

# Rare presentation of the generalized papular variant of elastolytic giant cell granuloma associated with follicular lymphoma



Derek J. Essegian, PhD,<sup>a</sup> Naiem T. Issa, MD, PhD,<sup>a</sup> Anna Nichols, MD, PhD,<sup>a</sup> and Clara Milikowski, MD<sup>b</sup>  
Miami, Florida

**Key words:** actinic granuloma; EGCG; granulomatous disease; lymphoma.

## INTRODUCTION

Elastolytic giant cell granuloma (EGCG) is a rare, benign granulomatous dermatosis with a chronic course that classically develops in sun-exposed areas of actinic elastosis.<sup>1-3</sup> EGCG is often self-limiting and asymptomatic but may present as pruritus and pain and have a relapsing, treatment-refractory course. The etiology of this condition is largely unknown, although it has been known to be associated with infection, autoimmune disorders, and malignancy. Few cases have been described as paraneoplastic syndromes in patients with hematologic malignancies, such as non-Hodgkin's lymphoma and leukemia. Of note, these instances have been known to be associated with the classic annular variant of EGCG. The papular variant has been rarely reported in patients with EGCG, and lymphoma-associated papular EGCG has not yet been described in the literature. Herein, we report a unique case of a middle-aged man with relapsed follicular lymphoma in whom a generalized eruption of the rare papular variant of EGCG involving both sun-exposed and sun-protected areas developed, which ultimately resolved after an allogeneic hematopoietic stem cell transplant.

## CASE REPORT

A 61-year-old Caucasian man with a past medical history of relapsed follicular lymphoma (14:18 translocation, a subtype of non-Hodgkin's lymphoma) and multiple treatments, including chimeric antigen receptor T-cell therapy, currently on copanlisib,

### Abbreviations used:

EGCG: elastolytic giant cell granuloma  
GA: granuloma annulare

presented to the emergency department with fever and shortness of breath. He was previously on immunotherapy with rituximab and lenalidomide, but this was discontinued because of hypercalcemia and pancytopenia. He was subsequently started on rituximab and copanlisib 7 weeks prior to presentation.

Upon admission, he presented with a generalized rash. The rash spread down his arms to the dorsal aspect of his hands, back, and lower extremities. Physical examination was notable for scattered, faint pink papules on the back; pink papules and atypical targetoid macules on the upper extremities, dorsal aspect and palms of the hands, and lower extremities; the absence of oral and mucosal lesions; and significant cervical lymphadenopathy (Fig 1).

Topical triamcinolone was initiated, and punch biopsies were performed on the left arm and left leg, followed by staining with hematoxylin and eosin. At low power, histology was significant for nodular aggregates within the dermis (Fig 2, A). Higher power revealed non-necrotizing granulomas with giant cells. There was elastolysis, and within the giant cells, there was elastophagocytosis (Fig 2, B). Elastic Verhoeff-Van Gieson stain confirmed elastolysis within the dermis and elastophagocytosis within the giant cells of the granulomas (Fig 3). The result

From the Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery,<sup>a</sup> and Department of Pathology, University of Miami Miller School of Medicine.<sup>b</sup>

Funding sources: None.

IRB approval status: Not applicable.

Correspondence to: Derek J. Essegian, PhD, Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, 1600 NW 10th Ave, RMSB 2023A, Miami, FL 33136. E-mail: [dje23@med.miami.edu](mailto:dje23@med.miami.edu).

JAAD Case Reports 2021;16:92-5.

2352-5126

© 2021 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.jidcr.2021.08.020>



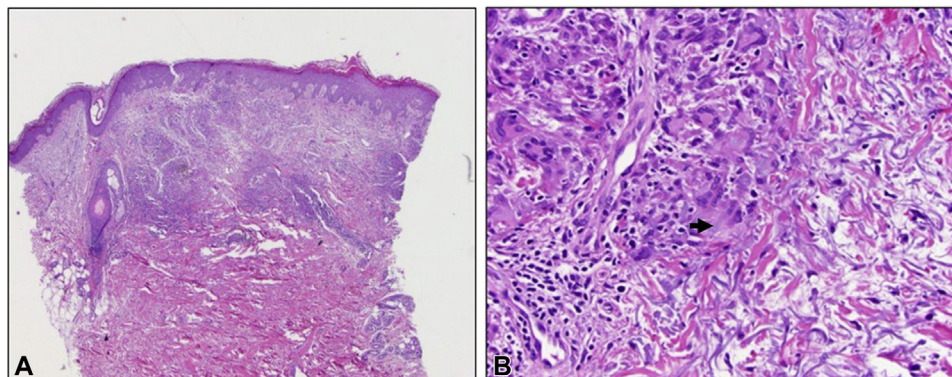
**Fig 1.** Erythematous discrete papules were observed on the (A) palmar aspect of the hand and flexor surface of the forearm, (B) legs, and (C) back (both sun-exposed and sun-protected areas). D, Left side of the neck shows significant palpable cervical lymphadenopathy.

of alcian blue staining was negative for mucin within the granulomas. These histopathologic features were consistent with those of EGCG.

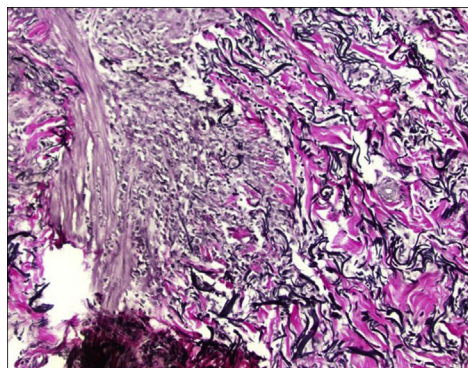
Three months after treatment initiation with triamcinolone, the patient reported minimal clinical improvement in the lesions, with persistent pruritus. At 6 months following presentation, the patient underwent an allogeneic stem cell transplant, with subsequent radiographic evidence of reduction in disease burden. At the 6-month post-transplant evaluation, all cutaneous lesions were resolved.

## DISCUSSION

The patient in this case had a complex 20-year medical history of follicular lymphoma with relapse, showing increased disease progression following 19 years in remission. He had recently started a new chemotherapy regimen, including a phosphoinositide 3-kinase inhibitor and a cluster of differentiation 20 monoclonal antibody. However, to date, there have been no reports of copanlisib or rituximab being associated with annular EGCG. The patient's skin lesions were recalcitrant despite



**Fig 2.** Elastolytic giant cell granuloma skin biopsy. **A**, A low-power view shows the involvement of the upper dermis based on the presence of nodular aggregates. **B**, A higher-power view shows nodular aggregates to be composed of lymphocytes, epithelioid histiocytes, and multinucleated giant cells. Within some of the giant cells, degenerated elastotic material was observed (arrow). (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**,  $\times 40$ ; **B**,  $\times 400$ .)



**Fig 3.** Elastic Verhoeff-Van Gieson stain highlights elastolysis and elastophagocytosis within the collections of histiocytes and giant cells, respectively (Elastic Verhoeff-Van Gieson stain; original magnification:  $\times 200$ .)

twice-daily treatment with topical triamcinolone over 3 months. However, after the successful allogeneic hematopoietic stem cell transplant and the radiographic evidence of decreased tumor burden at the time of follow-up 6 months after initial presentation, the patient's lesions had resolved. The association between the resolution of the patient's papular EGCG lesions due to the successful hematopoietic stem cell transplant lends credence toward the hypothesis of a malignancy-driven antigenic recognition process giving rise to a paraneoplastic T-cell-mediated granulomatous process.

EGCG is a rare, benign granulomatous dermatosis that typically develops in chronically sun-exposed areas of actinic elastosis.<sup>1,2,4</sup> However, several cases have been described in which such lesions developed in non-sun-exposed areas in association with solid tumors and blood malignancies,<sup>5</sup> including

squamous cell carcinoma,<sup>6</sup> acute myelogenous leukemia, adult T-cell leukemia,<sup>7</sup> prostate carcinoma,<sup>6</sup> and primary cutaneous T-cell lymphoma.<sup>5</sup> Reports of the resolution of EGCG following reduction in tumor burden support the theory that EGCG may be paraneoplastic in nature. In 1 case, the recurrence of malignancy brought about the return of EGCG.<sup>5</sup> The general pathophysiology of EGCG is largely unknown and highly debated upon. One leading theory is that damaged elastic fibers in actinic elastolytic skin are weakly antigenic and promote T-cell-mediated granulomatous inflammation in the dermis.<sup>2</sup> Some hypothesize that this paraneoplastic granulomatous disease may be a result of a cell-mediated systemic response to certain tumor antigens. Thus, physicians should be wary of new dermatoses in patients with malignancy and should perform a thorough physical examination and pathologic examination of biopsies of the suspicious lesions.

To our knowledge, there have been no reported associations between the papular EGCG variant and malignancy, although McGrae et al<sup>4</sup> described its association with monoclonal gammopathy of undetermined significance.<sup>4</sup> The annular variant most commonly manifests as lesions appearing on photo-distributed areas, including the neck, dorsal aspect of the hands, forearms, and face. Papular and reticular EGCG variants have also been reported, with lesions distributed in a generalized manner and a weaker association with sun exposure.<sup>2,3</sup> Papular EGCG was first reported in 1989 by Kato et al<sup>8</sup> as an unusual clinical variant, characterized by the development of asymptomatic, multiple, small red-to-skin-colored papules on the trunk and upper arms.

Few reports of this variant have been noted, including a pure papular variant, with the absence of centrifugal annular lesions, and the occurrence of a papular and reticular form in the same patient. Interestingly, the histopathologic features of all clinical variants do not differ from those of classic EGCG.<sup>3,8</sup>

Granulomatous dermatoses with papular or annular lesions have a broad differential, including many disorders with overlapping and loosely defined pathologic features and criteria.<sup>3,8</sup> Granulomatous eruption with elastolysis is not specific to EGCG and is observed in association with many cutaneous disorders.<sup>9</sup> Granuloma annulare (GA) is one such granulomatous disease, with 4 histopathologic subtypes, but is mainly defined by the presence of histiocytes surrounding degenerated collagen and increased mucin deposition. Reports of GA do not always demonstrate elastophagocytosis and may display a palisading pattern, with necrobiosis.<sup>9,10</sup> Actinic granuloma is a granulomatous cutaneous disorder of middle-aged adults that causes eruptions mainly on sun-exposed skin. Clinically, it is characterized by annular plaques with central atrophy and raised erythematous margins that are similar to those observed in patients with GA.<sup>4</sup> Its histopathology is notable for significant solar elastosis and the absence of mucin or necrobiosis.<sup>4</sup> Annular EGCG was first described by Hanke et al<sup>1</sup> as a cutaneous granulomatous disorder similar to GA, but it is more likely to be limited to sun-exposed areas and is associated with solar elastosis. The histology of annular EGCG lesions, like that of GA lesions, displays a multinucleated giant cell infiltrate, elastolysis, and elastophagocytosis in the mid-dermis. There exists some controversy about whether annular EGCG, actinic granuloma, and GA are separate entities or whether they are variants of the same spectrum. The other granulomatous cutaneous disorders that display elastolysis include granulomatous slack skin, granulomatous mycosis

fungoides, sarcoidosis, lichen sclerosus, and drug-induced elastophagocytosis.<sup>9</sup> Our patient lacked the clinical features of sarcoidosis, and there was absence of discrete epithelioid cell granulomas, as determined using histology. Classically, sarcoidosis is not associated with elastolysis, but there have been reports of elastolytic variants.<sup>5</sup> Given the clinical and histologic evidence, we hypothesize that in our patient, paraneoplastic granulomatous dermatitis associated with the follicular lymphoma developed, consistent with the diagnosis of papular EGCG.

#### Conflicts of interest

None declared.

#### REFERENCES

1. Hanke CW, Bailin PL, Roenigk HH Jr. Annular elastolytic giant cell granuloma: a clinicopathologic study of five cases and a review of similar entities. *J Am Acad Dermatol.* 1979;1(5):413-421.
2. Gutiérrez-González E, Pereiro M, Toribio J. Elastolytic actinic giant cell granuloma. *Dermatol Clin.* 2015;33(3):331-341.
3. Chen WT, Hsiao PF, Wu YH. Spectrum and clinical variants of giant cell elastolytic granuloma. *Int J Dermatol.* 2017;56(7):738-745.
4. McGrae JD. Actinic granuloma: a clinical, histopathologic, and immunocytochemical study. *Arch Dermatol.* 1986;122(1):43-47.
5. Tabata MM, Novoa RA, Martires KJ. Paraneoplastic granulomatous dermatitis in a patient with Hodgkin's disease: a diagnostic pitfall. *BMJ Case Rep.* 2018;2018:bcr2018224961.
6. Gyldenløve M, Faurschou A, Nielsen SL, Thyssen JP. Annular elastolytic giant cell granuloma in a patient with squamous cell carcinoma of the tonsil. *JAAD Case Rep.* 2014;1(1):34-35.
7. Kuramoto Y, Watanabe M, Tagami H. Adult T cell leukemia accompanied by annular elastolytic giant cell granuloma. *Acta Derm Venereol.* 1990;70(2):164-167.
8. Kato H, Uyeki Y, Yaoita H. Papular lesions associated with annular elastolytic giant cell granuloma. *J Am Acad Dermatol.* 1989;21(2):398-400.
9. El-Khoury J, Kurban M, Abbas O. Elastophagocytosis: underlying mechanisms and associated cutaneous entities. *J Am Acad Dermatol.* 2014;70(5):934-944.
10. Burket JM, Zelickson AS. Intracellular elastin in generalized granuloma annulare. *J Am Acad Dermatol.* 1986;14(6):975-981.