Granuloma Faciale: Distribution of the Lesions and Review of the Literature

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GOAL

To gain a thorough understanding of granuloma faciale (GF)

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Explain the clinical presentation of GF.
2. Discuss the differential diagnosis of GF.
3. List the treatment options for GF.

CME Test on page 208.

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Granuloma faciale (GF) is an uncommon inflammatory condition characterized by reddish brown papules and plaques that usually involve the facial area. Extrafacial lesions are rare. Histologically, the lesions are marked by leukocytoclastic vasculitis and extensive fibrin deposition. There are a variety of treatment options available for GF.

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Granuloma faciale (GF) is an uncommon disease of unknown etiology presenting with asymptomatic cutaneous papules, nodules, and plaques of the face. However, there has been some confusion and evolution of the term *granuloma faciale*. In 1937, the term *eosinophilic granuloma of the skin* was used to describe ulcerated lesions of the mouth and anus that were associated with tuberculosis.[1,2] Cobane et al[3] used the term *facial granuloma with eosinophilia*. Confusion continued until Lever and Leeper[4] subdivided eosinophilic granuloma of the skin into 3 groups. The first group consisted of cases with cutaneous lesions associated with and histologically identical to eosinophilic granuloma of the bone (Langerhans cell histiocytosis). The second group included cases with cutaneous lesions

consisting of torpid, asymptomatic purplish patches on the face. The last group was cases with a preponderance of eosinophils in a granulomatous infiltrate that were associated with a variety of diseases.[1,4] A case described by Wigley[5] in 1945 as *Sarcoid of Boeck* may, in fact, be the first reported case of GF.[6] It was Pinkus,[7] however, who in 1952 finally suggested the term *granuloma faciale*.

GF is characterized by papules, nodules, and plaques that are usually solitary, though multiple or disseminated lesions can be seen.[8] The lesions usually are soft, elevated, well-circumscribed nodules ranging in size from millimeters to centimeters.[3] The lesions can be shades of red, brown, or purple and may darken with sun exposure. Lesions usually have a smooth surface with follicular accentuation but may have telangiectasias. Ulceration or crusting rarely occurs. These lesions usually develop very slowly and remain unchanged, though occasionally they will involute.[6] Tenderness, burning, and pruritus also have been reported.[9,10]

Although extracutaneous involvement is rare, there are reports of oral mucosa/upper airway involvement. GF can occur in patients of any age, sex, or race but is usually found in middle-aged Caucasian men.[1,6,11-13]

Materials and Methods

The clinical presentation and treatment of 38 patients with GF was reviewed. Patient information was obtained from a database covering the past 10 years of patient activity at a large dermatopathology laboratory in Michigan. GF was diagnosed by clinical and histologic criteria including an infiltrate composed of lymphocytes, neutrophils, histiocytes, and eosinophils in the superficial and deep dermis and fibrin deposition within dermal blood vessels confirming the presence of vascular damage. The patients were reviewed according to demographics, location, treatment, and prognosis. Follow-up was obtained through a questionnaire sent to each referring physician. To our knowledge, this review represents the largest series of patients with GF ever described.

Results

The clinical features of the patients are summarized in the Table. Their ages ranged from 28 to 85 years, with a mean age of 51.9 years for men and 55.4 years for women. The study consisted of 24 men and 14 women, which is in concordance with an early study showing a predominance of GF in men.[1] One man and one woman (patients 1 and 7) had multiple lesions. Interestingly, five men (patients 19, 22, 25, 29, and 38) had extrafacial lesions; there are very few reported cases of extrafacial GF.

Comment

GF is characterized by solitary nodules and plaques.[1] Most lesions are asymptomatic red, brown, or purple nodules that are soft, elevated, well-circumscribed, and slow to develop (Figure 1).

Lesions usually are seen on the face but may occur elsewhere.[14] Particularly, lesions may appear on light-exposed areas, and some lesions are photoexacerbated.[10] Sites of predilection are the sides (30%) and tip (7%) of the nose, preauricular area (22%), cheeks (22%), forehead (15%), and helix of the ear (4%).[10,15] In a clinical and histopathologic review, Pedace and Perry[1] described 21 cases of GF seen at the Mayo Clinic from 1945 to 1965. They noted a predominance of the lesions on the face (nose, forehead, malar, preauricular and postauricular areas, and chin) and less frequently on the forearms and elsewhere.

A review of the literature reveals 14 reported cases of extrafacial involvement.[14-18] The clinical aspects of facial and extrafacial lesions are similar.[8] Extrafacial lesions usually are found on the trunk and proximal extremities.[19] Extrafacial lesions have been reported as isolated findings and in conjunction with facial lesions.[17,18] The infrequent reports of extrafacial lesions may reflect either the inconspicuous nature of extrafacial lesions or a failure to examine patients specifically for the lesions.[8]

Extrafacial GF may be difficult to differentiate from erythema elevatum diutinum (EED). In fact, some authors believe EED and GF represent different parts of the spectrum of the same disease.[20] Both are rare chronic forms of cutaneous small vessel vasculitis and may share some pathogenic mechanisms, but there are several clinical and histologic differences. EED is characterized by multiple lesions localized on the extensor surfaces of extremities in an acral, bilateral, and symmetrical distribution. Bulla formation and hemorrhagic crusting may be seen. The trunk is usually spared, and facial lesions are rare. Histopathologic features of EED include a dense superficial and deep polymorphous dermal infiltrate where neutrophils are prominent and eosinophils are scanty or absent. A grenz zone of normal collagen beneath the epidermis rarely exists and the epidermis is not always spared. EED may be associated with systemic conditions, primarily gammopathies. EED shows an excellent response to dapsone.[15,21,22]

There is a relatively large clinical differential diagnosis for GF including lupus erythematosus, polymorphous light eruption, fixed drug eruption,

Characteristics of Patients With Granuloma Faciale*

Patient No.	Age, y	Sex	Location	Treatment	Response
1	50	M	Nose, face	Unknown	Unknown
2	63	F	Cheek	Intralesional steroid	Fair improvement
3	35	F	Cheek	Unknown	Unknown
4	50	F	Cheek	Unknown	Unknown
5	57	M	Nose	Unknown	Unknown
6	43	M	Cheek	Unknown	Unknown
7	38	F	Cheek (2 lesions)	Unknown	Lost to f/u
8	44	M	Face†	Unknown	Unknown
9	58	F	Eyebrow	High-potency topical steroid	Marked improvement
10	58	F	Nose	Intralesional steroid	Resolved
11	79	M	Neck	Topical steroid	Resolved
12	46	M	Cheek	Unknown	Lost to f/u
13	63	M	Cheek	Steroid tape	Resolved
14	69	F	Cheek	Intralesional steroid	Improvement
15	45	M	Cheek	Unknown	Unknown
16	43	M	Forehead	Doxycycline 100 mg orally 4×/d and intralesional steroid	Marked improvement
17	68	F	Nose	Intralesional steroid	Marked improvement
18	48	M	Cheek	Unknown	Lost to f/u
19	78	M	Scalp	Unknown	Unknown
20	50	F	Cheek	Unknown	Unknown
21	42	M	Temple	Intralesional steroid, topical steroid, liquid nitrogen	Modest improvement
22	69	M	Arm	Unknown	Unknown
23	43	M	Cheek	Minocin, liquid nitrogen, topical steroid	Lost to f/u
24	78	F	Cheek	Topical steroid	Mild improvement
25	70	M	Scalp	Topical and intralesional steroids	Mild improvement
26	53	M	Cheek	Unknown	Unknown
27	50	M	Face	Unknown	Unknown
28	44	M	Forehead	Unknown	Unknown
29	28	M	Back	Unknown	Unknown
30	39	F	Face†	Unknown	Lost to f/u
31	57	M	Cheek	Topical steroid	Lost to f/u
32	47	M	Cheek	Unknown	No treatment desired
33	40	F	Upper lip	Unknown	Unknown
34	51	M	Forehead	Unknown	Lost to f/u
35	42	M	Nose	Unknown	Unknown
36	85	F	Nose	Unknown	Unknown
37	45	F	Face	Unknown	Unknown
38	54	M	Scalp	Unknown	Unknown

*M indicates male; F, female; f/u, follow-up.
†Site not specified.

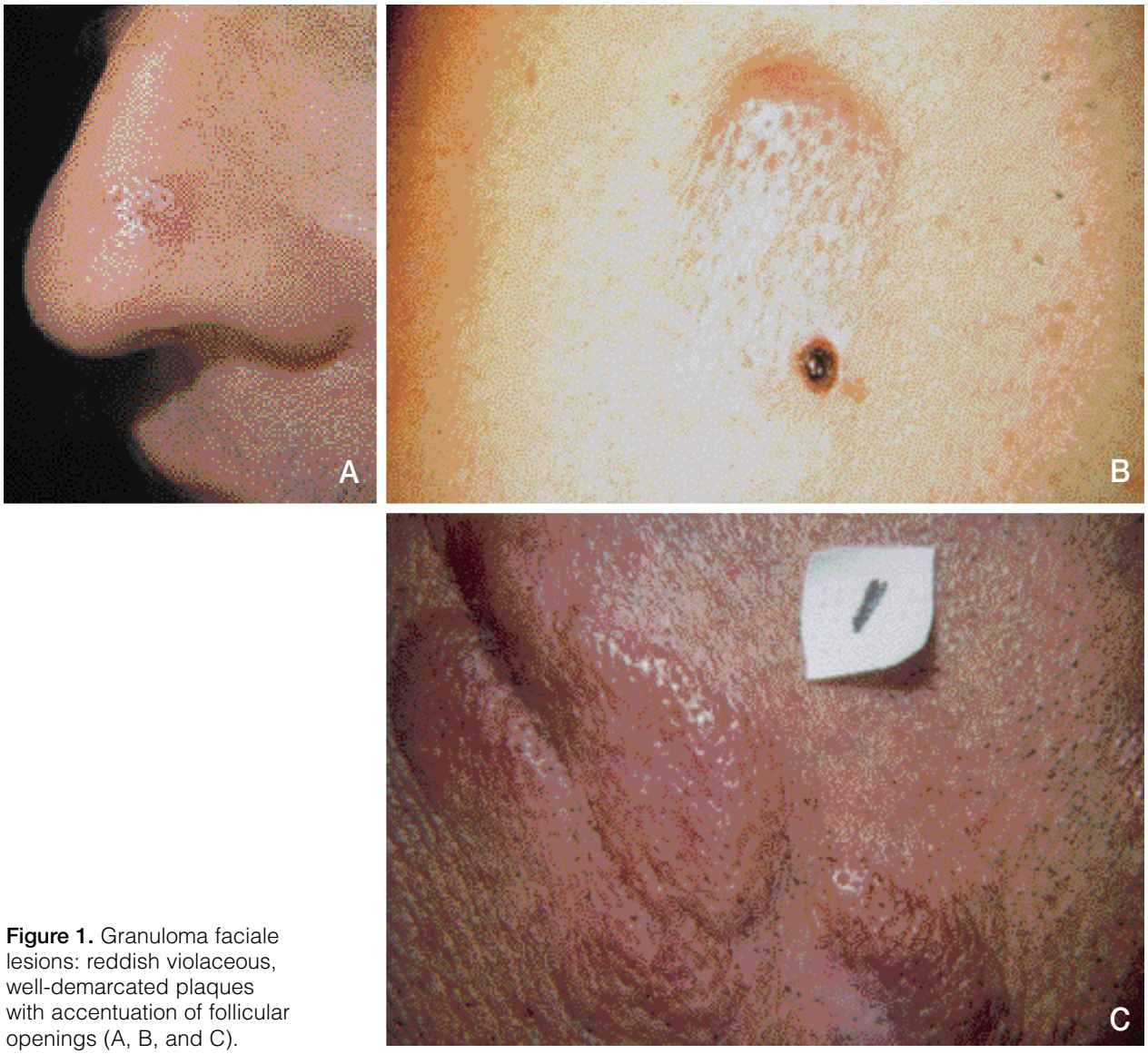

Figure 1. Granuloma faciale lesions: reddish violaceous, well-demarcated plaques with accentuation of follicular openings (A, B, and C).

benign and malignant lymphoid proliferations, sarcoidosis, granuloma annulare, foreign body reaction, tinea faciei, insect bite reaction, juvenile xanthogranuloma, mastocytoma, Spitz nevus, EED, mycosis fungoides, basal cell carcinoma, histiocytosis X, and rosacea.[1,6,23-26]

There is one case report of *Trichophyton rubrum* causing histologic changes similar to GF.[26] There also has been a case of GF mimicking rhinophyma.[27]

Histologic findings of GF show a normal epidermis that may be thinned and flattened by underlying infiltrate (Figure 2). There is a narrow grenz zone between the epidermis and the dermal inflammatory infiltrate consisting of lymphocytes, eosinophils, and neutrophils with leukocytoclasis (Figure 3). The infiltrate usually is distributed diffusely in the upper two thirds of the dermis. Fibrin deposition around blood vessels is evidence of vasculitis (Figure 4). In the later fibrotic stage, perivascular fibrin deposition predominates, and the number of inflammatory cells is greatly reduced.[6]

Microscopically, the primary differential diagnosis is EED, insect bite reaction, cutaneous lymphoma, or leukocytoclastic vasculitis. The exact pathogenesis is unclear, but some consider it a variant of leukocytoclastic vasculitis. Immunoglobulins, fibrin, and complement can be found at the dermal-epidermal junction and around blood vessels on direct immunofluorescence.[28-30]

GF usually lacks systemic symptoms or laboratory findings other than rare peripheral eosinophilia.[31] Immunohistochemical analysis revealed the majority of lymphocytes to be helper T-cell lymphocytes. The cells stained strongly with anti-

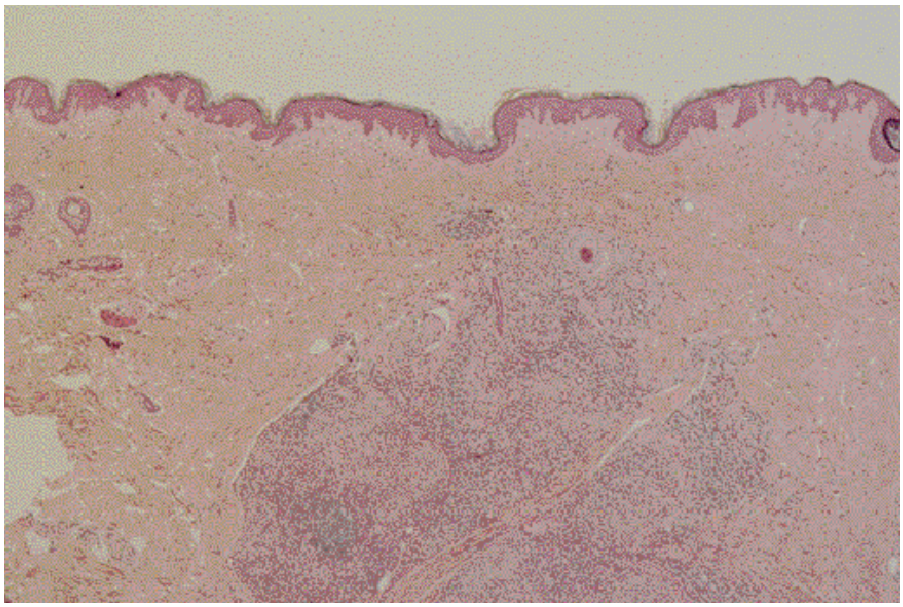

Figure 2. A nodular and diffuse infiltrate with sparing of the papillary dermis (H&E, original magnification ×4).

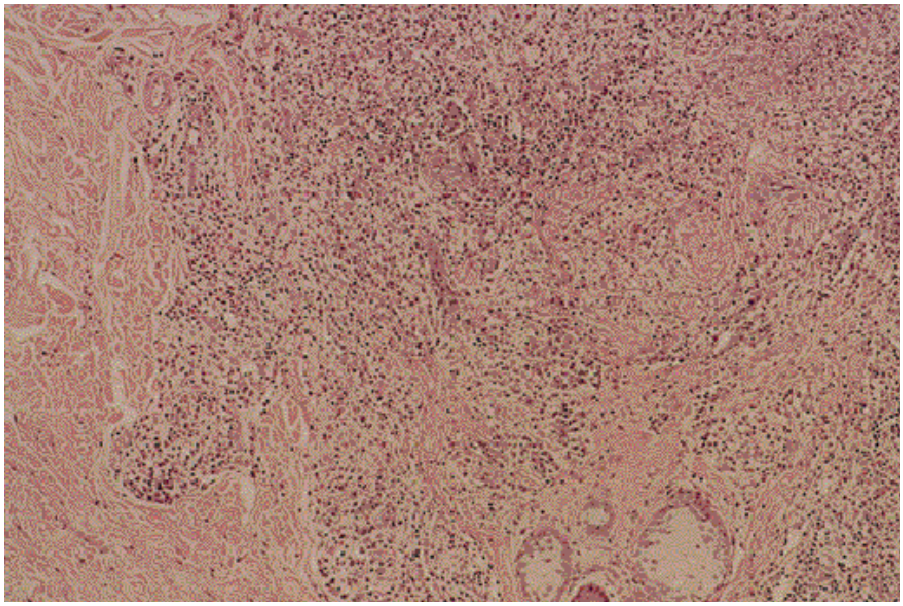

Figure 3. A mixed infiltrate of neutrophils, lymphocytes, eosinophils, and histiocytes (H&E, original magnification ×10).

bodies against IL-2 receptor and with antibodies to lymphocyte functional antigen-1 α. Overlying keratinocytes did not stain with intracellular adhesion molecule-1 or HLA-DR, which may account for the presence of the grenz zone in GF. These findings suggest that a γ–interferon-mediated process may play some role in the pathogenesis of this disorder.[32]

GF is known to be resistant to therapy. Numerous physical modalities and medical therapeutics have been tried. Laser therapy, including the CO_2,[33] argon,[34] pulsed dye, and long-pulsed tunable dye lasers,[35-38] all have been attempted with varying success. A study showed that lesions treated with a CO_2 laser and dermabrasion had a more even texture compared with lesions treated with electrosurgery alone. Healing times were similar between lesions treated with electrosurgery and CO_2 laser; however, lesions treated with dermabrasion healed more quickly.[39] Studies of patients treated with an argon laser resulted in total resolution of plaques of GF but had a remaining white collagenous scar.[34]

A case report by Elston[37] showed complete resolution of 3 lesions of GF when treated with a pulsed dye laser after the patient failed topical corticosteroids and oral dapsone. A case report by Ammirati et al[35] of a patient treated with the 585-nm pulsed dye laser showed clinical eradication of the lesion at 6-year follow-up. Another report by Welsh et al[36]

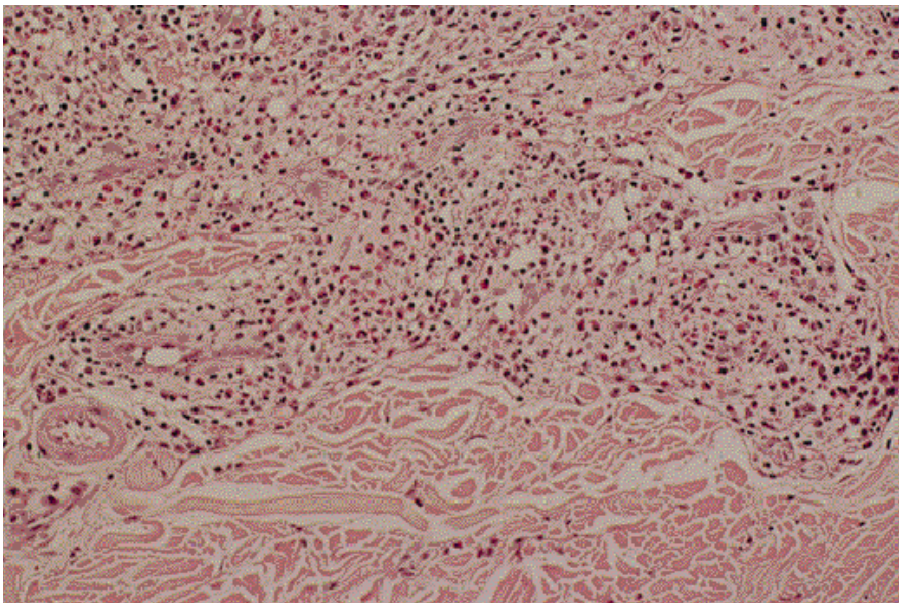

Figure 4. Blood vessels with perivascular fibrin deposition and mixed infiltrate (H&E, original magnification ×20).

showed good results when GF was treated with the pulsed dye laser. Recently, the long-pulsed tunable dye laser was used successfully with no scarring.[38] Other modalities that have been used include surgical excision,[7,10] dermabrasion, superficial ionizing radiation,[6,10] topical psoralen plus UV light,[40] cryosurgery,[41] intralesional corticosteroids,[42] combined cryosurgery and intralesional steroid injection,[43] and electrodesiccation.[10,39]

Medical treatment has included intralesional gold, colchicine, isoniazid, corticosteroids, potassium arsenite, testosterone, antimalarials, dapsone, and clofazimine.[9,10,25,27,34,39,44-46] Most medical therapies have shown varying success. No controlled trials are available because of the rarity of the condition.

In our review, most patients were treated with topical and intralesional steroids with varying results that ranged from mild improvement to complete resolution. Because there is a lack of scarring with steroid therapy, we recommend this as a good first-line therapy. Although none of the patients were treated with pulsed dye laser therapy, review of the literature demonstrates favorable results with this treatment modality. Pulsed dye laser should be considered as an alternative therapy.

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