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Pathogenesis and Diagnostic Complexities of Granuloma Faciale

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We present a case with granuloma faciale – a rare and idiopathic disorder characterized by the formation of asymptomatic red-brown plaque, most commonly on the face. Correct diagnosis of the disease requires a histopathological examination. Despite of the name, there are no granulomas but rather an eosinophil and neutrophil predominant infiltrate and a leucocytoclastic vasculitis with a typical grenz zone. Etiology is unknown and usually there is a therapeutic resistance, which determines a chronic-recurrent course with a psycho-emotional tension from the patient.

Key words: Granulona faciale, Grenz zone, tissue eosinophilia, histology

Introduction

Granuloma faciale (GF) is a rare, chronic inflammatory dermatosis that belongs to the group of idiopathic eosinophilic dermatoses. These conditions, which include several rare dermatological syndromes of unclear etiology, are characterized by tissue eosinophilia as a central pathogenetic feature. GF presents with a distinctive clinical appearance, characteristic histopathological findings, and a chronic-recurrent course, often with partial therapeutic resistance.

Granuloma faciale is generally benign, without systemic involvement, and its etiopathogenesis remains unclear. The disease most commonly affects middle-aged white men. Skin lesions typically appear as erythema-infiltrative plaques with a raised border and a slightly sunken, livid center. The disease may start with solitary papules or nodules that grow peripherally and may coalesce. The lesions can reach several

centimeters in diameter, with smooth surfaces, no ulceration, a slight accentuation of the follicular ostia, and peripheral telangiectasias. In some cases, the skin may develop a "peau d'orange" appearance.

The lesions are often asymptomatic and primarily localized to the face, particularly the perinasal, zygomatic, preauricular, or forehead areas [6]. However, extrafacial involvement of the scalp, trunk, and limbs can occur [9]. There is no known association with underlying diseases, and laboratory tests usually show only mild peripheral eosinophilia.

A biopsy is essential for diagnosing granuloma faciale. A key feature is the preservation of the subepidermal papillary dermis, known as the Grenz zone. Histopathologically, the upper dermis shows a dense mixed inflammatory infiltrate consisting of neutrophils, eosinophils, and lymphocytes, while skin adnexa remain unaffected. Leukocytoclastic vasculitis with typical nuclear debris may also be seen. Chronic lesions often show a histiocytic infiltrate with pronounced fibrosis and capillary proliferation [4].

GF is a chronic inflammatory dermatosis that does not involve systemic organs. The cutaneous lesions tend to persist for long periods, rarely resolving spontaneously. The disease's therapeutic resistance and unclear pathogenesis contribute to its chronic, persistent course, making treatment difficult and leading to patient dissatisfaction.

Case report

We present a case of a 45-year-old white male who developed an erythema-infiltrative plaque with a yellowish tint on his forehead four years ago. The lesion did not cause subjective symptoms and persisted despite treatment with potent topical corticosteroids. In the last few months, the patient developed a circumscribed erythematous livid lesion with follicular accentuation on the apex of the nose (**Fig. 1**). A dermato-oncologist recommended a biopsy to exclude basal cell carcinoma, and the lesion was initially diagnosed as primary T-cell cutaneous lymphoma due to pronounced infiltration by CD4-positive cells. The patient was referred to a hematology clinic for further staging.

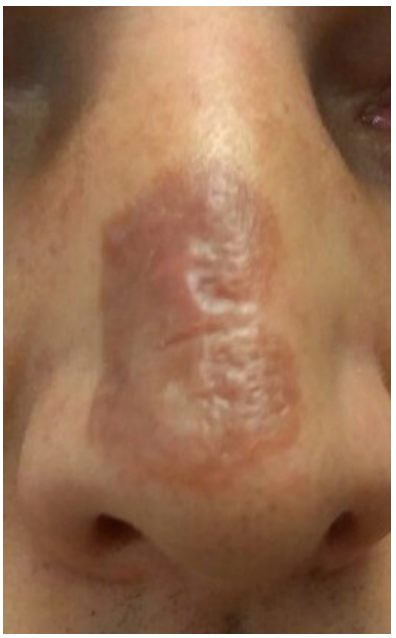

Fig. 1. Well-demarcated erythematous plaque with glossy appearance, localized to the dorsum of the nose.

At the clinic, a second dermatological consultation suggested granuloma faciale. Dermoscopy showed linear, arborizing vessels, dilated follicular openings, and brown dots, further supporting the diagnosis.

A new biopsy revealed the characteristic Grenz zone, a pronounced mixed inflammatory infiltrate in the upper dermis with many neutrophils, eosinophils, and lymphocytes, along

with single histiocytes and a more pronounced fibrous reaction in the lower dermis (**Fig. 2**). These findings were consistent with the clinical diagnosis of GF.

The patient underwent topical calcineurin inhibitors therapy (0.1% tacrolimus ointment). After one month of follow-up, a slight flattening and mild reduction in the lesion's diameter was observed.

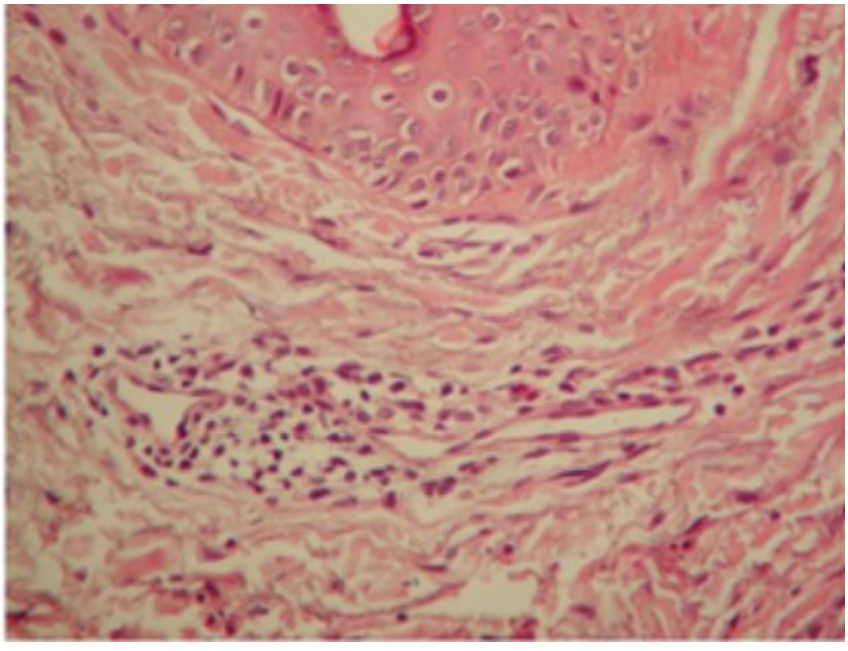

Fig. 2. Eosinophilic granuloma – follicular hyperkeratosis, uniform acanthosis, Grenz zone, mild to moderate perivascular infiltrate of lymphocytes, neutrophils and single eosinophils in the fibrous papillary dermis. (Hematoxylin-Eosin, ×400).

Discussion

Granuloma faciale is a rare, chronic inflammatory dermatosis with a benign course, no systemic involvement, and an unclear etiopathogenesis. First described in the 1950s [7], GF is characterized by erythematous livid plaques, primarily affecting the face, with a persistent course and pronounced therapeutic resistance. The exact pathogenesis remains unclear, but several theories have been proposed.

One hypothesis speculates that chronic actinic damage plays a significant role in its development, as cutaneous efflorescences are commonly found on photoexposed areas and may flare up following photoexposure [10]. Other researchers suggest that granuloma faciale could be a localized reaction to the deposition of circulating immune complexes, resembling a form of limited small vessel vasculitis [5]. Studies have also shown that tissue eosinophilic infiltration in GF correlates directly with the migration of CD4-positive lymphocytes that produce interleukin-5 (IL-5) in the affected tissues. As a result, GF is suspected to be a dermatological prodrome of monoclonal expansion of a specific lymphocyte subset, which induces eosinophilic chemotaxis

and the proliferation of tissue macrophages, leading to a subsequent local, persistent fibrous reaction [8]. Some researchers argue that a gamma-interferon-mediated process directly activates the complement system, causing tissue destruction and resulting in chronic fibrous changes mediated by tissue macrophages [1].

The correct diagnosis of GF can be established through its distinctive clinical features and characteristic histopathological findings. Biopsy analysis is essential to rule out key differential diagnoses, including erythema elevatum diutinum, chronic discoid lupus erythematosus, sarcoidosis, lymphoid infiltration, primary cutaneous lymphomas, basal cell carcinoma, and skin infections such as lupus vulgaris [13].

The treatment of GF remains challenging, as there are no universally effective therapeutic options. A variety of treatments have been attempted, including dapsone, clofazimine, antimalarials, isoniazid, topical corticosteroids, intralesional injections with gold salts and depo-corticoids, dermabrasion, laser ablation, surgical excision, local PUVA therapy, and calcium-neurin inhibitors [3,11]. However, the clinical responses to these treatments are highly variable, and no single therapy has proven to be consistently effective.

Recently, topical JAK inhibitors such as tofacitinib and ruxolitinib have emerged as promising treatments for GF. Given that inflammatory mediators associated with the development of this disorder – specifically interleukin-5 and interferon-gamma – signal through the JAK pathway, these inhibitors may offer a targeted approach to managing GF [2, 12]. However, further randomized controlled studies are needed to confirm their efficacy, safety, and optimal dosing for this condition.

Conclusion

Granuloma faciale is a rare chronic inflammatory dermatosis with an unclear etiopathogenesis, characterized by persistent violaceous plaques primarily on the face. Its diagnosis is challenging due to clinical similarity to other dermatological conditions, but the characteristic histopathological findings, including the preservation of the Grenz zone and a mixed inflammatory infiltrate, are key to confirming the condition. While the exact cause remains uncertain, various theories suggest that chronic actinic damage, immune complex deposition, or T-cell-mediated immune responses may play important roles in its development.

Treatment of GF remains difficult and often unsatisfactory, with variable responses to therapies such as topical corticosteroids, dapsone, and calcineurin inhibitors. Despite this, newer treatments, such as topical JAK inhibitors like ruxolitinib, show promise, targeting inflammatory pathways involved in the condition. However, further randomized controlled trials are necessary to establish their long-term efficacy, safety, and optimal use in managing granuloma faciale.

This case highlights the diagnostic complexities and treatment challenges associated with GF. As a condition that is both clinically and histopathologically distinctive, it requires careful attention from healthcare providers. Continued research and clinical trials will be crucial to improving our understanding of the disease and optimizing therapeutic strategies.

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