Clofazimine in Inflammatory Facial Dermatosis—Granuloma Faciale and Lipogranulomatosis Subcutanea (Rothmann-Makai)

Sir,

Chronic inflammatory diseases with a facial manifestation may lead to a remarkable disability. Granuloma faciale (GF) is a rare inflammatory skin disease, found mainly in middle-aged men. It shows chronic relapsing and slow progression. GF is characterized by a mixed lympho-histiocytic dermal infiltrate with a Grenz zone against the overlying epidermis. By immunohistochemistry, the majority of non-myelocytic hemopoietic cells are T-helper lymphocytes which express the interleukin-2 receptor and the lymphocyte functional antigen (LFA-1). Recently, a gamma interferon (IFN)-mediated process has been suggested in GF (1). It is difficult to treat, though corticosteroids may be of some value. Lipogranulomatosis subcutanea (Rothmann-Makai; LGS) is a panniculitis variety, which evolves rapidly with general malaise and fever. Subcutaneous nodules develop on the limbs, the trunk and

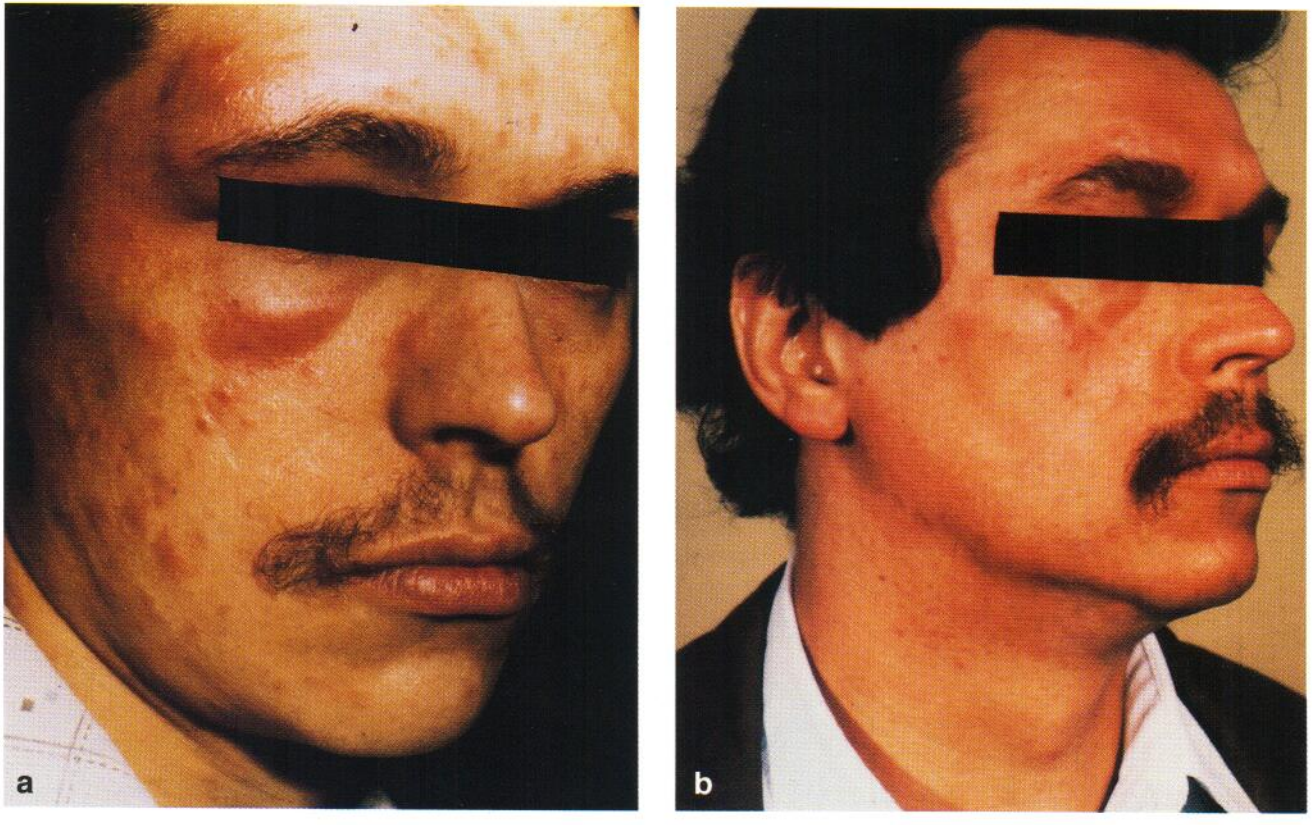

Fig. 1. Granuloma faciale (case 1): (*a*) before and (*b*) after 3 months of treatment with 300 mg clofazimine daily.

occasionally the face; these may perforate. The disease peaks in children and middle-aged women. Corticosteroids, oral or topical, tetracycline and non-steroidal anti-inflammatory drugs (NAIDS) may be helpful in many cases (2). We report on both one patient with longstanding GF and one with LGS showing an impressive response to clofazimine.

CASE REPORTS

Case 1

A 41-year-old otherwise healthy man with a 10-year rapidly relapsing course of GF was admitted to our hospital. On examination he showed facial inflammatory brown-reddish plaques and larger lesions on the cheeks (Fig. 1a). A skin biopsy was taken which showed a mixed infiltrate with numerous lymphocytic cells and histiocytes. The latter were also localized within the papillary layer, but in general a subepidermal zone of normal collagen was found. Vascular proliferations and dilated capillaries were seen. We performed immunoperoxidase stainings on unfixed frozen sections. The histiocytes were positive for alpha1-antichymotrypsine and MAC387 (DAKO), arguing for activated cells. Polymorphonuclear leukocytes and granulocytes expressed neuroglandular antigen as defined by monoclonal antibody LS59 [3]. Since the patient experienced a relapse almost every second month and topical steroids were uneffective, we decided to treat him with oral prednisolone 40 to 50 mg/day. This was efficient for the acute symptoms but failed to prevent relapses. Therefore, we started clofazimine 300 mg daily in October 1992. During the next months we were able to reduce the steroids down to 3 mg/day and clofazimine 200 mg/day. The clinical response was remarkable after 3 months (Fig. 1b). Until now, no relapse has occurred.

Case 2

A 40-year-old woman was admitted to our hospital 10 years ago. At that time she had several subcutaneous nodules on the upper limbs, the back and latero-facial. A deep skin biopsy was taken from a nodule of the right upper arm, which showed an enlargement of subcutaneous septa by an interstitial oedema and lymphohistiocytic infiltration. Areas of granulomatous structure with histiocytic foam cells were seen in the subcutaneous fat. In the lower stratum reticulare, the stratum papillary and the epidermis were free of inflammation. The diagnosis of LGS was made. Treatment with topical steroids under occlusion, oral prednisolone and NAIDS did not have any significant effect. The patient discontinued this treatment within the first 2 years. One year ago, she developed a slowly growing tumorous mass in the right angle of the mandible (Fig. 2a). Magnetic resonance imaging revealed an infiltrating process with an enhancement of gadolinium. A re-biopsy was taken from her cheek. The subcutaneous fat was almost completely replaced by broad fascicles of connective tissue. There were areas of granuloma formation, focal lymphofollicular structures, oedema and hyaline degeneration of collagen fibres. Perivascular mixed infiltrates and an epidermal acanthosis were evident. We started a daily treatment with 100 mg clofazimine for half a year. The swelling and infiltrating disease responded very well (Fig. 2b), so we decided to reduce the dosage to 50 mg/day and observed no relapse but further improvement during the last year.

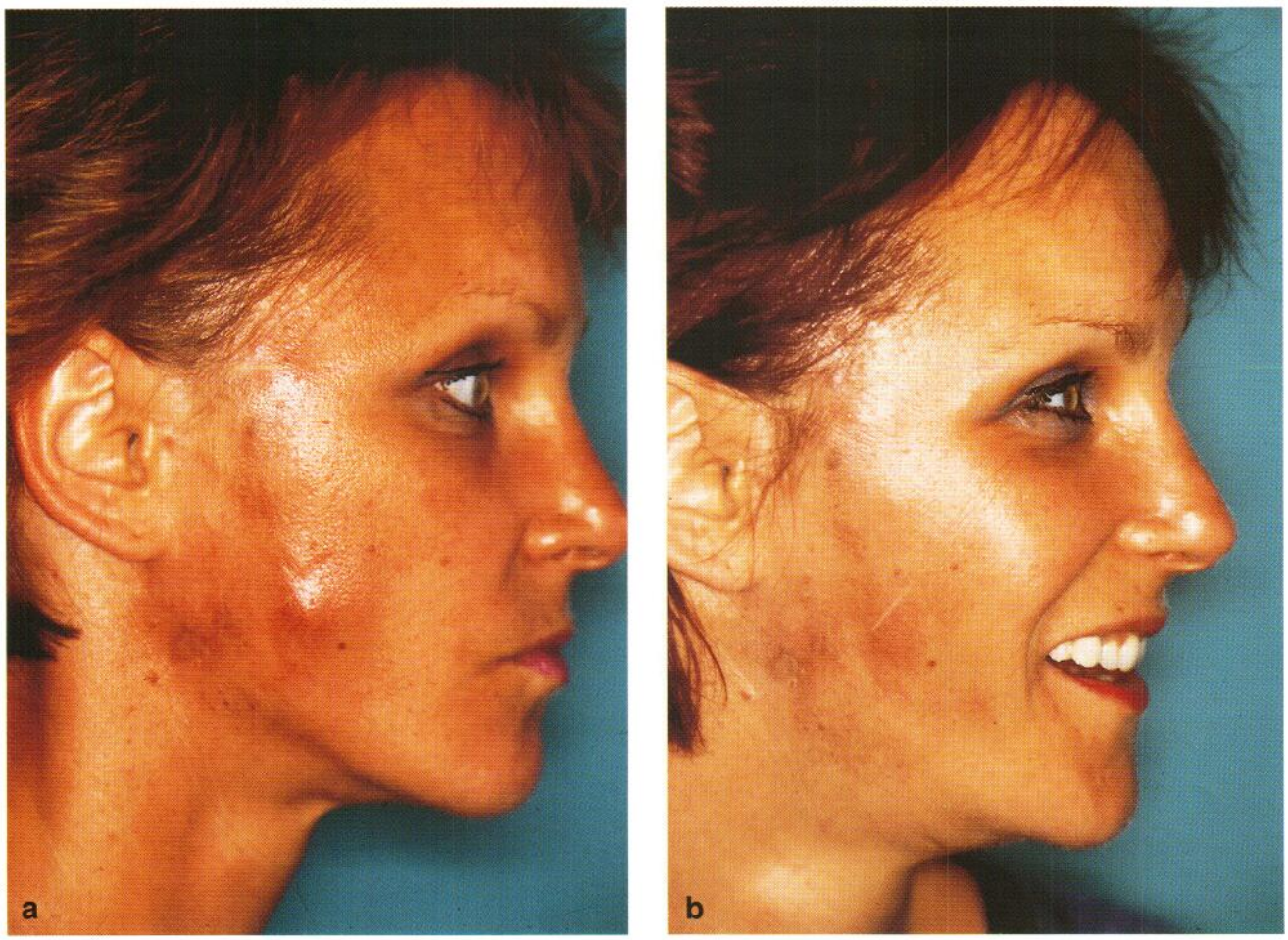

Fig. 2. Lipogranulomatosis subcutanea (case 2): (*a*) before and (*b*) after 3 months of treatment with 100 mg clofazimine daily.

DISCUSSION

Chronic relapsing inflammatory diseases of the face may be particularly disabling for the patient. Both GF and LGS belong to this type of skin disease. Their treatment may often be unsatisfying and frustrating. Corticosteroids and dapsone have been used with some benefit in some cases of GF (2). We observed a very good effect of clofazimine in widespread GF. To the best of our knowledge, there is only one additional report on a 36-year-old Nigerian man treated with 300 mg clofazimine daily for 3 months (4).

Our second patient, a 40-year-old woman, suffered from a longstanding, mainly facial LGS. The course is one of chronic relapsing and its treatment sometimes frustrating. Clofazimine was of outstanding benefit in this case. The initial dosage of 100 mg/day was well tolerated and without any side-effects.

Clofazimine is a phenothiazine drug with antibacterial and anti-inflammatory effects. Recently anti-proliferative activity has been observed for lymphocytes and carcinoma cells (5, 6). Unwanted side-effects have been reported in high-dosage and longstanding treatment regimens, as for leprosy, including skin hyperpigmentation, toxic erythema, gastrointestinal irritation, eosinophilic enteritis, renal infarction and pedal oedema (7–9). In our first patient a mild hyperpigmentation of the skin was seen, but no other side-effects were noted. On the other hand, the clinical reponse was obviously very good and the dosage of potentially hazardous corticosteroids could be minimized.

We suggest that clofazimine seems to be a beneficial and reliable alternative to other therapeutic efforts in certain cases of disabling inflammatory skin diseases.

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