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 from 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: urinanalysis, 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.

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 birefringent elastic fibers in the slightly edematous dermis, and granulomatous reaction, consisting of histiocytes and multinucleate giant cells. Between the mildly necrobiosis collagen fibers, present in the mid- and deep-dermis and the subcutaneous tissue. Small epithelioid (sarcoïdal-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. Ablain 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 elastic 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
condition. Histopathology of the hands showed a lymphohistiocytic granulomatous reaction involving the whole dermis and the subcutaneous fat tissue, 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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ANNOUNCEMENTS

17th Colloquium of the International Society of Dermatopathology (ISD) and Swiss Group of Dermatopathology (SGDP) will be held in Zürich, Switzerland on July 18–20, 1996. For further information please contact Conference management: Dermatopathologie 96, c/o AKM Congress Service, Clarastr. 57, CH-4005 Basel, Switzerland. Tel: +41-61 691 51 11. Fax: +41-61 691 81 89.

XI. Fortbildungsschule für Praktische Dermatologie and Venerologie 1996 will be held in München, Germany on July 21–26, 1996. For further information please contact Prof. Dr. Gerl Plewig, Dermatologische Klinik and Poliklinik der Ludwig-Maxillians-Universität, München, Frauenlobstr. 9–11, D-80337, München. Tel: +49-89 5160 4600. Fax: +49-89 5160 4527.

The Thirteenth International Congress, Medical Informatic Europe will be held in Copenhagen, Denmark on August 19–22, 1996. For further information please contact MIE 96, c/o DIS Congress Service, Copenhagen A/S, Herlev Ringvej 2c, DK-2730 Herlev, Denmark. Tel: +45 4492 4402. Fax: +45 4492 4500.

The 12th International Congress on Photobiology will be held in Vienna, Austria on September 1–6, 1996. For further information please contact Vienna Academy of Postgraduate Medical Education and Research, Alser Straße 4, A-1090 Vienna, Austria. Tel: +43 1 405 138313. Fax: +43 1 405 138323.

Third European Chlamydia Meeting will be held in Vienna, Austria on September 11–14, 1996. For further information please contact Dr. Angelika Stuy, Vienna Academy of Postgraduate Medical Education and Research, Alser Straße 4, A-1090 Vienna, Austria. Tel: +43 1 405 138313. Fax: +43 1 405 138323.

IV. International Dermatology Symposium Berlin. Schleimhaut Gland and its Disorders will be held in Berlin, Germany on September 13–15, 1996. For further information please contact Doc. Dr. Ch. C. Zouboulis, Department of Dermatology, University Medical Center Benjamin Franklin, The Free University of Berlin, Hindenburgdamm 20, D-12200 Berlin, Germany. Tel: +49 30 8445 2628. Fax: +49 30 8445 4262.

Seventh Dermatopathology Self Assessment Workshop and Mammary Gland Neoplasms Self Assessment Workshop will be held in Rome, Italy on September 19–21, 1996. For further information please contact Dr. Guido Massi, Department of Pathology, Catholic University, Largo F. Vito 1, I-00168 Rome, Italy. Tel: +39 6 3503481. Fax: +39 6 3503483.

11th International Symposium on Bioengineering and the Skin will be held in Zürich, Switzerland on October 2–5, 1996. For further information please contact Dr. William D. Carey, Vice Chairman, Division of Education for Continuing Education, 9500 Euclid Avenue, Cleveland, Ohio 44195, USA. Tel: +1 216 444 4606. Fax: +1 216 444 4606.

The Cleveland Clinic Foundation Dermatopathology Self Assessment Workshop will be held in Cleveland, Ohio on October 5, 1996. For further information please contact Dr. William D. Carey, Vice Chairman, Division of Education for Continuing Education, 9500 Euclid Avenue, Cleveland, Ohio 44195, USA. Tel: +1 216 444 4606. Fax: +1 216 444 4606.

Skin Therapy Forum III will be held in Cardiff, United Kingdom on October 7–9, 1996. For further information please contact Prof. R. Marks, Professor of Dermatology, University of Wales College of Medicine, Heath Park, Cardiff, CF4 4XN, United Kingdom. Tel: +44 1222 747747. Fax: +44 1222 762314.

Fifth Congress of the European Academy of Dermatology will be held in Lisbon, Portugal on October 13–17, 1996. For further information please contact Prof. A. Cabral Ascenso, Clinica Universitaria de Dermatologia e Venerologia, Hospital Pulido Valente, Alam, Lindares de Torres, P-1700 Lisbon, Portugal.

European Regional IUVDT Conference on STDs and Euvugian Conference on Herpes Viruses and Genital Pathology will be held in Paris, France on October 25–26, 1996. For further information please contact Congress Secretariat, BAXON Communication, 69/73 Avenue du Général Leclerc, BP 304-92102 Beugnon, France. Fax: +33 146 21 50 80.

Clinic Seminars in Dermatology will be held in Cleveland, Ohio on November 1–3, 1996. For further information please contact Dr. William D. Carey, Vice Chairman, Division of Education for Continuing Education, 9500 Euclid Avenue, Cleveland, Ohio 44195, USA. Tel: +1 216 444 4606. Fax: +1 216 444 4606.

Second International Congress on Cataracta Drug Reactions Devoted to “Drug Related Skin Diseases in the Immunocompromised Patients” will be held in Rome, Italy on November 14–15, 1996. For further information please contact ASFE, Viale Certosa 233, I-20151 Milano, Italy. Tel./Fax: +39 2 3340359.