Elastolytic Actinic Giant Cell Granuloma

Enrique Gutiérrez-González, MD, Manuel Pereiro Jr, MD, PhD*, Jaime Toribio, MD, PhD

KEYWORDS

• Actinic granuloma • Annular elastolytic giant cell granuloma • Elastophagocytosis • Elastosis • Diabetes mellitus

KEY POINTS

- Elastolytic actinic giant cell granuloma is a distinct condition characterized by annular lesions with erythematous borders and central clearance.
- Actinic damage is recognized as the main triggering factor, although the pathogenesis of cases in sun-covered areas remains unclear.
- A radial ellipse biopsy taken across the ring is recommended for diagnosis. Histologic features are the presence of an inflammatory infiltrate with nonpalisading granulomas and multinucleated giant cells limited to superficial dermis, as well as the absence of mucin and necrobiosis.
- Diabetes mellitus is the most frequently associated systemic disease.

INTRODUCTION

Annular elastolytic giant cell granuloma, also termed actinic granuloma (AG), when it affects sun-exposed skin, is an uncommon granulomatous skin disease. It is characterized clinically by annular plaques with raised erythematous borders that grow centrifugally and leave an atrophic center (**Fig. 1**). On histopathology the lesions show elastophagocytosis by multinucleated giant cells and marked loss of elastic tissue (**Fig. 2**). Elastophagocytosis is the phagocytosis of elastic fibers that can be seen microscopically in the cytoplasm of multinucleated giant cells and histiocytes (**Fig. 3**). This phenomenon is not exclusive to granulomatous disorders; it has been also described in cutaneous malignancies and infections, and can also be drug induced.[1] Although the pathogenesis of elastolytic actinic giant cell granuloma (EAGCG) remains unclear, it is thought that ultraviolet radiation, heat, and other unknown factors might change the antigenicity of elastic fibers.

ETIOPATHOGENESIS

AG was first described by O'Brien[2] in 1975. He postulated that actinically degenerated elastotic tissue was the antigenic basis of this condition, suggesting that elastotic fibers could be the direct stimulus for the development of granulomas and considering it as a phenomenon of repair of the damaged connective tissue. O'Brien[2] considered actinic injury as the primary event, supported by the observation that most of the lesions appear in sun-exposed areas of skin, with a characteristic solar elastosis that manifests as basophilic in sensitive hematoxylin-eosin stains (**Fig. 4**).[3,4]

Whether it should be considered a specific entity or a subtype of granuloma annulare (GA) is a topic of discussion. The original concept was disputed by Ragaz and Ackerman,[5] who thought that the lesions described by O'Brien[2] were variants of GA in sun-damaged skin. Al-Hoqail and colleagues[6] compared the histologic features of AG and GA located both in sun-exposed and

Conflict of Interests: None.

Department of Dermatology, Faculty of Medicine, Complejo Hospitalario Universitario, Santiago de Compostela, Spain

* Corresponding author. Departamento de Dermatología, Facultad de Medicina, C/. San Francisco, s/n, Santiago de Compostela 15782, Spain.

E-mail address: manuel.pereiro.ferreiros@usc.es

Dermatol Clin 33 (2015) 331–341

http://dx.doi.org/10.1016/j.det.2015.03.002

0733-8635/15/$ – see front matter

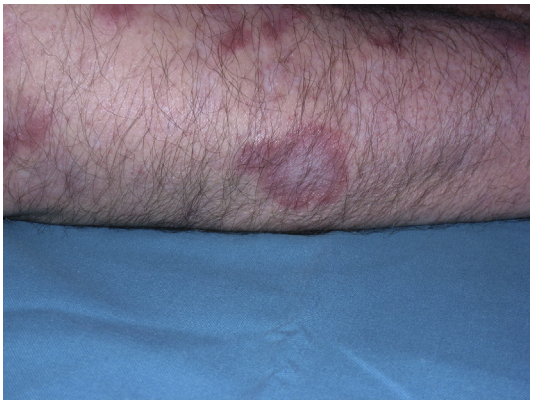

Fig. 1. Annular plaque showing central clearing on the dorsum of the forearm.

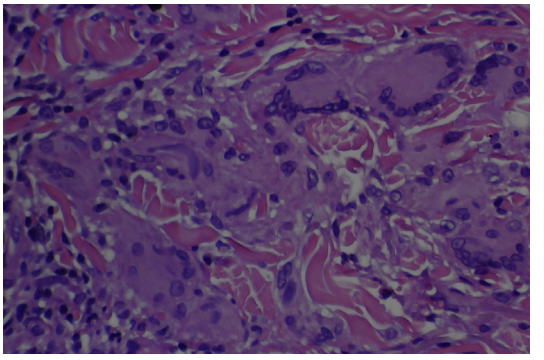

Fig. 3. Foreign body giant cell infiltrate in the middermis (hematoxylin and eosin; original magnification, ×250).

nonexposed areas, concluding that AG was an independent condition that must be differentiated from GA, even in those located in sun-exposed sites. Other investigators supported O'Brien's[2] concept of AG as a distinct entity.[7–10] Cases showing characteristics of both GA and EAGCG have been also reported.[11]

The descriptive term annular elastolytic giant cell granuloma was proposed by Hanke and colleagues[12] for lesions identical to AG but located not only in sun-exposed skin. Under this term he grouped other similar conditions, like Miescher granuloma of the face or atypical necrobiosis lipoidica of the scalp and the face. According to this investigator, the association of solar elastosis and granulomatous inflammation does not imply a cause-effect relationship. They prefer a term that is based on the main histologic features. There have been other descriptions that agree with this concept.[11,13]

O'Brien and Regan[3] refused this term and preferred the original term of AG because "it conceals the intrinsic and true nature of the lesion, that is, it represents an inflammatory reaction in response to actinically degenerated tissue."

The pathogenesis of EAGCG remains unclear. McGrae[8] suggested an immune response mediated by cells to degenerated elastic tissue, with a predominance of helper T cells in the lymphocytic infiltrate. He also observed differences between the enzymes of the histiocytes of AG and those of GA,[8] supporting that these are different conditions. Elastin peptides are responsible for inducing factor XIIIa(+) cells and macrophages to form granulomas and multinucleated giant cells.[14] Matrix metalloproteinase (MMP)-12, produced by macrophages, is expressed in the infiltrates of EAGCG, explaining the degradation of elastic fibers and inducing the formation of multinucleated giant cells.[15]

Ultraviolet (UV) radiation, especially UVA, because of its longer wavelength, and heat are recognized as causal factors, by changing the antigenicity of elastic fibers and producing an immune response.[2,16] However, collagen is not

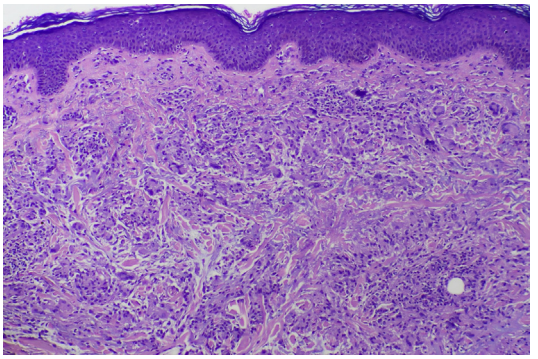

Fig. 2. Interstitial inflammatory infiltrate constituted by giant cell and lymphocytes surrounded by elastotic connective tissue (hematoxylin and eosin; original magnification, ×100).

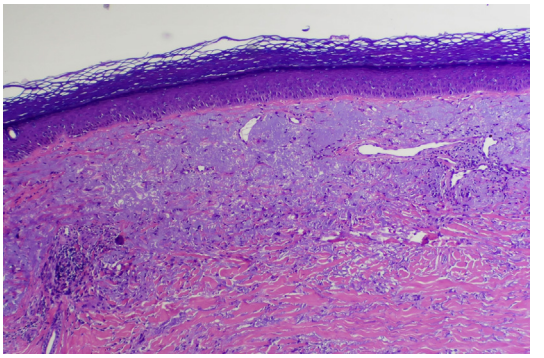

Fig. 4. Basophilic, elastotic degeneration of the dermis: elastic fibers appear thickened, coiled, and bluish (hematoxylin and eosin; original magnification, ×100).