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Spontaneous or photo-induced resolution of papular elastolytic giant cell granuloma? A case report with considerations on its etiopathogenesis and clinical approach

Andrea Marani,[1] Davide Bertolla,[2] Alessia Caligiure,[2] Anna Rita Lombardi,[3] Andrea Conti[1]

[1]Dermatologic Unit, Department of Surgery, Infermi Hospital, AUSL Romagna, Rimini; [2]Section of Dermatology and Infectious Diseases, Department of Medical Sciences, University of Ferrara; [3]Anatomical Pathology Unit, Department of Oncohematology, Infermi Hospital, AUSL Romagna, Rimini, Italy

Correspondence: Andrea Conti, Dermatologic Unit, Department of Surgery, Infermi Hospital of Rimini, AUSL Romagna, Viale Settembrini 2, 47924 Rimini, Italy.
Tel.: +39 3472380244
Fax: +39 0541705002
E-mail: a.conti.dermo@gmail.com

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Abstract

Papular elastolytic giant cell granuloma (PEGCG) is a rare subtype of elastolytic giant cell granuloma (EGCG), typically presenting as asymptomatic papules in non-photo-exposed areas and lacking annular or photo-distributed lesions. Histologically, it overlaps with other EGCG variants, showing features like elastolysis, elastophagocytosis, and multinucleated giant cell infiltrates. The etiopathogenesis remains unclear, particularly the role of ultraviolet radiation (UV), and its clinical management is not well defined. We report a case of PEGCG that, after a one-year history, achieved complete clinical remission following two and a half months of sun exposure during the summer (heliotherapy). This case offers insights into its etiopathogenesis and clinical management, supported by a review of the existing literature.

Introduction

Papular elastolytic giant cell granuloma (PEGCG) is an uncommon clinical variant of annular elastolytic giant cell granuloma (AEGCG), a rare granulomatous skin disorder. AEGCG is characterized by annular, centrifugally expanding lesions primarily on sun-exposed areas, with histological features including elastolysis, elastophagocytosis, and multinucleated giant cell infiltration.[1,2] Recently, the term "elastolytic giant cell granuloma" (EGCG) has been adopted to encompass a broader spectrum of clinical subtypes, replacing earlier terms such as "AEGCG" and "actinic granuloma" (AG), the latter introduced by O'Brien in 1975.[1,2] This shift reflects reports indicating that EGCG lesions are not always annular or limited to photo-exposed areas, supporting the concept of a family of EGCG subtypes rather than defining AEGCG as a singular entity with rare variants.[3]

PEGCG, as a papular clinical subtype of EGCG, typically lacks annular or photo-distributed lesions. Instead, it presents as multiple, asymptomatic, erythematous to skin-colored, non-scaly, indurated papules on the trunk and extremities. Its recognition challenges traditional assumptions about EGCG pathogenesis and nosology. While elastic fiber degeneration remains central to EGCG, the role of ultraviolet radiation has become increasingly debated.[3] Recent reports describe EGCG in non-photo-distributed areas, highlight the papular PEGCG subtype, and even document paradoxical remission of PEGCG with narrow-band UVB irradiation.[4,5]

Here, we present a case of PEGCG that resolved following prolonged summer sun exposure. This case provides insights into the pathogenesis, nosology, and clinical management of PEGCG, supported by a review of the existing literature.

Case Report

A 79-year-old woman presented with a one-year history of asymptomatic macules and papules distributed across her trunk and extremities. The lesions initially appeared flat and gradually became palpable. During the consultation, she expressed significant concern about her condition.

Her medical history included osteoporosis, diverticulosis, and hereditary thrombophilia. She had been under angiologic follow-up and on anticoagulant therapy for thrombophilia but was not taking medication for osteoporosis or diverticulosis. She reported no recent introduction of new drugs but noted mild asthenia over the past year, without other systemic symptoms.

On examination, the patient had pink to red, firm, smooth macules and papules on her back, thighs, and arms (Figures 1 A,B). The lesions were confluent but did not form annular patterns, with the back being the most affected area (Figure 1C). The body surface area (BSA) involved was approximately 20%. Differential diagnoses included EGCG, disseminated granuloma annulare (GA), lichen myxedematosus, and clinically atypical sarcoidosis.

A skin biopsy revealed orthokeratotic epidermis, chronic granulomatous inflammation with histiocytes, multinucleated Langhans-type giant cells, and focal mucin deposits (Figures 2 A,B). Higher magnification showed multinucleated giant cells phagocytosing broken elastic fibers (elastophagocytosis) with associated elastolysis in the dermal interstitium (Figure 2C). There was no evidence of necrobiosis or palisading granulomas. Superficial and deep perivascular lymphocytic inflammation was observed. Fungal elements and alcohol-acid-resistant bacilli were absent.

The histological finding was compatible with EGCG, and, considering the clinical presentation, a diagnosis of PEGCG was made.

Based on the literature, investigations of the patient included chest radiography, abdominal ultrasound, ophthalmological evaluation, and routine blood tests to rule out underlying systemic pathology and consider systemic treatment options, such as hydroxychloroquine.[2,6]

The first visit occurred in July 2024. The patient came to follow up at the end of September 2024, in complete clinical remission.

Instrumental and laboratory findings were normal, and her asthenia had resolved. Physical examination revealed normal, lesion-free but markedly tanned skin (Figures 3 A-C), as demonstrated by iconographic comparison with July 2024 (Figures 2 and 3). The patient reported significant sun exposure during the summer without sunscreen and recognized much greater sun exposure than the previous summer. At a subsequent follow-up in December 2024, the patient remained in remission. The resolution of asthenia was attributed to the alleviation of psychological distress associated with her condition.

Discussion

The first description of PEGCG was reported in 1989 by Kato *et al.*, detailing a 55-year-old patient with multiple annular lesions on the trunk and numerous papules on the upper back and forearms. The histological examination of a skin lesion confirmed EGCG, marking the initial diagnosis of its papular subtype.[7] Since then, other atypical papular variants have been identified. In 1999, Morita *et al.* described a generalized papular variant without annular lesions, while Misago *et al.* reported a case with both papular and reticular lesions.[8,9] In 2009, Rongioletti *et al.* documented a case resembling Morita's, though with notable histopathological differences.[10] More recently, larger case series of PEGCG have emerged, although it remains rare, with limited literature.[2,6,11] We owe to these recent scientific studies the first attempt to classify the EGCG family into clinically distinct variants: annular, popular, and mixed,[6] or annular, papular, giant, generalized, and mixed.[2]

An important contribution by Limas *et al.* established histological criteria for EGCG diagnosis, distinguishing it from GA by the presence of predominant elastolysis and elastophagocytosis without necrobiosis or palisading granulomas.[12] The key histological features of EGCG include: i) absence of mucin and necrobiosis; ii) prominence of multinucleated giant cells, elastolysis, and elastophagocytosis; and iii) absence of palisading granulomas.[9] These criteria are consistent across EGCG variants, including PEGCG, as no definitive histological differences exist among them. However, histological overlap with GA has been reported. For instance, de Oliveira *et al.* described a case of EGCG with features of granulomatous inflammation, elastophagocytosis, and elastolysis, alongside necrobiosis and palisading granulomas.[13] Similarly, our case demonstrated focal mucin deposits, a finding uncommon in EGCG but insufficient to exclude a diagnosis of PEGCG given the overall clinical and histopathological presentation.

Another possible differential diagnosis could have been type III mid-dermal elastolysis. It clinically presents with persistent reticulated erythema and skin wrinkling localized to the trunk. Its clinical presentation may resemble our case, although coalescence of papules is the characteristic clinical finding of PEGCG. In addition, histologically, mid-dermal elastolysis characteristically presents with loss of elastic fibers in the mid-dermis and only occasionally multinucleated giant cells and elastophagocytosis.[14]

PEGCG has been linked to various clinical conditions, including hyperlipidemia, sideropenic anemia, angina, shingles,[6] and monoclonal gammopathy.[10] Notably, there is only one reported case of PEGCG presenting as a paraneoplastic manifestation of relapsed follicular lymphoma, which resolved following allogeneic hematopoietic stem cell transplantation.[15] In our case, the patient's medical history does not appear to be directly related to the development of PEGCG, and thorough investigations ruled out other underlying conditions.

The treatment of PEGCG remains unstandardized, with reported therapeutic attempts including topical steroids,[6] topical tacrolimus,[10] hydroxychloroquine, and griseofulvin.[16] Medications effectively used for AEGCG, such as methotrexate, cyclosporine, and fumaric acid, have not yet been reported for PEGCG. Interestingly, at least five cases of spontaneous regression of PEGCG have been documented, a phenomenon not observed in AEGCG, suggesting that the papular subtype may have a unique tendency for resolution without treatment.[1,6,9,17,18]

Notably, Takata *et al.* reported a case of PEGCG successfully treated with NB-UVB phototherapy.[5] This case is particularly intriguing given that UV radiation is considered a potential trigger or exacerbating factor for EGCG. The authors attribute the therapeutic effects to the specific mode of irradiation: while chronic exposure to low doses and broad UV wavelengths may induce granulomatous reactions by altering connective tissue antigenicity, acute exposure to high doses and selective wavelengths, such as NB-UVB, may have therapeutic benefits.[5] NB-UVB is particularly effective because it targets the upper dermis, where granulomatous infiltration occurs.[5]

Our case closely resembles those described above, as our patient experienced non-pharmacological resolution of PEGCG. However, it remains uncertain whether this resolution was truly spontaneous or photo-induced. The disease's persistence over one year, followed by remission during two and a half months of summer sun exposure, suggests a potential causal role for heliotherapy. This represents the second reported case, after Takata *et al.*, where UV radiation – a presumed causative factor – appears to have therapeutic or potentially therapeutic effects.

Uniquely, our case involved remission associated with natural sun exposure, which, although an exposure made over two and a half months, may be considered "acute", is by radiation other than NB-UVB phototherapy (*e.g.*, about 99% of the ultraviolet that reaches the earth's surface is UVA).

The remission linked to intense or prolonged sun exposure raises questions about the pathogenesis and classification of a disease historically associated with actinic damage.[3,16]

Early pathogenic theories, such as those by O'Brien, posited that EGCG's clinical variants depend on the degree of immune response and the type of elastic tissue involved.[19] Annular lesions were thought to result from complete, centrifugal elastophagocytosis of actinically damaged fibers, while generalized papular lesions were linked to a systemic immune response to mildly damaged or intact elastic tissue.[9] Although elastic fiber degeneration remains central to EGCG, the role of UV radiation in its pathogenesis – particularly in PEGCG – appears less definitive.

For instance, Caldas *et al.* described PEGCG in an obese, diabetic patient with papules localized to adipose areas.[16] They proposed that the adipose tissue's cytokine profile might trigger a granulomatous reaction against nearby glycated, damaged elastic fibers. A similar mechanism may

explain EGCG cases associated with systemic conditions like hematologic malignancies, underscoring the need for further investigation into their pathogenesis.[15,16]

Although further validation is needed, we support the pathogenic model proposed by Caldas *et al.*, for which our report provides additional evidence. The pathogenesis of PEGCG may differ from that of AEGCG, even though both are driven by damage to elastic fibers. AEGCG could represent a granulomatous, cell-mediated inflammatory response to elastic fibers severely damaged by sunlight, which explains its predilection for photo-exposed areas. In contrast, PEGCG may result from a similar inflammatory response to mildly damaged elastic fibers, with damage potentially triggered by factors other than sunlight, such as diabetes, malignancies, or unknown processes.

Elastic fibers can be compromised not only by sun exposure but also by endogenous and exogenous factors (*e.g*, glycation or calcification), collectively contributing to the so-called "aging" of elastic fibers, even if photo-exposed areas consistently show greater elastic fiber damage compared to non-exposed regions.[20] This hypothesis aligns with early models by O'Brien and other authors and more recent studies.

A distinct pathogenesis could explain the differing clinical presentations and disease courses, with PEGCG demonstrating potential for spontaneous remission if the "non-solar" stimulus is removed. This may also clarify why, in our patient, PEGCG was not induced but instead resolved during sun exposure, suggesting that the pathogenesis of PEGCG may not be as tightly linked to actinic damage as traditionally thought.

Conclusions

In conclusion, our case report offers three key insights when compared with other PEGCG cases in the literature. First, a "wait-and-watch" approach, where the patient is informed but no immediate treatment is given, appears justified for asymptomatic PEGCG, as spontaneous remission has been reported in several cases.[1,6,9,17,18] Ongoing monitoring with laboratory and instrumental investigations is recommended to rule out underlying causes and anticipate potential therapy. Second, phototherapy and heliotherapy may be viable treatment options, though they should be used cautiously given the incomplete understanding of PEGCG's pathogenesis, and since Chen *et al.* reported a moderate to strong correlation of PEGCG with sun exposure in some cases.[6] In contrast, photoprotection is advised for AEGCG. Finally, a more precise nosography and classification of PEGCG within the spectrum of EGCG, and in relation to AEGCG and GA, is certainly needed to clarify its etiopathogenesis and improve its clinical approach.

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Figure 1. Clinical picture at first evaluation. Pink or small red, firm to touch, smooth macules and papules diffuse to the back (**A**), thighs (**B**), and arms. (**C**) Higher magnification detail of the lesions, purely papular, without annular structures.

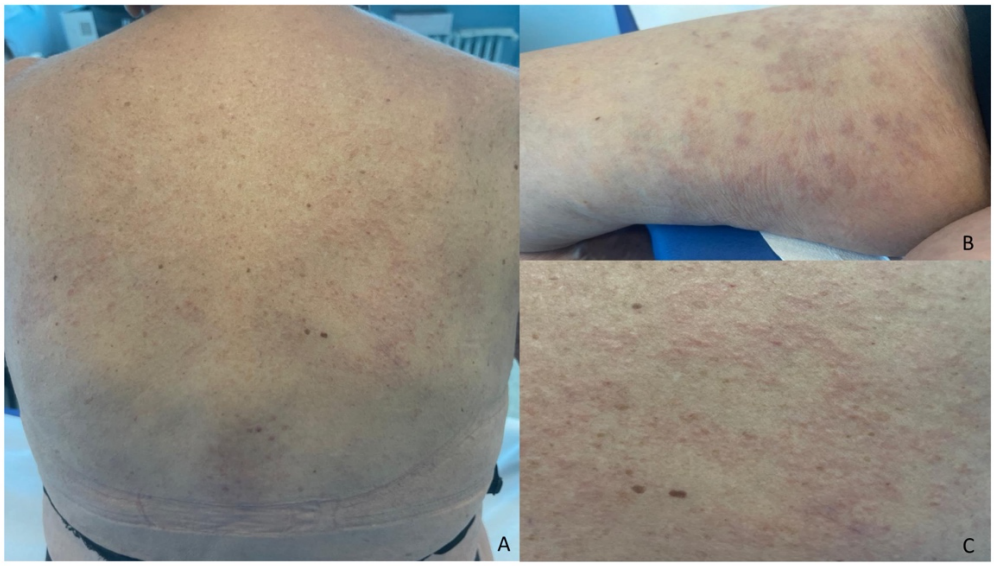

Figure 2. Histopathological picture in hematoxylin and eosin at 10x (**A**), 20x (**B**), and 40x (**C**) magnification. At 10x and 20x magnification (**A**,**B**) orthokeratotic epidermis and chronic granulomatous inflammation with histiocytes and multinucleated Langhans-type giant cells phagocytosing (elastophagocytosis) broken elastic fibers (elastolysis) are observed. Elastophacytosis and elastolysis are best seen at 40x; elastophagocytosis is highlighted by arrows (**C**). Mucin deposits are evidenced by histochemical staining with Alcian blue (**D**).

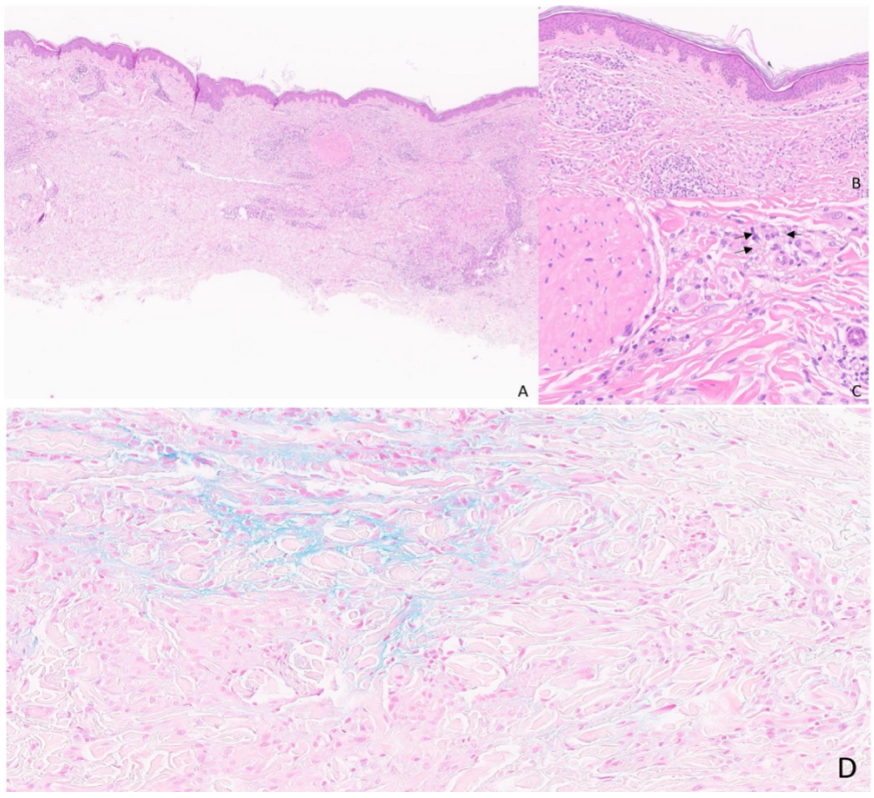

Figure 3. Clinical picture at second evaluation. The areas previously affected by PEGCG at both low (**A**,**B**) and high magnification (**C**) were free of lesions. Only clearly tanned skin is observed (**A**-**C**).