney Skin and to Kleresca® for facilitating compassionate access to chromophore gel-assisted phototherapy for our patient and to the University of New South Wales MD program for their support of Xin Lin Wong.

CONFLICT OF INTEREST

Dr Sebaratnam has received a travel grant from FB Dermatology Denmark.

ORCID

Deshan F. Sebaratnam https://orcid.org/0000-0001-5896-8178

Akalya Mahendran[1]
Xin L. Wong[2]
Steven Kao[3]
Deshan F. Sebaratnam[2]

[1]*Concord Repatriation General Hospital, Concord, New South Wales, Australia*
[2]*University of New South Wales, Kensington, New South Wales, Australia*
[3]*Chris O'Brien Lifehouse, Camperdown, New South Wales, Australia*

Correspondence
Deshan F. Sebaratnam, Skin and Cancer Foundation Australia, Westmead, NSW, Australia.
Email: deshan@unsw.edu.au

REFERENCES

1. Rapp SR, Feldman SR, Graham G, Fleischer AB, Brenes G, Dailey M. The acne quality of life index (Acne-QOLI). *Am J Clin Dermatol*. 2006;7(3):185-192.
2. Martin A, Lookingbill D, Botek A, Light J, Thiboutot D, Girman C. Health-related quality of life among patients with facial acne-assessment of a new acne-specific questionnaire. *Clin Dxp Dermatol*. 2001;26(5):380-385.
3. Kiyohara Y, Yamazaki N, Kishi A. Erlotinib-related skin toxicities: treatment strategies in patients with metastatic non-small cell lung cancer. *J Am Acad Dermatol*. 2013;69(3):463-472.
4. Antoniou C, Dessinioti C, Sotiriadis D, et al. A multicenter, randomized, split-face clinical trial evaluating the efficacy and safety of chromophore gel-assisted blue light phototherapy for the treatment of acne. *Int J Dermatol*. 2016;55(12):1321-1328.
5. Nikolis A, Fauverghe S, Scapagnini G, et al. An extension of a multicenter, randomized, split-face clinical trial evaluating the efficacy and safety of chromophore gel-assisted blue light

phototherapy for the treatment of acne. *Int J Dermatol*. 2018;57(1):94-103.
6. Braun SA, Gerber PA. A photoconverter gel-assisted blue light therapy for the treatment of rosacea. *Int J Dermatol*. 2017;56(12):1489-1490.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.