TITLE PAGE

Full Title: Two cases of generalised granuloma annulare successfully treated with acitretin and narrowband UVB therapy

Short running title: Generalised granuloma annulare treatment

Authors:

H.Rajgopal Bala [1], S.Khan [2] and A.H.Chong [1]

[1]Skin and Cancer Foundation Inc, University of Melbourne, Melbourne, Australia

[2] Melbourne Pathology, Melbourne, Australia

Dr Harini Rajgopal Bala

Email: hbala@skincancer.asn.au

Address: Skin and Cancer Foundation, Level 1, 80 Drummond St, Carlton, Victoria 3053, Australia

Fax: 96393575

Telephone: 0396239400

Dr Sant Khan

Email: sant.khan@mps.com.au

Address: Melbourne Pathology, Private Bag 5, Collingwood, VIC, 3066, AUSTRALIA

Telephone: +61 3 9287 7700

Dr Alvin H Chong

Email: Alvin.CHONG@svha.org.au

Address: Skin and Cancer Foundation, Level 1, 80 Drummond St, Carlton, Victoria 3053, Australia

Fax: 96393575

Telephone: 0396239400

Word Count: 434

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.12500

Received Date: 25-Nov-2015

Revised Date: 02-Apr-2016

Accepted Date: 04-Apr-2016

Article Type: Letter to the Editor

Two cases of generalised granuloma annulare successfully treated with acitretin and narrowband UVB therapy

Granuloma annulare (GA) is an inflammatory skin condition with various morphological presentations including generalised forms.[1, 2] Generalised GA is a challenging disease due to its recalcitrant, widespread nature and lack of evidence-based treatment.[2] Previously reported therapies include steroids, immunosuppresants, biologics, phototherapy, lasers, retinoids and fumaric acid.[2] Treatment of GA with acitretin has rarely been described.[1] We report two cases of complete clearance of generalised GA following combination therapy with acitretin and narrowband UVB phototherapy.

A 68-year-old male presented with a 2-month history of generalised GA over the trunk and legs (Figure 1.1). Prior unsuccessful treatments included topical betamethasone diproprionate ointment 0.5mg/g daily and a tapering dose of 25mg prednisolone daily. Acitretin was introduced at 10mg daily, with concurrent narrowband UVB therapy (cumulative total of 15.5J/cm^2) over 31 sessions for 10 months. Combination therapy lead to a total clearance of the GA (Figure 1.2). On review, 6 months post-cessation of therapy, mild GA was observed. The patient was restarted on acitretin 10mg daily as monotherapy and the GA rash responded with an almost complete clearance at 5-month review.

Figure 1:

A 62-year-old female presented with a two-year history of generalised GA involving her flank, abdomen and legs (Figure 1.3). Prior unsuccessful treatments included betamethasone 0.05% cream, intralesional triamcinolone 10mg/ml, minocycline 50mg twice daily and hydroxychloroquine 200mg twice daily. Acitretin 10mg daily was initiated for 11 months, with narrowband UVB therapy twice weekly (cumulative dose of 13.9J/cm^2) for 32 sessions over 4 months. During this period, the generalised GA had cleared entirely (Figure 1.4). Six months post-cessation of acitretin, the patient presented with a mild recurrence of GA on the trunk. Acitretin 10mg daily and narrowband UVB was restarted and an almost complete clearance of the rash was noted after two months.

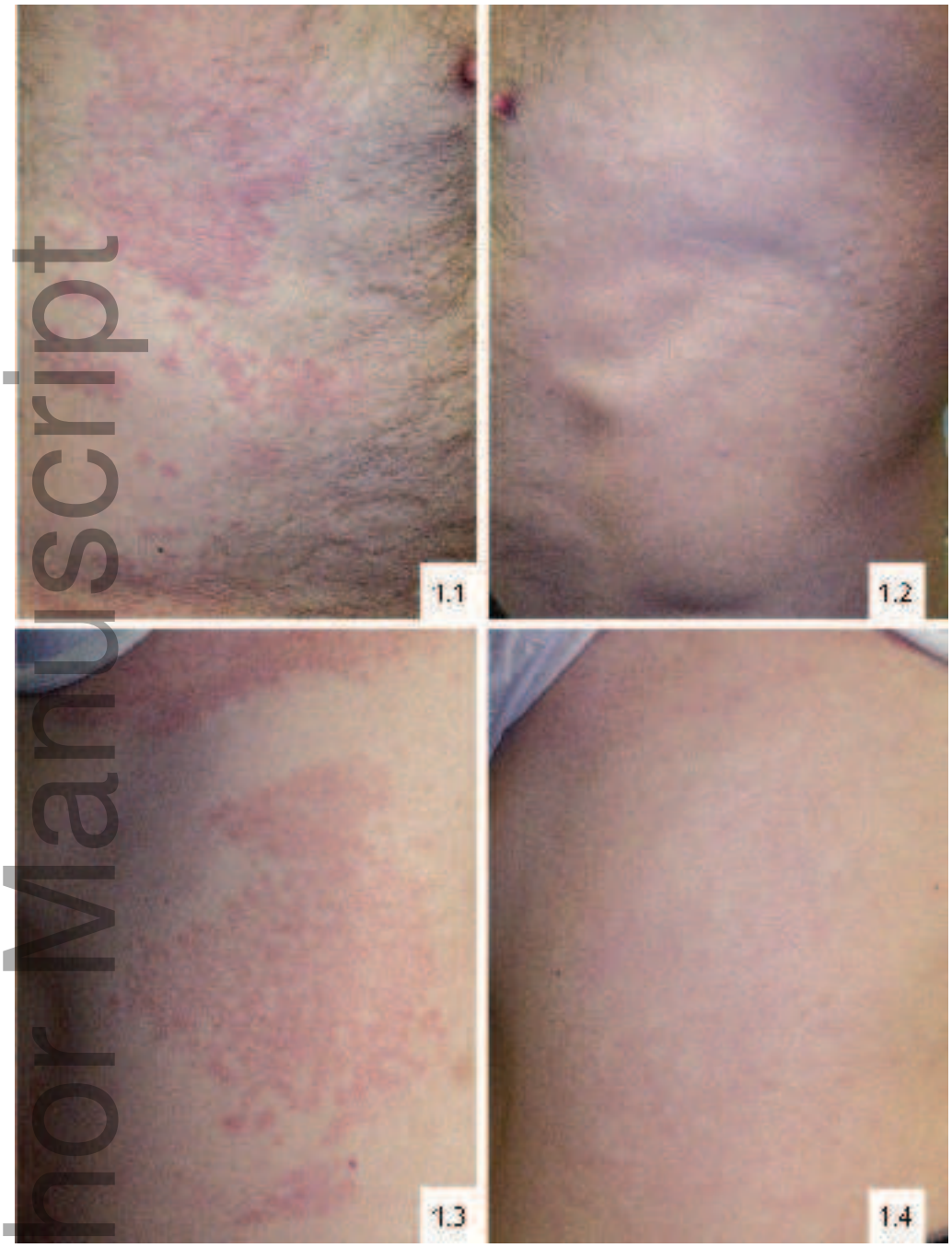
GA is thought to represent a delayed-type hypersensitivity reaction to an unknown stimulus.[3] This

produces various inflammatory cytokines including tumour necrosis factor, interferon gamma and interleukin-2, which cause matrix degradation.[3, 4] Acitretin, a potent second-generation retinoid, acts at an intranuclear level to alter the expression of epidermal growth factor genes.[5] Its immunomodulatory effects inhibit both neutrophil migration and dermal microvascular endothelial cells.[5] The resulting anti-keratinising, anti-inflammatory properties of acitretin help to normalise epidermal proliferation, differentiation and cornification.[5]Narrowband UVB therapy has also shown to be useful in the treatment of generalised GA by suppressing lymphocyte proliferation and cytokine production.[6]

We acknowledge the limitation that only combination therapy was used; however in case 1 the patient responded to acitretin as monotherapy for recurrence. The authors recommend future studies to compare acitretin and narrowband UVB as monotherapies and in combination to further define treatment for generalised GA.

References:

1. Gopal MG, Gupta D, Sharath Kumar BC et al. Granuloma Annulare mimicking sarcoidosis and treated with acitretin: a case report. *JEMDS.* 2013: 2(48): 9297-9301.
2. Thornsberry LA, English JC. Etiology, diagnosis, and therapeutic management of granuloma annulare: an update. *Am J Clin Dermatol*. 2013: 14(4): 279-90.
3. Keimig EL. Granuloma Annulare. *Dermatol Clin*. 2015. 33(3): 315-29.
4. PasmatziE, Georgiou S, Monastirli A, et al. Temporary remission of disseminated granuloma annulare under oral isotretinoin therapy. *Int J Dermatol*. 2005: 44(2): 169-71.
5. Ormerod AD, Campalani E, Goodfield MJ. British Association of Dermatologists guidelines on the efficacy and use of acitretin in dermatology. *Br J Dermatol*. 2010: 162(5): 952-63.
6. Inui S, Nishida Y, Itami S, et al. Disseminated granuloma annulare responsive to narrowband ultraviolet B therapy. *J Am Acad Dermatol*. 2005: 53(3): 533-4.



ajd_12500_f1.tif