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

Short running title: Generalised granuloma annulare treatment

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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. Generalised GA is a challenging disease due to its recalcitrant, widespread nature and lack of evidence-based treatment. Previously reported therapies include steroids, immunosuppressants, biologics, phototherapy, lasers, retinoids and fumaric acid. Treatment of GA with acitretin has rarely been described. 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 dipropionate 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/cm²) 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.

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/cm²) 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.
produces various inflammatory cytokines including tumour necrosis factor, interferon gamma and interleukin-2, which cause matrix degradation.\textsuperscript{[3, 4]} Acitretin, a potent second-generation retinoid, acts at an intranuclear level to alter the expression of epidermal growth factor genes.\textsuperscript{[5]} Its immunomodulatory effects inhibit both neutrophil migration and dermal microvascular endothelial cells.\textsuperscript{[5]} The resulting anti-keratinising, anti-inflammatory properties of acitretin help to normalise epidermal proliferation, differentiation and cornification.\textsuperscript{[5]} Narrowband UVB therapy has also shown to be useful in the treatment of generalised GA by suppressing lymphocyte proliferation and cytokine production.\textsuperscript{[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:
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