lymphocytes with complement receptors were within the normal range. No eosinophilia was present. There was no evidence of hemolysis.

DISCUSSION

The etiology of the SJS reported here remained enigmatic. Respiratory disease has been recognized as one of the main causes of mortality in SJS (1). Earlier reports have pointed to the association of SJS with pneumomediastinum and pneumothorax (4, 5). The fatal respiratory distress was most likely due to severely destructive bronchiolitis, which has been demonstrated in autopsy studies in SJS (1, 3).

Liver disease in association with SJS seems rare. In most reported cases a variety of drugs had been administered before involvement of the liver was diagnosed (7, 9). Cholestasis was demonstrated biochemically or histologically in most patients. The protracted intrahepatic cholestasis observed here might be related to SJS in some undefined way, but a cholestatic drug reaction must also be considered (12). Erythromycin ethyl succinate was the only drug given systemically before jaundice was observed, and therefore this drug is incriminated. To our knowledge, cholestatic reactions to erythromycin ethyl succinate have not been reported before, although the hepatotoxicity of other derivatives of the erythromycin base, i.e. the estolate, is well known (6, 11).

Severe hepato-pulmonary pathology equal to that described here has been reported in a 6-year-old girl with SJS (2). In both cases the prodromal period was short and no systemic therapy preceded the development of SJS. The unique features of these cases may constitute a hitherto unrecognized subtype of SJS.

ACKNOWLEDGEMENTS

The author is indebted to Professor, Dr Med. Steen Olsen, Department of Pathology, and Dr M. Friis Andersen, Department of Radiology, The Municipal Hospital, Aarhus, for contributions to the case history. Furthermore I am grateful to Dr N. Rajani, and Dr Med. K. Thestrup-Pedersen for valuable suggestions during preparation of the manuscript.

REFERENCES

1. Ashby, D. W. & Lazar, T.: Erythema multiforme exudativum major (Stevens-Johnson syndrome). Lancet *i:* 1091, 1951.
2. Broadbent, R. V.: Stevens-Johnson disease presenting with pneumothorax. Rocky Mt Med J *64:* 69, 1967.
3. Claxton, R. C.: A review of 31 cases of Stevens-Johnson syndrome. Med J Aust *50* (1): 963, 1963.
4. Genieser, N. B., Becker, M. H. & Rothman, J.: Mediastinal emphysema complicating Stevens-Johnson syndrome. Arch Dermatol *105:* 421, 1972.
5. Jonsson, A. S.: Mediastinal emphysema and mucocutaneous syndrome. Lancet *i:* 208, 1969.
6. Plaa, G. L. & Priestly, B. G.: Intrahepatic cholestasis induced by drugs and chemicals. Pharmacol Rev *28:* 207, 1977.
7. Ritland, S.: Syndroma mucocutanea febrilis, sepsis og leveraffeksjon. Tidsskr Nor Laegeforen *92:* 175, 1972.
8. Sontheimer, R. D., Garibaldi, R. A. & Krueger, G. G.: Stevens-Johnson syndrome associated with *Mycoplasma pneumoniae* infections. Arch Dermatol *114:* 241, 1978.
9. Sternlieb, P. & Robinson, R. M.: Stevens-Johnson syndrome plus toxic hepatitis due to ibuprofen. NY State J Med *78:* 1239, 1978.
10. Ström, J.: Actiology of febrile mucocutaneous syndromes with special reference to the provocative role of infections and drugs. Acta Med Scand *201:* 131, 1977.
11. Tolman, K. G., Sannella, J. J. & Freston, J. W.: Chemical structure of erythromycin and hepatotoxicity. Ann Intern Med *81:* 58, 1974.
12. Zimmerman, H. J.: Intrahepatic cholestasis. Arch Intern Med *139:* 1038, 1979.

Acute Diffuse Scleroderma

E. Nunzi,[1] A. Rebora[1] and R. H. Cormane[2]

Departments of Dermatology, [1]University of Genova, Genova, Italy, and [2]University of Amsterdam, Binnengasthuis, Amsterdam, The Netherlands

Received July 14, 1980

Abstract. A case of acute diffuse scleroderma without contemporaneous visceral involvement is described. Antibodies to endothelial cells have been found in the skin.

Key words: Acute scleroderma; Immunofluorescence

Acute diffuse scleroderma (ADS) or malignant scleroderma is an exceedingly rare kind of systemic sclerosis, with acute onset, involving the trunk, sparing face and hands, and without Raynaud's phenomenon (8). The involvement of

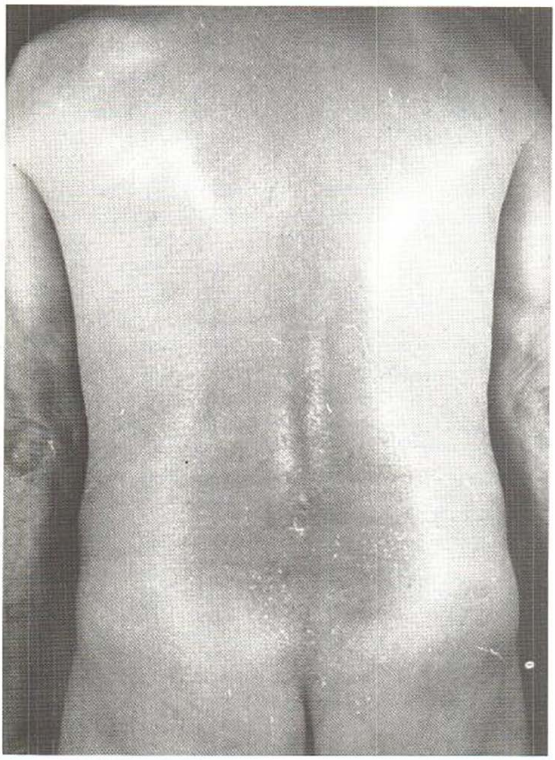

Fig. 1. Diffuse, not sharply demarcated induration of the skin of the back.

visceral organs is said to be simultaneous (9) and the prognosis very poor, patients dying in a few years. The prevalence of ADS ranges between 5% (5, 6) and 8% (8) of all cases of systemic sclerosis.

We have observed a patient with ADS who, after 9 months, still did not display evident signs of visceral involvement with the routine methods of investigation.

CASE REPORT

A 56-year-old Caucasian male with a 3-month history of itching and hyperpigmentation of the lower back was referred to our Department. After a few days a skin induration occurred in the same region which, soon after, spread dramatically all over the trunk. At present, a shiny, hyperpigmented, hardened and hairless skin extends over the arm and the thighs. There is no sharp demarcation from adjoining, normal skin (Figs. 1 and 2). The patient had never complained of Raynaud's phenomenon.

Laboratory investigations

ESR 14 mm/h; haemoglobin 13.5 g/100 ml; haematocrit 40%; RBC 5 110000; WBC 7400. The differential leukocyte count was normal. Serum electrophoresis revealed a normal total protein value (8.2 g/100 ml) with normal albuminemia (60.4%) and normal levels of beta-globulins (11%) and gamma-globulins (17.5%). Immunoelectrophoresis: IgA and IgG were normal, while IgM were slightly elevated to 203 mg% (normal values up to 170 mg%). No paraproteins were demonstrated. Liver and renal function tests were normal but a slight proteinuria (30 mg%) with a few red cells was present.

Rheumatoid serology, LE and syphilis tests were negative. ANA were absent. C3 and C4 components of complement were normal. E and EAC rosettes were within normal limits. Direct and indirect Coombs' tests were negative. LDH and isoenzymes, CPK, aldolases, pseudocholinesterases, SGOT and SGPT were normal.

ECG and EMG in the deltoid muscle were within normal limits. X-rays of chest and oesophagus were normal. Blood was repeatedly absent from the feces. Vital capaci-

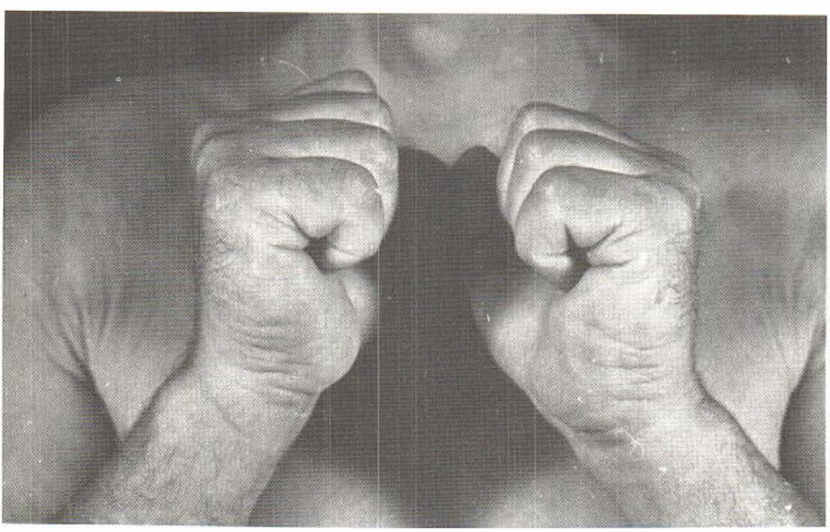

Fig. 2. Hands appear uninvolved; their movement is conserved.

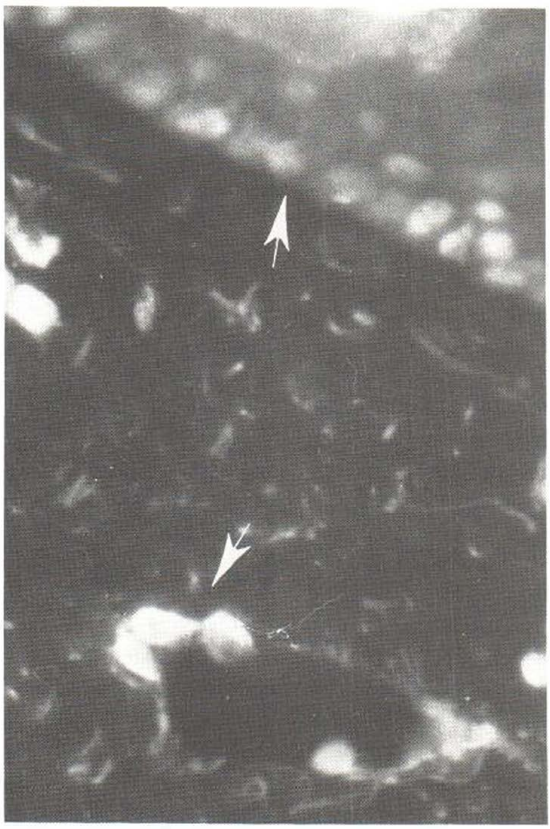

Fig. 3. Cryostat section of involved skin. IIF. The section was incubated with eluate from isolated circulating lymphocytes of the patient and subsequently with SW Hu IgE/FTC. Antibody present in eluate is reactive with nuclei of basal layer cells (*upper arrow*) and endothelial cells of blood vessels of dermis (*lower arrow*).

ty appeared to be insignificantly reduced. Blood pressure was and remained normal.

Histology

Biopsies were performed in both involved and clinically uninvolved skin. In the former, the epidermis was slightly thinned; the dermis appeared compact with tightly packed collagen bundles. Fairly dense perivascular lymphocytic infiltrates were apparent all over the dermis and deep into the subcutis. A biopsy specimen of the deltoid muscle did not reveal any sign of inflammation. The clinically uninvolved skin appeared normal.

Immunofluorescence studies

Direct immunofluorescence studies were negative in both the involved and uninvolved skin. The indirect immunofluorescence with serum on clinically normal skin and on rat tongue was negative. Indirect immunofluorescence with antibodies eluted from circulating lymphoid cells (1) showed antibodies to nuclei of epidermal basal cells and to nuclei of endothelial cells of the middle portion of the dermis in both involved and uninvolved skin. On rat tongue, such findings were absent. These antibodies did not bind complement 'in vivo' and appertained to the IgA, IgM and IgE classes (Fig. 3).

Treatment

A treatment with griseofulvin (1.5 g/day) was prescribed and was continued for 3 months. The hardening continued to spread to the present limits, although in the initial regions the skin now appears more tender. At present the spreading of the disease seems to have ceased.

DISCUSSION

ADS is a rare disease with a rapid and fulminating course with death occurring in a few years. In a case of Tuffanelli series, a 15-year-old girl died 8 months after the onset of symptoms. Our case appears to be unusual in that after 9 months the patient does not yet show any significant sign of visceral involvement and the skin hardening seems to have ceased.

The lack of visceral involvement may suggest other diagnoses, however. Generalized morphea is a quite different disease, in which numerous plaques are present, having a well defined border. The lack of eosinophilia and hypergammaglobulinemia, the non-involvement of fascia planes and muscle, as well as the lack of initial acral symptoms and of the memory of unaccustomed physical exertion exclude the Shulman syndrome (7).

In addition, the prodromic febrile illness and the involvement of the face and neck, typical of scleredema adultorum, are not present in our case.

The unusual, apparently benign course in our case could well be due to the griseofulvin treatment the patient was given.

Griseofulvin has been advocated by many authors (2, 3, 10) for the treatment of Raynaud's phenomenon and its beneficial effects were attributed to its alleged direct action on the vascular smooth muscle. In our case, however, this kind of effect seems to be unlikely, since our patient has never complained of digital vasospasms.

As far as the immunofluorescence findings are concerned, they confirm the data of Cormane et al. (1979) in that, in our case too, two antibodies have been isolated from circulating lymphoid cells, one to basal cells the other to endothelial cells.

Although it was tempting to assume that the involvement of internal organs in scleroderma depended on antibodies reactive to endothelial cells of

the organs in question, as suggested by Cormane et al. (1979), a cross reactivity of such antibodies with substrates taken from internal organs, such as oesophagus and kidney for example, has not been tested in our case; this might have revealed a possible visceral involvement before its clinical signs have become apparent.

ACKNOWLEDGEMENT

The immunofluorescence technique was performed in the immunopathology laboratory of the Department of Dermatology, University of Amsterdam.

REFERENCES

1. Cormane, R. H., Hamerlinck, F. & Nunzi, E.: Antibodies eluted from lymphoid cell membrane. Occurrence in certain varieties of scleroderma. Arch Dermatol *115:* 709, 1979.
2. Creery, R. D. G., Voyce, M. A., Preece, A. W. & Evanson, A. R.: Raynaud's disease treated with griseofulvin. Arch Dis Child *43:* 344, 1968.
3. Giordano, M., Ara, M. & Tirri, G.: La griseofulvina nella terapia delle periartriti della spalla e di altre malattie reumatiche. Atti XII Giornate Reumatologiche Romane, p. 371. Morara, Roma, 1965.
4. Giordano, M.: Griseofulvin for scleroderma. Lancet *ii:* 260, 1967.
5. — La sclerosi sistemica progressiva, p. 105. Pozzi, Roma, 1977.
6. Sackner, M. A.: Scleroderma. Grune & Stratton, New York–London. 1966. Quoted by Giordano: La sclerosi sistemica progressiva, p. 103. Pozzi, Roma, 1977.
7. Shewmake, S. W., Lopez, D. A. & McGlamory, J. C.: The Shulman syndrome. Arch Dermatol *114:* 556, 1978.
8. Tuffanelli, D. L. & Winkelmann, R. K.: Diffuse systemic scleroderma. A comparison with acrosclerosis. Ann Int Med *57:* 198, 1962.
9. Winkelmann, R. K.: Classification and pathogenesis of scleroderma. Mayo Clin Proc *46:* 83, 1971.
10. Wiskemann, A. & Korff, F.: Der Einfluss von Procain, Griseofulvin und Cloroquin auf die Hautdurchblutung bei progressiver Sklerodermie. Dermatol Wochenschr *153:* 1033, 1967.

Granulomatous Reaction in a Red Tattoo

Jesper Verdich

Department of Dermatology University of Copenhagen, Rigshospital, Copenhagen, Denmark

Received June 13, 1980

Abstract. A granulomatous reaction developed in the red part of a professsionally executed tattoo. The reaction appeared a few weeks after tattooing. A patch test for mercuric bichloride proved negative. The localization to the red part of the tattoo implies a specific reaction to an unknown antigen, and that the reaction may denote a localized delayed hypersensitivity.

Key words: Tattoo; Granulomatous reaction; Localized delayed hypersensitivity

The practice of tattooing is age-old and has flourished in modern civilizations among certain groups such as sailors and members of the armed forces. The tattoos are executed by professional tattooists by introducing pigmented particles into the dermis by means of an electric needle. The pigments used are in most cases mercuric sulphide (red colour), cobaltous aluminate (light blue), chromic oxide (green), cadmium sulphide (yellow), iron oxide (brown) and carbon (blue-black). All tattoos are followed by an acute inflammatory reaction which subsides within 3 weeks (7). Late or persistent reactions occur, but seem to be rare, considering the large number of tattoos performed.

This paper reports a case of granulomatous reaction in a red tattoo.

CASE REPORT

A 17-year-old marine had been tattooed by a professional tattooist on the left forearm 4½ months before attending this clinic. The tattooing was followed by the usual acute inflammatory reaction which subsided within a few weeks. Shortly after the inflammatory reaction had subsided, he developed small, slightly itching nodules in the red parts of the tattoo. He was otherwise well and sought advice because he considered the tattoo cosmetically unacceptable.

On inspection, a professional tattoo with red, green and blue colours was seen on the left forearm. All the red parts were elevated, with thickened and slightly scaling nodules (Fig. 1). A punch biopsy was made and histological examination showed the epidermis to be slightly hyperkeratotic. In the dermis there were areas heavily infiltrated with inflammatory cells, mostly lymphocytes and histiocytes. Some parts of the tissue showed granuloma-like infiltrates of lymphocytes and histiocytes. No epithelioid or foreign body types of giant cells were seen. Tiny pigment particles were seen, both intra- and extracellularly. In addition slight fibrosis was found in the dermis. The tattoo was excised surgically and the defect covered with a split-skin graft. A standard patch test series of the ICDRG (International Contact Dermatitis Research Group, Al-test), which includes mercuric bichloride 1 : 500 proved negative. The patient refused further investigations.