

# Granuloma faciale – analysis of 5 cases

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## Abstract

**Introduction:** Granuloma faciale (GF) is an uncommon inflammatory dermatosis. The treatment of GF remains a challenge considering the unclear aetiopathogenesis. Various therapeutic methods have been described.

**Aim:** To analyse the clinical picture and treatment results in a group of patients with GF.

**Material and methods:** Five adults with GF were analysed and treated. Diagnosis was confirmed by histological examination. Patients were treated with surgery, cryosurgery, topically with corticosteroids and tacrolimus. The follow-up period varied from 5 to 15 months.

**Results:** Complete resolution was observed in 3 cases, partial remission was noted in 1 case. In 1 case the treatment was unsuccessful.

**Conclusions:** The treatment of GF remains a challenge. It is difficult to determine the most effective therapy. Topical tacrolimus and cryosurgery seem to be the first line treatment.

**Key words:** granuloma faciale, treatment, tacrolimus, calcineurin inhibitors.

## Introduction

Eosinophilic granuloma (*granuloma faciale* – GF) is a rare, benign, inflammatory dermatosis. The aetiology of this disease remains unclear. Non-specific clinical and histological picture may cause diagnostic difficulties. In the medical literature, there are only few reports concerning GF. This report is a clinical analysis based on the largest number of patients with GF (5 cases) in Polish literature.

## Aim

To perform a clinical analysis of patients with GF diagnosed and treated in the Dermatology, Venereology and Allergology Clinic of the Medical University of Gdansk.

## Material and methods

Five patients with GF, including 3 women and 5 men (mean age 47.6), were retrospectively analysed. The definitive diagnosis was based on the histopathological picture of the skin biopsy. Patients were treated with topical tacrolimus, topical steroids, with cryosurgery and surgery. The follow-up period varied from 5 to 15 months.

## Results

All lesions occurred in the face area (especially the forehead and cheeks). The number of lesions varied from 1 to 8, of diameter from 0.8 to 6 cm. In all cases, flat elevated, reddish-brownish nodules were observed (tab. 1). Time from the first manifestation of lesions to the diagnosis of GF varied from 2 months to 5 years. In 1 case, GF was diagnosed only on the basis of the clinical picture. Patients did not present any subjective complaints. In 3 cases, UV-induced deterioration of skin lesions was observed.

0.1% tacrolimus ointment was used in 4 patients (patients 1, 3, 4, 5). The drug was applied twice a day and for the night under occlusion. Only in 1 patient a complete remission was obtained. In the others, no significant improvement was noticed. In 2 patients (patients 1, 2) topical steroids of medium or high strength were used, resulting in a complete regression of nodular eruptions in 1 patient (fig. 1 A, B). In the second case, due to, regarding reconstruction possibilities, beneficial size and location, a surgical excision was performed with an excellent aesthetic effect, with no recurrence (fig. 2). In 1 case (patient 3), eruptions were treated with cryosurgery, following unsuccessful topical tacrolimus treatment (spraying method

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**Tab. 1.** Patients' clinical data

No.	Sex	Age [year]	Number of lesions	Location	Morphology
1	F	46	4	forehead, cheek	flat elevated, infiltrative nodules
2	F	44	1	cheek	flat elevated, infiltrative nodule
3	M	47	8	forehead, cheeks, nose	flat elevated, infiltrative nodules
4	F	45	1	cheek	flat elevated, infiltrative nodule
5	M	56	2	cheek	flat elevated, infiltrative nodules with atrophy in central part

**Fig. 1. A.** *Granuloma faciale*, flat elevated, cyanotic-reddish lesions of forehead skin (patient 1)**Fig. 1. B.** Complete remission after topical clobetasol propionate treatment

2 x 20 sec. 3 cycles). Afterwards, topical tacrolimus was used, obtaining significant flattening of lesions (fig. 3 A, B). During the follow-up period varying from 5 to 15 months, new disease outbreaks were found only in 1 patient. Complete remission was obtained in 3 (60%) patients, partial in 1 (20%) case, and in 1 patient the treatment was unsuccessful.

## Discussion

Granuloma faciale is a rare subject of clinical interest. Until now, only few dozen of cases of GF have been described. Benign course, non-specific clinical picture and the absence of subjective complaints influence the low interest in this disease. The number of patients with GF observed in a relatively short period of time (15 months) suggest that this entity occurs more frequently than it was previously thought. GF is more commonly observed in male Caucasians. The higher proportion of females in our material might result from the greater interest in their appearance. However, the age range did not vary from the literature data (4<sup>th</sup>-6<sup>th</sup> decade of life). Flat elevated, infiltrative reddish blue nodules were observed in all cases [1-3]. According to the literature data, nodular, ulcerative and sometimes annular shaped lesions were observed in 15% of cases. A very rare type of GF may present as glan-

**Fig. 2.** A single, small lesion of GF (patient 2)



Fig. 3. A. Numerous lesions of GF (patient 3)



Fig. 3. B. Significant flattening of lesions after combined treatment (cryosurgery and topical tacrolimus). New lesions are visible

dular hypertrophy of the nose; so far, 3 cases have been described [4-6]. Exceptionally rarely, GF is accompanied by subjective complaints (usually burning, pruritus).

In a definite majority of GF cases the lesions occur on the face. Up till now, only few cases of extrafacial involvement have been described (scalp, trunk, extremities) [7, 8].

Due to the non-specific clinical picture, the diagnosis of GF causes some difficulties. Ortonne *et al.* [1] estimated that only in 15% of all cases the diagnosis can be made basing only on the clinical picture. The differential diagnosis includes: tuberculosis, sarcoidosis, lupus, skin lymphomas, lymphocytic skin infiltrations, Kimura Disease, erythema fixum and skin cancer. Considering the significant similarity in the clinical and histological picture, some authors include GF, erythema elevatum diutinum and erythema fixum in the same nosological entity [1-3].

In the studied group, the average time from the first outbreak of lesions to the definitive diagnosis was 21 months. What is interesting, only classical course of GF was observed in the analysed material. Apparently, the majority of cases of atypical morphology and location are not recognized.

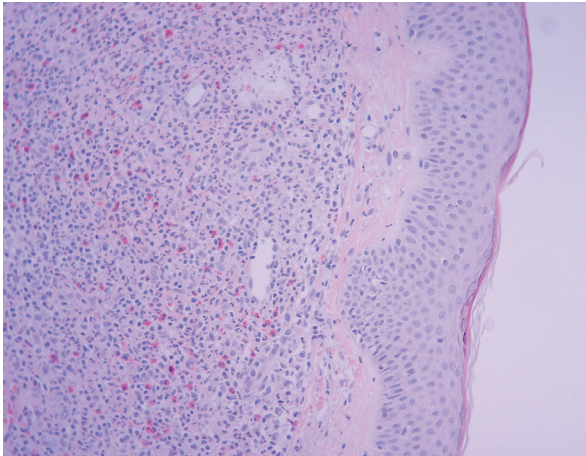
The histological picture of GF is characterized by significant heterogeneity. Normal epidermis and Grenz zone of normal papillary skin layer are observed. Early infiltra-

tion includes perivascular neutrophil and eosinophil aggregations. Foam cells and giant cells can be found in small amount as well. In early eruptions, characteristics of leukocytoclastic vasculitis can be found; and in the later period: eosinophils, lymphocytes, plasmatic and mast cells, haemosiderin deposits and markers of fibrosis. Despite the name, the disease does not have a granulomatous character; however, eosinophilic infiltration can be observed only in half of cases of GF (fig. 4 A, B) [1-3].

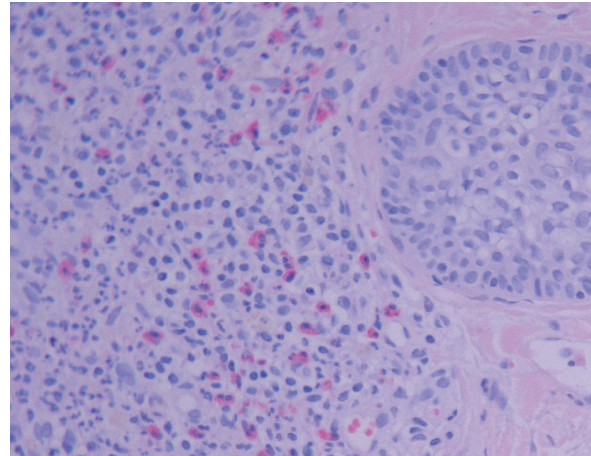
The aetiopathogenesis of GF remains unclear. Infectious background of the disease has not been confirmed. The role of trauma and UV radiation has been taken into consideration. Deterioration of the skin condition following UV exposure indicates the possible role of this factor. It appears that the essence of GF is a skin vasculitis in which type III hypersensitivity is involved in immune complex production and deposition [1-3, 9-12].

Considering the unclear aetiology, there is no causal treatment. The multiplicity of therapeutic options indicates limited effectiveness of each of them. The therapeutic spectrum includes anti-inflammatory agents and destructive methods (tab. 2, 3).

The most commonly chosen medications are topical steroids. Some authors [13] deny their effectiveness. Nevertheless, in our material, in 1 patient complete remission



**Fig. 4. A.** Histological picture. Diffused inflammatory infiltration in dermis, composed of polynuclear leucocytes, eosinophilic granulocytes, lymphocytes and histiocytes, separated from epidermis with a band of normal connective tissue



**Fig. 4. B.** In mixed inflammatory infiltration, a large number of eosinophilic granulocytes are noticeable.

after clobetasol treatment was observed. However, in a different case, topical fluticasone appeared to be ineffective. The risk of side effects, particularly skin atrophy, significantly restricts long-term use of this group of drugs. Intralesional steroid injection appears to be a more effective therapeutic option. There are some promising reports concerning use of topical calcineurin inhibitors (tacrolimus). In recent years, there have been 8 casuistic reports confirming the efficacy of this treatment. In all cases, the ointment had been used for many months [14]. In our material, only in 1 out of 4 patients treated with tacrolimus was a clinical improvement observed. Despite the limited efficacy, the use of tacrolimus as a first line agent in GF patients appears to be reasonable due to its high safety profile.

Among ablation methods, cryosurgery has the most established position. Its efficacy in GF treatment was

proven for the first time by Graham and Steward in 1977 [15]. So far, over 20 cases of GF treated with cryosurgery have been described [13, 16-18]. Panagiotopoulos *et al.* [13] presented a highly valuable report. The authors treated 9 patients with GF using the spray or contact method (2 times for 20 sec; 1 to 3 cycles), obtaining an improvement in all patients. Only in 2 cases a temporary hyperpigmentation of the treated area was observed. However, Dowlati *et al.* [19] combined cryosurgery with intralesional steroid injection in 9 patients, obtaining satisfactory results. Our experience suggests potential usefulness of cryosurgery combined with topical tacrolimus.

Attempts at laser treatment have been made as well. Apfelberg *et al.* [20] described 3 cases of GF treated with argon laser with very satisfactory results. Cheung *et al.* [21] treated 4 patients with pulsed-dye laser, but only in 2 patients a satisfactory response was achieved.

**Tab. 2.** Treatment results

No.	Treatment	Results	Follow-up period [months]
1	<b>Tacrolimus 0.1%</b> 2 × day for 5 months, <b>Clobetasol propionate 0.05% ointment</b> 2 × day for 2 months (under occlusion)	no improvement complete remission	15
2	<b>Fluticasone propionate 0.05 mg/g ointment</b> 2 × day for 2 months (occlusion) <b>Surgical excision</b>	no improvement complete remission	8
3	<b>Tacrolimus 0.1%</b> 2 × day for 6 months <b>Cryosurgery and tacrolimus 0.1% ointment</b>	no improvement, progression of disease partial remission (flattening of lesions), new eruptions	15
4	<b>Tacrolimus 0.1%</b> 2 × day for 3 months (under occlusion)	complete remission	6
5	<b>Tacrolimus 0.1% ointment</b> 2 × day for 2 months (under occlusion)	no improvement	5

Tab. 3. Methods of treatment

Non-invasive treatment	Destructive treatment
steroids (topical, intralesional, systemic)	surgery
calcineurin inhibitors	cryosurgery
colchicine	electrosurgery
dapsone	dermabrasion
clofazimine	laser therapy
isoniazid	roentgenotherapy
gold salts	
PUVA	

Among systemic medications we can distinguish: dapsone, chloroquine, clofazimine and isoniazid [1-3, 10, 13, 22].

Despite contradictory reports in the literature, we take the position that surgical excision of lesions with beneficial, from the aspect of reconstruction, size and location should be considered as a first line therapeutic method.

In conclusion, the frequency of GF is higher than the literature data indicate. Treatment of GF is difficult. Due to the lack of randomized trials, in the face of contradictory reports, an objective assessment of the effectiveness of individual methods of treatment is doubtful. Literature data indicate the efficacy of cryosurgery. Despite the limited efficacy, topical tacrolimus appears to be a first line treatment due to the high safety profile. Combining ablation methods with conservative treatment is an interesting alternative for patients who do not respond to monotherapy.

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