Generalized Granuloma Annulare Showing the Unusual Clinical Feature of Marked Swelling of the Hands

Sir,

Generalized granuloma annulare (GGA) is an uncommon cutaneous disease of unknown origin. The eruption is characterized by predominantly papular primary lesions, a tendency toward annular grouping, and a potential to involve virtually any area of the skin. We describe a patient with GGA who showed features of markedly swollen lesions of the hands and numerous infiltrated erythematous macules on the extremities. The lesions were successfully treated with cyclosporine.

CASE REPORT

In October 1994, a 61-year-old man presented with a 20-day history of conspicuous swelling of the hands. Physical examination revealed skin-colored tender and markedly swollen glove-like lesions on both hands, and numerous infiltrated erythematous macular lesions on both forearms (Fig. 1). Moderately elevated hypertension, treated with diltiazem hydrochloride, and non-insulin-dependent diabetes mellitus had been present for several years. In addition, the patient had been taking Chlorella® tablets, a kind of health food supplement pom green algae, produced by Aspro Co. Ltd. (Japan), for 3 months before the lesions appeared.

Initial laboratory examinations revealed the following normal or negative results: urinalysis, blood sedimentation rate, liver and renal function tests, immunological examinations, serum tumor marker levels, angiotensin-converting enzyme and serum lysozyme level. Abnormal laboratory findings were: WBC 8,200/μl (eosinophils 8.0%); IgE 546 IU/ml; fasting blood sugar 161 mg/dl. Blood pressure was 171/98 mmHg. Tuberculin intradermal test was negative. Chlorella® demonstrated a positive result, stimulation index 20.1 on drug-lymphocyte-stimulation test, whereas diltiazem hydrochloride control was negative. In addition, no remarkable findings were noted on chest X-ray, ultrasound investigation of the abdomen, or upper gastrointestinal series.

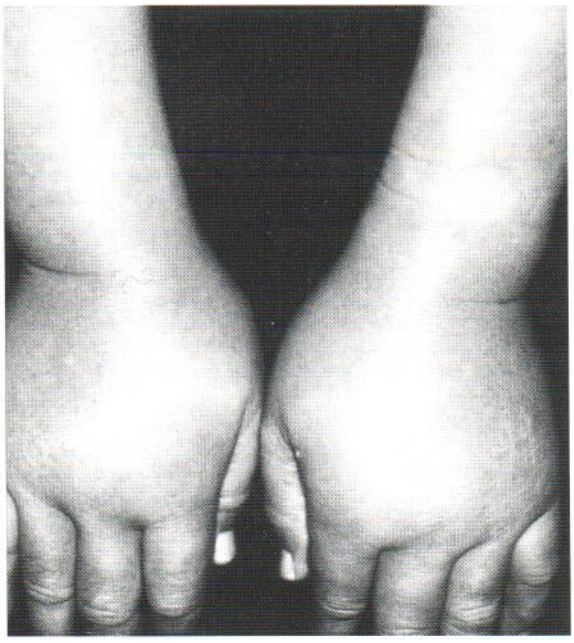

Fig. 1. Marked swelling of both hands and multiple erythematous macules on the forearms.

Skin biopsy specimens were taken from the swollen lesions on the hands and an infiltrated erythematous lesion on the forearm. Histopathology of the hands showed the following findings: coarse collagen and bluish-stained elastic fibers in the slightly edematous dermis, and granulomatous reaction, consisting of histiocytes and multinucleate giant cells, between the mildly necrobiotic collagen fibers, present in the mid- and deep-dermis and the subcutaneous tissue. Small epithelioid (sarcoidal-appearing) nodules at the periphery of the degenerative focus were partially observed (Fig. 2). In addition, an inflammatory infiltrate composed of lymphocytes and numerous eosinophils was present throughout the dermis. Alcian blue stain showed mucin deposits between the degenerative collagen fibers. Elastica van Gieson stain revealed prominent solar elastosis in the whole dermis and abrupt loss of elastotic materials within the granulomatous infiltrate. Ziel-Neelsen stains were negative for acid fast organisms. Furthermore, the histology of the erythematous lesion of the forearm disclosed findings consistent with granuloma annulare, with mild granulomatous changes compared to those of the hands. On clinicopathological findings, a diagnosis of GGA was made.

Treatment with betamethasone 0.5 mg daily and d-chlorpheniramine maleate 4 mg daily yielded no relief. Subsequently, the numerous infiltrated erythematous macular lesions extended into the upper and lower thigh (sun-protected areas). Then the treatment with cyclosporine 5 mg/kg daily was started. The swelling of the hands regressed completely after 2 weeks, leaving numerous discrete papules, measuring 1–2 mm in diameter. Histopathology of the biopsy specimen of these papules demonstrated multiple large granulomatous foci, consisting of histiocytes and multinucleate giant cells, between the disorderly arrangement of collagen bundles in various stages of degeneration. Mucin deposits were evident within the area of necrobiosis. The conspicuous swelling of the hands recurred 2 days after this biopsy. However, the swollen lesions of the hands regressed and erythematous macules regressed gradually within the following 3 weeks, and the treatment of cyclosporine was stopped 1 month after the complete resolution of the lesions. No relapse has been observed 8 months later.

DISCUSSION

This case presented the uncommon feature of markedly swollen lesions of the hands, which we had not previously seen in this

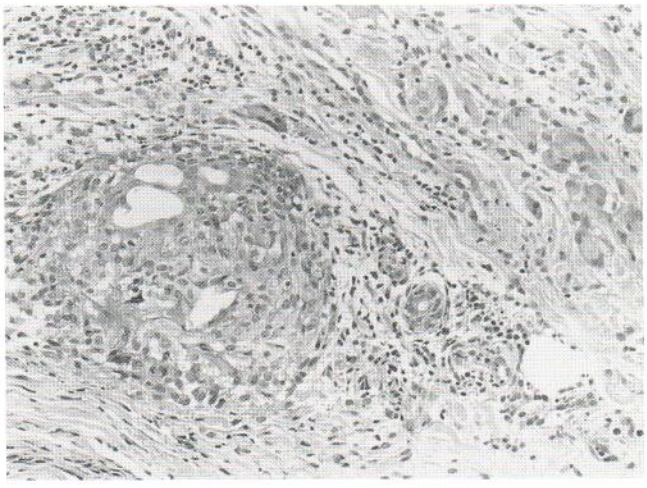

Fig. 2. Small histiocytic epithelioid nodules and numerous infiltrated multinucleate giant cells in the deep dermis (× 100).

condition. Histopathology of the hands showed a lymphohistiocytic granulomatous reaction involving the whole dermis and the subcutaneous fat tissues, with some histiocytic sarcoidal-appearing nodules and numerous eosinophil infiltrations. These clinicopathological findings were somewhat similar to those of the subcutaneous type of GGA, which usually develops in the subcutaneous fat tissue with the histology of complete collagen necrosis surrounded by an infiltrate of palisaded histiocytes and numerous eosinophils (1).

This patient had taken Chlorella® tablets for 3 months before lesions appeared and he demonstrated a positive drug-lymphocyte-stimulation test, indicating a possible allergic response to this agent. A combination with sun exposure might have triggered the reaction.

Many treatments for GGA have been used, with varying results. Recently the successful use of cyclosporine (2) was reported. The treatment of this agent also provided good results in this case. The role of the cell-mediated immune mechanisms in the pathogenesis of GGA has been described by some authors (1). Cyclosporine is highly effective in suppressing cell-mediated immunity and inhibiting chronic inflammatory reactions. The most important action of cyclosporine is inhibition of interleukin 2 production, elaborated by activated T-cells.

REFERENCES

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