The interaction of inflammatory cells in granuloma faciale

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Abstract

Granuloma faciale (GF) is a rare chronic inflammatory skin disease characterized by single or multiple reddish-brown cutaneous plaques or nodules. Although this condition is benign, its clinical course is extremely chronic with poor response to therapy. The typical histopathological features of GF include vasculitis with mixed cellular infiltration; however, its etiopathogenesis remains unknown. Here, we describe the case of a 76-year-old man with GF resistant to topical steroids. Biopsy of the lesion revealed i) dense mixed inflammatory cellular infiltrates of lymphocytes, histiocytes, neutrophils, and eosinophils, ii) mild perivascular nuclear dust and swollen endothelium of blood vessels, and iii) a narrow Grenz zone beneath the epidermis. Immunohistochemical staining demonstrated mixed cellular infiltrates intermixed with CD1a+ dendritic cells, CD68+ histiocytes, and CD4+ and CD8+ T cells.

Introduction

Granuloma faciale (GF) is a chronic inflammatory skin disorder appearing as a solitary lesion or multiple reddish-brown infiltrating lesions on the face, usually on the cheeks, nose, and forehead. Although its etiopathogenesis remains unknown, vasculitis with mixed cell inflammation is considered to be the typical histological feature.1 Exposure to sunlight is regarded as a triggering factor; however, other causative factors such as infections, immunological disorders and associated malignancies might be responsible for its pathogenesis.2 Recently, the production of interleukin (IL)-5 by the clonal T-cell population has been implicated in the attraction of eosinophils to the lesions.1 Here, we report a male patient who was clinically and histopathologically diagnosed with GF. Mixed cellular infiltrates intermixed with CD1a+ dendritic cells (DCs), CD68+ histiocytes, and CD4+ and CD8+ T cells were detected immunohistochemically.

Case Report

The patient was a 76-year-old male who developed a reddish-brown cutaneous plaque with exaggerated follicular openings on the left cheek (Figure 1a and b). The lesion was slightly elevated and slowly progressive, and showed no response to topical steroids. No underlying associated disease was detected, and his routine laboratory examinations were all within the normal limits. Screening for antinuclear antibodies was negative. Clinically, GF, sarcoidosis, discoid lupus erythematosus, follicular mucinosis and pseudolymphoma were considered as differential diagnosis. Punch biopsy from the lesion showed a dense dermal inflammatory and granulomatous infiltrate of mononuclear cells with numerous eosinophils and neutrophils. The features of mild leukocytoclastic vasculitis: perivascular neutrophilic infiltrate with debris and swollen endothelium of blood vessels were also evident. Stromal fibrosis was found around the granulomatous lesions. A narrow Grenz zone was also observed beneath the epidermis, and adnexal structure was intact (Figure 2a and b). These histopathological findings were consistent with GF. Immunohistochemically, both CD8+ lymphocytes and CD68+ histiocytes were present mainly inside the granulomatous lesions (Figures 3a and b), whereas scattered CD4+ lymphocytes and CD1a+ DCs surrounded the lesions, and to a lesser extent, occurred within the lesions (Figure 3c and d). The cutaneous plaque lesion was treated with local injection of a corticosteroid. In a few months of treatment, infiltration was reduced but the reddish-brown cutaneous plaque lesion persisted.

Discussion

GF is a rare inflammatory skin disease with typical clinical and histopathological entity. A previous extensive review of GF comprising 66 patients revealed that more than 90% of the patients had only facial lesions and 62% of the patients of this series had a solitary lesion. GF has a tendency to appear in areas exposed to sunlight, such as the forehead, cheek, and nose.4 It is mostly asymptomatic but occasional burning or itching sensation is experienced. Dense granulomatous infiltration of lymphocytes, plasma cells, neutrophils, histiocytes and eosinophils is observed in the reticular dermis. Interestingly, a typical granulomatous lesion predominantly composed of histiocytes does not normally occur in GF, making GF one of the mismomers in dermatology. Fibrous tissue accompanying capillary proliferation can be observed in old lesions. One of the most important...
histopathological findings in GF is the presence of the Grenz zone, which is an area between the epidermis and the upper dermis devoid of cells. Thus, the present case showed representative clinical and histopathological features of GF.

For the clinical differential diagnosis, sarcoidosis, lupus vulgaris, fungal infections, discoid lupus erythematosus, follicular mucinosis, and pseudolymphoma should be considered. Histopathological examination is useful in distinguishing GF from other diseases. Histopathological differential diagnosis of GF should be made with erythema elevatum diutinum (EED). Similar to GF, EED starts with the appearance of neutrophils and neutrophilic nuclear dust around small vessels containing fibrin in their wall. In most EED cases, the eruption is bilateral and symmetric. Histopathologically, eosinophils are few or absent and neutrophils predominate with plasma cells only present episodically. The sites of EED predilection are different — the face is usually spared, and the skin on the dorsal aspects of joints is usually the target site.

Different etiologies regarding the pathogenesis of GF have been suggested, but most of them remain controversial. Because light-exposed areas are favored as exemplified in the majority of GF cases with facial involvement, actinic exposure has been suggested to play an important role. It is suggested that it may be a form of vasculitis mediated by localized Arthus-like response. It might also be due to a localized persistent immune complex disease or persistent allergic hypersensitivity reaction to a retained antigen or both. Histopathologically, eosinophils are few or absent and neutrophils predominate with plasma cells only present episodically. The sites of EED predilection are different — the face is usually spared, and the skin on the dorsal aspects of joints is usually the target site.

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