Evaluating the Clinical and Demographic Features of Extrafacial Granuloma Faciale

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PRACTICE **POINTS**

- Extrafacial lesions are rare in granuloma faciale (GF).
- Extrafacial GF should be included in the differential diagnosis of well-demarcated plaques and nodules found on the trunk or extremities.
- Diagnosis of extrafacial GF is based on the presence of distinct histologic features identical to GF.
- Granuloma faciale is a chronic benign leukocytoclastic vasculitis that can be difficult to treat.

Granuloma faciale (GF) is an uncommon cutaneous disease of uncertain etiology that predominantly affects the face. Extrafacial lesions are rare. The purpose of this study was to describe the clinical and demographic features of a series of patients with extrafacial manifestations of GF who were diagnosed and treated at a single center over more than 5 decades. We performed a retrospective medical record analysis for all patients diagnosed with extrafacial GF who were treated at Mayo Clinic (Rochester, Minnesota) from 1959 through 2013. During the study period, extrafacial GF was diagnosed in 10 patients (6 men, 4 women), all of whom were white. The mean age was 58.7 years (range, 26–87 years). Seven patients presented with both facial and extrafacial lesions. Although extrafacial lesions are rare in GF, this condition should be included in the differential diagnosis of well-demarcated plaques and nodules found on the arms and legs.

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Granuloma faciale (GF) is a chronic benign leukocytoclastic vasculitis that can be difficult to treat. It is characterized by single or multiple, soft, well-circumscribed papules, plaques, or nodules ranging in color from red, violet, or yellow to brown that may darken with sun exposure.[1] Lesions usually are smooth with follicular orifices that are accentuated, thus producing a peau d'orange appearance. Lesions generally are slow to develop and asymptomatic, though some patients report pruritus or burning.[2,3] Diagnosis of GF is based on the presence of distinct histologic features. The epidermis usually is spared, with a prominent grenz zone of normal collagen separating the epidermis from a dense infiltrate of neutrophils, lymphocytes, and eosinophils. This mixed inflammatory infiltrate is seen mainly in the superficial dermis but occasionally spreads to the lower dermis and subcutaneous tissues.[4]

As the name implies, GF usually is confined to the face but occasionally involves extrafacial sites.[5-15] The clinical characteristics of these rare extrafacial lesions are not well understood. The purpose of this study was to identify the clinical and demographic features of extrafacial GF in patients treated at Mayo Clinic (Rochester, Minnesota) during a 54-year period.

Methods

This study was approved by the Mayo institutional review board. We searched the Mayo Clinic Rochester dermatology database for all patients with a diagnosis of GF from 1959 through 2013. All histopathology slides were reviewed by a board-certified dermatologist (A.G.B.) and dermatopathologist (A.G.B.) before inclusion in this study. Histologic criteria for diagnosis of GF included the presence of a mixed inflammatory infiltrate of neutrophils, eosinophils, lymphocytes, and histiocytes in the superficial or deep dermis; a prominent grenz zone separating the uninvolved epidermis; and the presence of vascular damage, as seen by fibrin deposition in dermal blood vessels.

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Medical records were reviewed for patient demographics and for history pertinent to the diagnosis of GF, including sites involved, appearance, histopathology reports, symptoms, treatments, and outcomes.

Literature Search Strategy—A computerized Ovid MEDLINE database search was undertaken to identify English-language articles concerning GF in humans using the search terms *granuloma faciale* with *extrafacial* or *disseminated*. To ensure that no articles were overlooked, we conducted another search for English-language articles in the Embase database (1946-2013) using the terms *granuloma faciale* and *extrafacial* or *disseminated*.

Statistical Analysis—Descriptive clinical and histopathologic data were summarized using means, medians, and ranges or proportions as appropriate; statistical analysis was performed using SAS software (JMP package).

Results

Ninety-six patients with a diagnosis of GF were identified, and 12 (13%) had a diagnosis of extrafacial GF. Of them, 2 patients had a diagnosis of extrafacial GF supported only by histopathology slides without accompanying clinical records and therefore were excluded from the study. Thus, 10 cases of extrafacial GF were identified from our search and were included in the study group. Clinical data for these patients are summarized in Table 1. The mean age was 58.7 years (range, 26–87 years). Six (60%) patients were male, and all patients were white. Seven patients (70%) had facial GF in addition to extrafacial GF. Six patients reported no symptoms (60%), and 4 (40%) reported pruritus, discomfort, or both associated with their GF lesions.

Extrafacial GF was diagnosed in the following anatomic locations: scalp (n=3 [30%]), posterior auricular area (n=3 [30%]), mid upper back (n=1 [10%]), right shoulder (n=1 [10%]), both ears (n=1 [10%]), right elbow (n=1 [10%]), and left infra-auricular area (n=1 [10%]). Only 1 (10%) patient had multiple extrafacial sites identified.

The lesions were characterized clinically as violet, red, and yellow to brown smooth papules, plaques, and nodules (Figure 1). Biopsies from these lesions showed a subepidermal and adnexal grenz zone; a polymorphous perivascular and periadnexal dermal infiltrate composed of neutrophils, eosinophils, lymphocytes, histiocytes, and plasma cells; and a mild subtle leukocytoclastic vasculitis with subtle mild vascular necrosis (Figure 2).

For the 9 patients who elected to undergo GF treatment, the average number of treatments attempted was 2.8 (range, 1–5). The most common method of treatment was a combination of intralesional and topical corticosteroids (n=5 [50%]). Other methods included surgery (n=3 [30%]), dapsone (n=2 [20%]), radiation therapy (n=2 [20%]), cryosurgery (n=1 [10%]), nitrogen mustard (n=1 [10%]), liquid nitrogen (n=1 [10%]), and tar shampoo and fluocinolone acetonide solution 0.01% (n=1 [10%]).

Treatment outcomes were available for 8 of 9 treated patients. Three patients (patients 7, 8, and 10) had long-term successful resolution of their lesions. Patient 7 had an extrafacial lesion that was successfully treated with intralesional and topical corticosteroids, but the facial lesions recurred. The extrafacial GF lesion in patient 8 was found adjacent to a squamous cell carcinoma and was removed with a wide surgical excision that included both lesions. Patient 10 was successfully treated with a combination of liquid nitrogen and topical corticosteroid. Patients 2 and 4 were well controlled while on dapsone; however, once the treatment was discontinued, primarily due to adverse effects, the lesions returned.

Literature Search—Our search of the English-language literature identified 20 patients with extrafacial GF (Table 2). Fifteen (75%) patients were male, which was similar to our study (6/10 [60%]). Our patient population was slightly older with a mean age of 58.7 years compared to a median age of 54 years among those identified in the literature. Additionally, 3 (30%) patients in our study had no facial lesions, as seen in classic GF, which is comparable to 8 (40%) patients identified in the literature.

Comment

Extrafacial GF primarily affects white individuals and is more prevalent in men, as demonstrated in our study. Extrafacial GF was most often found in association with facial lesions, with only 3 patients having exclusively extrafacial sites.

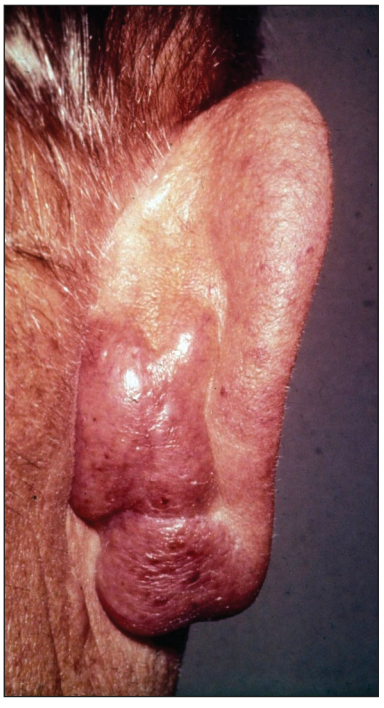

FIGURE 1. Extrafacial granuloma faciale. Smooth, red-brown plaque in the posterior auricular area.

TABLE 1. Summary of Patient Clinical Data

Patient	Age, y/ Sex	Extrafacial Site(s)	Facial Involvement?	Symptoms	Treatment	Outcome
1	61/M	Left and right scalp	Yes	Asymptomatic	Cryosurgery	Recurrence
2	61/F	Mid upper back	Yes	Asymptomatic	1. Dapsone 2. Surgery 3. Intralesional corticosteroid 4. Topical corticosteroid	1. Discontinued due to adverse effects; recurrence after stopping treatment 2. Recurrence 3. Recurrence 4. Recurrence after stopping treatment
3	87/F	Right posterior auricular area	No	Asymptomatic	Patient declined treatment	N/A
4	60/M	Vertex scalp and right shoulder	Yes	Pruritus	1. Dapsone 2. Intralesional corticosteroid 3. Topical corticosteroid	1. Discontinued due to adverse effects; recurrence after stopping treatment 2. Recurrence after stopping treatment 3. Recurrence after stopping treatment
5	26/M	Ears	Yes	Asymptomatic	1. Radiation 2. Intralesional corticosteroid 3. Topical corticosteroid	1. Recurrence 2. Recurrence 3. Recurrence after stopping treatment
6	49/M	Right posterior auricular area	Yes	Pruritus, discomfort	1. Nitrogen mustard 2. Radiation 3. Intralesional corticosteroid 4. Topical corticosteroid 5. Surgery	1. Recurrence 2. Recurrence 3. Recurrence 4. Recurrence after stopping treatment 5. Recurrence
7	62/M	Right elbow	Yes	Asymptomatic	Topical and intralesional corticosteroids	Successful resolution of elbow lesion, but facial lesions recurred after stopping treatment
8	68/M	Left infra-auricular area	No	Asymptomatic	Surgical resection[a]	No recurrence
9	75/F	Scalp	Yes	Pruritus	1. Topical corticosteroid cream 2. Cyproheptadine 3. Tar shampoo 4. Fluocinolone acetonide solution 0.01%	Unknown
10	38/F	Right posterior auricular area	No	Pruritus	Liquid nitrogen, topical corticosteroid	Successful resolution after 6 mo of treatment

Abbreviations: M, male; F, female; N/A, not applicable.
[a]Patient 8 had surgical resection for squamous cell carcinoma, which was biopsied in an area adjacent to a granuloma faciale lesion.

Data from the current study indicate that diverse modalities were used to treat extrafacial GF with variable outcomes (chronic recurrence to complete resolution). The most common first-line treatment, intralesional corticosteroid injection, was used in 5 (50%) patients but resulted in only 1 (10%) successful resolution. Other methods frequently used in our study and prior studies were surgical excision, cryotherapy, electrosurgery, and dermabrasion.[1,20] These treatments do not appear to be uniformly definitive, and the ablative methods may result in scarring.[1] Different laser treatments are emerging for the management of GF lesions. Prior reports of treating facial GF with argon and CO_2 lasers have indicated minimized residual scarring and pigmentation.[21-23] The use of pulsed dye lasers has resulted in complete clearance of facial GF lesions, without recurrence on long-term follow-up.[20,24-26]

The latest investigations of immunomodulatory drugs indicate these agents are promising for the management of facial GF. Eetam et al[27] reported the successful use of topical tacrolimus to treat facial GF. The relatively low cost and ease of use make these topical medications a competitive alternative to currently available surgical and laser methods. The appearance of all of these novel therapeutic modalities creates the necessity for a randomized trial to establish their efficacy on extrafacial GF lesions.

TABLE 2. Summary of 20 Cases of Extrafacial Granuloma Faciale Reported in the English-Language Literature

Reference (Year)	Age, y/ Sex	Extrafacial Site(s)	Facial Involvement?
Lever et al[16] (1948)	53/M	Trunk	Yes
Okun et al[11] (1965)	54/F	Arms	Yes
Pedace and Perry[17] (1966)	45/M	Arms	Yes
	47/F	Trunk, arms	Yes
Rusin et al[13] (1976)	44/M	Trunk	Yes
	50/F	Trunk	Yes
Frost and Heenan[18] (1984)	64/M	Scalp, arms	Yes
Sears et al[14] (1991)	57/M	Legs	Yes
Konohana[19] (1994)	59/M	Trunk	Yes
Kavanagh et al[9] (1996)	62/M	Scalp	No
Castano et al[5] (1997)	51/F	Trunk	No
Roustan et al[12] (1999)	37/M	Trunk, forearm	Yes
Castellano-Howard et al[6] (2001)	57/M	Anterior chest, upper back	Yes
Inanir and Alvur[8] (2001)	47/F	Right arm	Yes
Radin and Mehregan[1] (2003)	79/M	Neck	No
	78/M	Scalp	No
	69/M	Arm	No
	70/M	Scalp	No
	28/M	Back	No
	54/M	Scalp	No

Abbreviations: M, male; F, female.

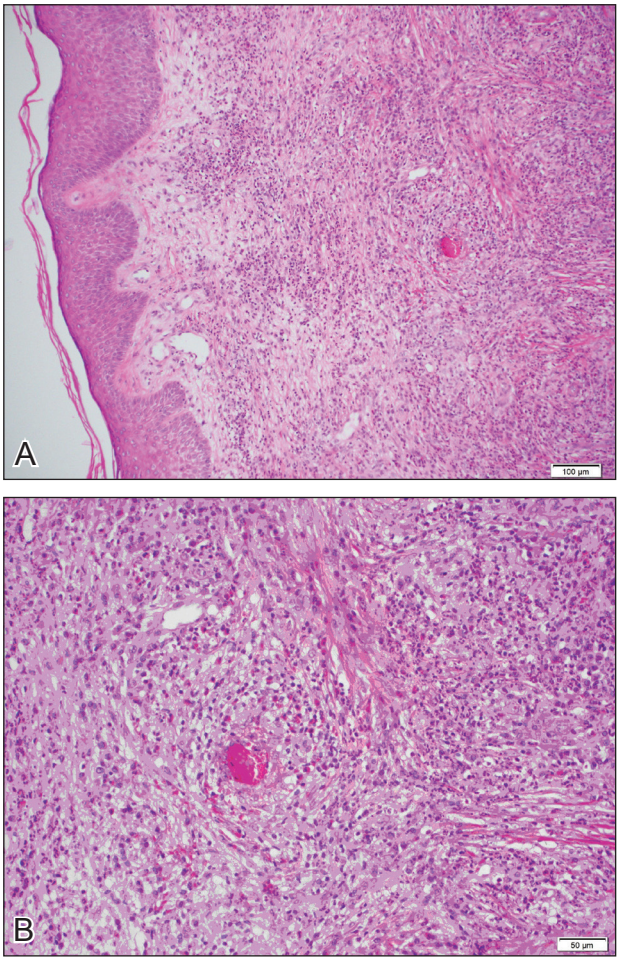

FIGURE 2. Extrafacial granuloma faciale. Low-power view demonstrated a grenz zone and a dense diffuse polymorphous infiltrate in the dermis (A)(H&E, original magnification ×10). High-power view showed that the infiltrate was composed of neutrophils, eosinophils, lymphocytes, and histiocytes. Findings of chronic leukocytoclastic vasculitis were seen with an area of fibrin deposition in dermal blood vessels (B)(H&E, original magnification ×20).

The wide array of treatments reflects the recalcitrant nature of extrafacial GF lesions. Further insight into the etiology of these lesions is needed to understand their tendency to recur. The important contribution of our study is the observed predilection of extrafacial GF for sun-exposed areas such as the scalp, upper trunk, and arms and legs. This pattern of extrafacial distribution along with the lack of mucosal involvement suggests a possible connection with UV light exposure. Furthermore, one of the extrafacial GF lesions in our study occurred in association with a squamous cell carcinoma, which may be an additional indication that these sites have been subjected to sun damage. This finding strengthens the importance of obtaining an adequate skin biopsy of any well-demarcated plaque or nodule found on the trunk, arms, and legs. The observed GF prevalence on sun-exposed areas and association with photoexacerbation have been speculated in prior studies, but no clear connection has been established.[1,28]

Conclusion

The findings from this study and the cases reviewed in the literature provide a unique contribution to the understanding of the clinical and demographic characteristics of extrafacial GF. The rarity of this condition is the single most important constraint of our study, reflected in the emblematic limitations of a retrospective analysis in a select group of patients. The results of analysis of data from our patients were similar to the findings reported in the English-language medical literature. Serious consideration should be given to the development of a national registry for patients with GF. A database containing the clinicopathologic features, treatments, and outcomes for patients with both facial and extrafacial manifestations of GF may be invaluable in evaluating various treatment options and increasing understanding of the etiology and epidemiology of the disease.

REFERENCES

1. Radin DA, Mehregan DR. Granuloma faciale: distribution of the lesions and review of the literature. *Cutis.* 2003;72:213-219.
2. Dowlati B, Firooz A, Dowlati Y. Granuloma faciale: successful treatment of nine cases with a combination of cryotherapy and intralesional corticosteroid injection. *Int J Dermatol.* 1997;36:548-551.
3. Guill MA, Aton JK. Facial granuloma responsive to dapsone therapy. *Arch Dermatol.* 1982;118:332-335.
4. Ryan TJ. Cutaneous vasculitis. In: Champion RH, Burton JL, Burns DA, et al, eds. *Rook/Wilkins/Ebling Textbook of Dermatology*. 7th ed. Malden, MA: Blackwell Science; 2004.
5. Castano E, Segurado A, Iglesias L, et al. Granuloma faciale entirely in an extrafacial location. *Br J Dermatol.* 1997;136:978-979.
6. Castellano-Howard L, Fairbee SI, Hogan DJ, et al. Extrafacial granuloma faciale: report of a case and response to treatment. *Cutis.* 2001;67:413-415.
7. Cecchi R, Paoli S, Giomi A. Granuloma faciale with extrafacial lesions. *Eur J Dermatol.* 2002;12:438.
8. Inanir I, Alvur Y. Granuloma faciale with extrafacial lesions. *Br J Dermatol.* 2001;14:360-362.
9. Kavanagh GM, McLaren KM, Hunter JA. Extensive extrafacial granuloma faciale of the scalp. *Br J Dermatol.* 1996;134:595-596.
10. Marcoval J, Moreno A, Peyr J. Granuloma faciale: a clinicopathological study of 11 cases. *J Am Acad Dermatol.* 2004;51:269-273.
11. Okun MR, Bauman L, Minor D. Granuloma faciale with lesions on the face and hand. *Arch Dermatol.* 1965;92:78-80.
12. Roustan G, Sanchez Yus E, Salas C, et al. Granuloma faciale with extrafacial lesions. *Dermatology.* 1999;198:79-82.
13. Rusin LJ, Dubin HV, Taylor WB. Disseminated granuloma faciale. *Arch Dermatol.* 1976;112:1575-1577.
14. Sears JK, Gitter DG, Stone MS. Extrafacial granuloma faciale. *Arch Dermatol*. 1991;127:742-743.
15. Zargari O. Disseminated granuloma faciale. *Int J Dermatol.* 2004; 43:210-212.
16. Lever WF, Lane CG, Downing JG, et al. Eosinophilic granuloma of the skin: report of three cases. *Arch Derm Syphilol.* 1948; 58:430-438.
17. Pedace FJ, Perry HO. Granuloma faciale: a clinical and histopathologic review. *Arch Dermatol.* 1966;94:387-395.
18. Frost FA, Heenan PJ. Facial granuloma. *Australas J Dermatol.* 1984;25:121-124.
19. Konohana A. Extrafacial granuloma faciale. *J Dermatol.* 1994; 21:680-682.
20. Ludwig E, Allam JP, Bieber T, et al. New treatment modalities for granuloma faciale. *Br J Dermatol.* 2003;149:634-637.
21. Apfelberg DB, Druker D, Maser MR, et al. Granuloma faciale: treatment with the argon laser. *Arch Dermatol.* 1983;119:573-576.
22. Apfelberg DB, Maser MR, Lash H, et al. Expanded role of the argon laser in plastic surgery. *J Dermatol Surg Oncol.* 1983;9:145-151.
23. Wheeland RG, Ashley JR, Smith DA, et al. Carbon dioxide laser treatment of granuloma faciale. *J Dermatol Surg Oncol.* 1984; 10:730-733.
24. Cheung ST, Lanigan SW. Granuloma faciale treated with the pulsed-dye laser: a case series. *Clin Exp Dermatol.* 2005;30:373-375.
25. Chatrath V, Rohrer TE. Granuloma faciale successfully treated with long-pulsed tunable dye laser. *Dermatol Surg.* 2002;28:527-529.
26. Elston DM. Treatment of granuloma faciale with the pulsed dye laser. *Cutis.* 2000;65:97-98.
27. Eetam I, Ertekin B, Unal I, et al. Granuloma faciale: is it a new indication for pimecrolimus? a case report. *J Dermatolog Treat.* 2006;17:238-240.
28. Johnson WC, Higdon RS, Helwig EB. Granuloma faciale. *AMA Arch Derm.* 1959;79:42-52.