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CLINICAL CORRESPONDENCE

Refractory Disseminated Annular Elastolytic Giant Cell Granuloma Successfully Treated With Upadacitinib: A Case Report

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Annular elastolytic giant cell granuloma (AEGCG) is an uncommon granulomatous dermatosis variant, first described by O'Brien in 1975. Clinically, it presents with annular or arciform plaques, distributed over sun-exposed areas. The disease course is usually chronic and slowly progressive. Histologically, AEGCG is characterized by a dermal granulomatous infiltrate composed of multinucleated giant cells, histiocytes, and lymphocytes, accompanied by widespread elastophagocytosis and loss of elastic fibers [1]. The pathogenesis of AEGCG remains incompletely understood; however, chronic ultraviolet exposure is believed to play a central role. Some associations have been reported, including diabetes mellitus, sarcoidosis, giant cell arteritis, polymyalgia rheumatica, polychondritis, vitiligo, anemia, leukopenia, hepatitis C (HCV), focal segmental glomerulosclerosis, and Hashimoto's thyroiditis [2].

Therapeutic options include topical and systemic corticosteroids, antimalarials, retinoids, and immunosuppressants, but outcomes are often inconsistent, particularly in disseminated forms. For this reason, lately interests have progressively shifted toward targeted therapies, particularly Janus kinase (JAK) inhibitors, which have been successfully used in other chronic granulomatous dermatoses [3].

In this report, we describe a case of disseminated AEGCG successfully treated with upadacitinib.

A 43-year-old Caucasian male presented with a diffuse, slightly pruritic papular eruption. Clinical examination showed erythematous papules distributed over the face, trunk, and limbs. The papules coalesced into plaques over the posterior aspects of the arms (Figure 1A–C). The patient reported the initial onset of the lesions approximately 1 year prior, with a relapsing and progressive course over time. Medical history revealed type 1 diabetes mellitus treated with insulin. No other comorbidities were reported. Histopathology showed a granulomatous dermal infiltrate, predominantly composed of multinucleated giant cells with scattered histiocytes, associated with a dense perivascular and interstitial lymphoplasmacellular infiltrate. Widespread elastophagocytosis and elastolysis were noted, with minimal interstitial mucin deposition (Figure 2A–D). Palisading granulomas and necrobiosis were absent. A diagnosis of annular elastolytic giant cell granuloma was made. Treatment with topical corticosteroids and hydroxychloroquine 400 mg/d, cyclosporine 200 mg/d, or methotrexate 15 mg/week yielded minimal clinical improvement. Consequently, upadacitinib 30 mg/day was initiated, with early benefit after 4 weeks and substantial improvement by Month 4 (Figure 1D–F). Follow-up visit at 1 year showed persistent remission. The treatment was well tolerated, without side effects.

AEGCG is a rare granulomatous dermatosis characterized by annular or arciform plaques, often localized to sun-exposed areas such as the face, neck, and upper extremities. The diagnosis is confirmed histologically by the presence of a dermal

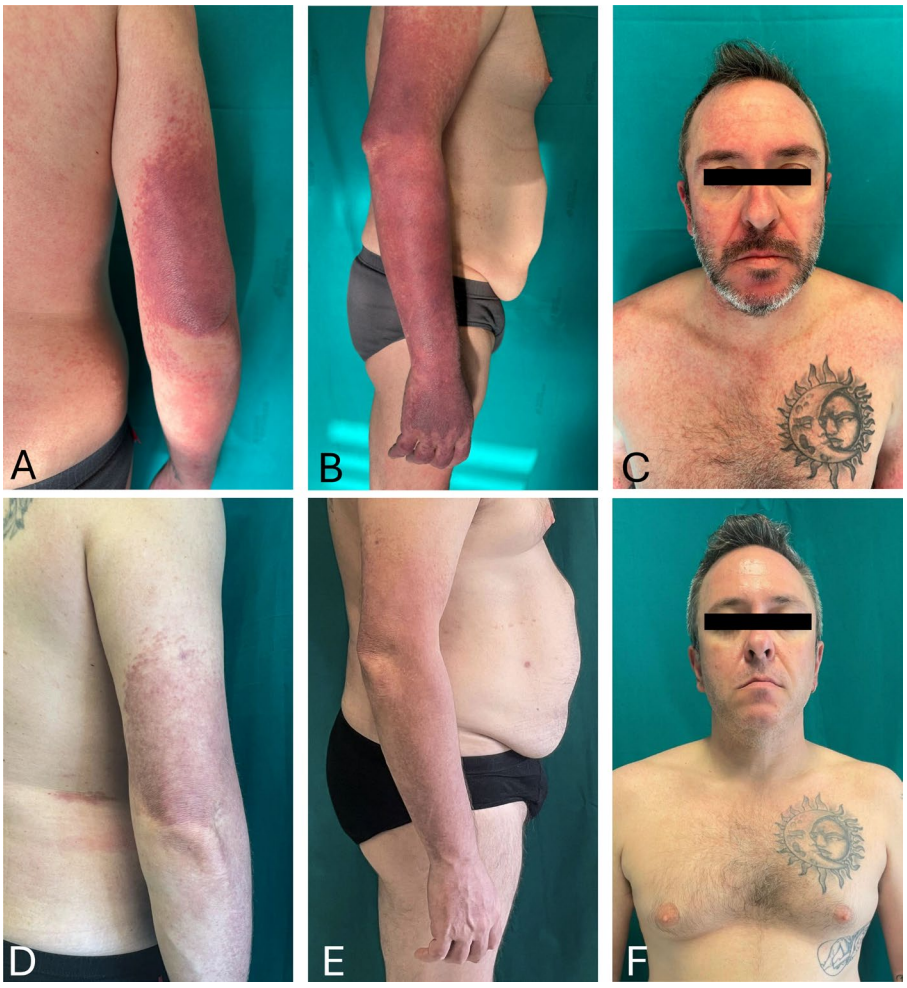

FIGURE 1 | (A)–(C): Erythematous papules distributed over the trunk and upper limbs. The papules progressively coalesced into plaques over the posterior aspects of the arms. (D)–(F): Significant improvement of the lesions, which appeared less erythematous and infiltrated.

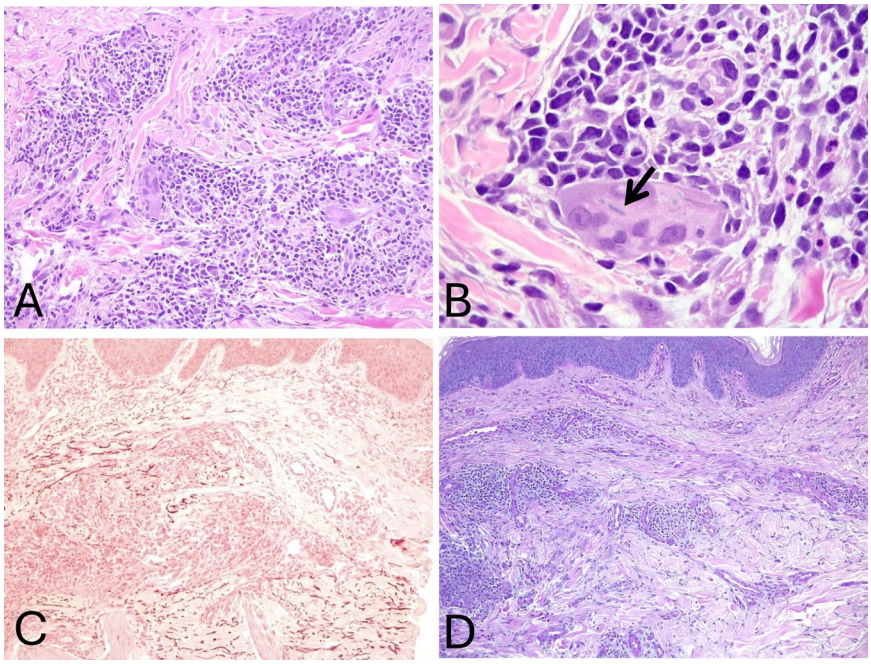

FIGURE 2 | (A) A dense inflammatory infiltrate with numerous multinucleated giant cells in the upper dermis (Hematoxylin & eosin, 20X). (B) Elastophagocytosis with engulfment of degraded elastin fiber (arrow) in a giant cell (Hematoxylin & eosin, 63X). (C) Significant reduction and fragmentation of elastic fibers (modified orcein, 5X). (D) Interstitial mucin deposition is minimal (Alcian-PAS, 10X).

granulomatous infiltrate composed of multinucleated giant cells, accompanied by elastophagocytosis and a loss of elastic fibers, without necrobiosis [1]. Traditional therapies are often associated with variable clinical responses and are frequently ineffective in disseminated cases. The pathogenesis of AECCG remains unclear; however, some evidence suggests that the granulomatous response can be driven by persistent activation of Th1 and Th17-mediated immune pathways, with overrelease of pro-inflammatory cytokines [3]. Interleukin (IL)-15, IL-21, tumor necrosis factor-alpha, and interferon-gamma have been implicated in sustaining granulomatous inflammation in various conditions. These cytokines activate the JAK/STAT pathway signaling, thus suggesting a potential therapeutic target [3]. JAK inhibitors (JAKi) have been used effectively in the treatment of disseminated or refractory granulomatous skin conditions, achieving rapid remission. Previous reports have documented the use of non-selective JAK inhibitors such as tofacitinib with conflicting results, as well as other selective ones with clinical benefit, supporting the potential therapeutic role of JAK pathway modulation in chronic granulomatous dermatoses [4, 5].

To the best of our knowledge, this is the first reported case of AEGCG successfully treated with upadacitinib, suggesting that selective JAKi may represent a novel and promising therapeutic option for recalcitrant forms of such disease. Further studies are necessary to demonstrate the efficacy of JAKi in the management of non-infectious cutaneous granulomatous diseases.

Ethics Statement

Ethical approval was not required for this case report in accordance with institutional guidelines.

Consent

Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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