Actinic granuloma responding to doxycycline

George M. Jeha, BS,[a] Kathryn Olivier Luckett, MD,[b] and Lauren Kole, MD[b]
New Orleans, Louisiana and Birmingham, Alabama

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INTRODUCTION

Actinic granuloma (AG) is an idiopathic granulomatous dermatosis first described in 1975. AG presents with single or multiple annular lesions on sun-exposed areas of the skin such as the face, neck, and scalp.[1,2] Although AG was once thought to be a variant of granuloma annulare (GA), it is now regarded as a distinct clinical entity. AG is a relatively rare disorder, and its exact pathogenesis is unknown. Although there is no specific treatment for AG, several therapeutic agents have been tried with mixed results. Previous reports speak to the efficacy of doxycycline for treating similar granulomatous dermatoses such as GA or annular elastolytic giant cell granuloma (AEGCG) but not AG. Here we present the case of a 67-year-old man with a 3-year history of biopsy-proven AG who was treated with doxycycline after showing no improvement with topical or intralesional triamcinolone. The patient responded dramatically within 2 months of initiating doxycycline and has had continued resolution of skin lesions after completing an additional 6 months of treatment.

CASE REPORT

A 67-year-old white man with a history of chronic kidney disease, type 2 diabetes mellitus, coronary artery disease, and leukopenia presented for evaluation of an erythematous rash on the arms and thighs that had slowly been progressing for the last 3 years. The patient had no associated complaints and denied pain, pruritus, or burning related to the skin lesions. Physical examination found erythematous, thin plaques with central clearing ranging from approximately 0.25 cm to 7 cm in diameter distributed on the bilateral ventral forearms and bilateral proximal thighs (Fig 1, *A*).

Abbreviations used:

AEGCG:	annular elastolytic giant cell granuloma
AG:	actinic granuloma
GA:	granuloma annulare

The patient reported no improvement after treatment with triamcinolone ointment. Histopathologic examination found multinucleated giant cells exhibiting elastophagocytosis on a background of dermal elastosis, consistent with AG (Fig 2). The patient received intralesional 10% triamcinolone injections to the upper extremity lesions, which provided minimal improvement. A trial of doxycycline (100 mg twice per day) was started with the possibility of later initiating hydroxychloroquine or light therapy if no improvement was seen. The patient experienced marked improvement of in the appearance of his lesions within 2 months after initiating doxycycline with continued improvement after 8 months (Fig 1, *B*).

DISCUSSION

Doxycycline, a semisynthetic tetracycline derivative with both antimicrobial and anti-inflammatory properties, has been used for the treatment of a variety of infectious and noninfectious dermatologic conditions, but not for AG. We present an original case of AG improving after treatment with doxycycline in a patient whose history of leukopenia and kidney disease limited the available treatment options.

First described by O'Brien in 1975, AG is thought to result from inflammation in response

From Louisiana State University Health Sciences Center School of Medicine[a] and the Department of Dermatology, University of Alabama at Birmingham School of Medicine.[b]
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Correspondence to: Kathryn Olivier Luckett, MD, Department of Dermatology, University of Alabama at Birmingham School of Medicine, 500 22nd St S., Birmingham, AL 35294. E-mail: koluckett@uabmc.edu.

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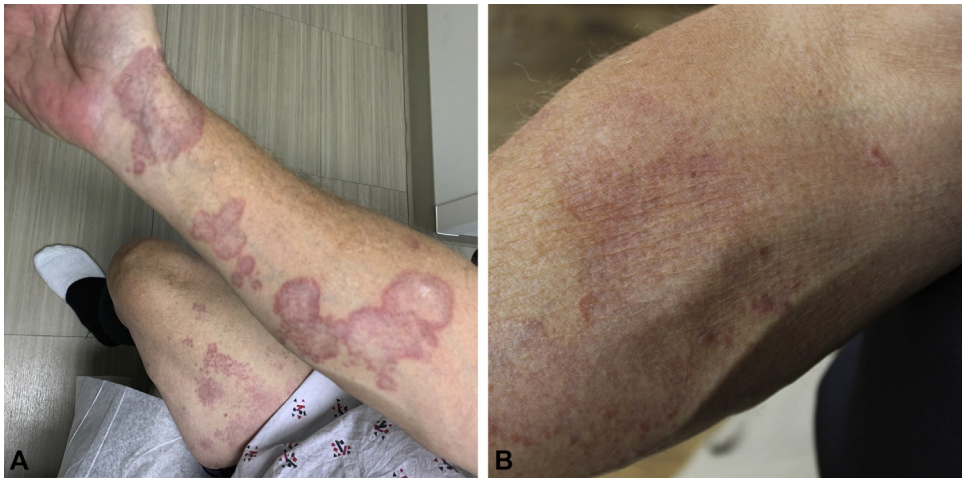

Fig 1. AG **A**, Pretreatment image shows annular lesions with erythematous scalloped borders and central atrophy on the right upper forearm and thigh. **B**, Image of the right upper forearm shows marked improvement after 6 months of doxycycline therapy.

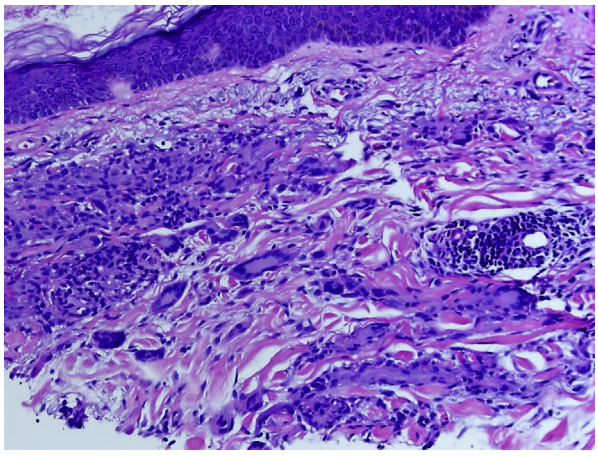

Fig 2. Histopathology of actinic granuloma. Skin biopsy shows superficial granulomatous dermal infiltrate with multinucleated giant cells and areas of dermal elastosis. (Hematoxylin-eosin stain; original magnification: ×200.)

to solar-damaged elastic fibers in sun-exposed areas of skin.[1] Histologically, the lesions of AG are characterized by a granulomatous reaction composed of multinucleated foreign body giant cells with elastophagocytosis on a background of dermal elastosis.[1,3] The differential diagnosis of AG includes GA and AEGCG. Clinically, the lesions of AG initially appear as erythematous papules and progress to annular plaques with raised edges and atrophic central skin or central hypopigmentation.[2-4] Lesions tend to affect the face, chest, neck, or upper limb and are mostly asymptomatic.[2,4]

AG has a slight predominance for middle-aged women but should be suspected in any patient presenting with annular plaques in a photo distribution, such as the patient described in this report.[2] Solar exposure is thought to be an inciting factor, but the exact pathogenesis of the disease is unknown. AG is a relatively rare disorder with less than 20 cases reported in PubMed over the last 5 years; its exact prevalence remains uncertain.

Although AG is a self-limiting disorder, the lesions may persist for up to 10 years.[1,3] Therapy is often desired given the slow disease course and topography involving cosmetically sensitive sites, but no specific treatment is universally recommended. Given the inflammatory nature of AG, it is thought that therapeutic agents with anti-inflammatory or immunosuppressive properties may be beneficial for its treatment. Varying success has been reported with agents such as hydroxychloroquine, cyclosporine, intralesional steroids, acitretin, isotretinoin, and retinoid psoralen plus ultraviolet A therapy.[5-7]

This patient posed a therapeutic conundrum for his treatment team. The patient did not respond to topical treatment and intralesional corticosteroids; however, we were hesitant to attempt treatment with cyclosporine, dapsone, or acitretin given the patient's personal history of leukopenia and chronic kidney disease. The decision to initiate doxycycline stemmed from previous reports of successful treatment of GA and AEGCG using tetracyclines.[8] Given some degree of shared patho-biologic factors between the AG, GA, and AEGCG, we felt inspired to pursue doxycycline treatment in our patient. Doxycycline is generally well tolerated, has shown utility in treating a variety of dermatologic conditions, and has minimal myelosuppressive or nephrotoxic activity.

The decision to begin treatment with doxycycline was weighed against the risk of dose-dependent phototoxicity of the drug as well as the photosensitive nature of AG. There have been two reports of AG developing in association with prolonged doxycycline phototoxicity. Accordingly, the patient was counseled on limiting sun exposure and wearing sun-protective clothing.

The patient was started on a course of 100 mg of doxycycline by mouth twice per day. Within 2 months, the patient had marked improvement of his lesions. After 6 months of continued improvement, the patient was started on a doxycycline taper and was instructed to discontinue the drug after 1 month of the taper. Two months after discontinuing doxycycline, the patient's lesions continued to resolve.

Because of the rarity of the disease, established treatment guidelines for AG do not exist. We hope that documentation of this patient's presentation and favorable clinical course helps characterize possible treatment modalities for future AG patients in whom therapy with other medications is ineffective or not feasible.

REFERENCES

1. O'brien JP. Actinic granuloma: an annular connective tissue disorder affecting sun and heat-damaged (elastotic) skin. *Arch Dermatol*. 1975;111(4):460-466.
2. Al-Hoqail IA, Al-Ghamdi AM, Martinka M, Crawford RI. Actinic granuloma is a unique and distinct entity: a comparative study with granuloma annulare. *Am J Dermatopathol*. 2002;24(3):209-212.
3. Thacker PM, Nayak K, Lobo F, Pavithra G. O'Brien's granuloma- a case report. *J Clin Diagn Res*. 2016;10(10):WD05-WD06.
4. Coutinho ID, Ramos LIC, Brites MM, Tellechea O. O'Brien actinic granuloma: a case report and brief review of literature. *Indian J Dermatol*. 2015;60(4):391-393.
5. Stefanaki C, Panagiotopoulos A, Kostakis P, Stefanaki K, Petridis A. Actinic granuloma successfully treated with acitretin. *Int J Dermatol*. 2005;44:163-166.
6. Lazzarini R, Rotter A, Cadore de Farias D, Muller H. O'Brien's actinic granuloma: an unusually extensive presentation. *An Bras Dermatol*. 2011;86:339-342.
7. Yaghoob R, Ranjbari N, Feily A. Actinic granuloma. *Dermatol Pract Concept*. 2014;4(3):2013-2014.
8. Lim DS, Triscott J. O'Brien's actinic granuloma in association with prolonged doxycycline phototoxicity. *Australas J Dermatol*. 2003;44(1):67-70.