

THE EFFECT OF TRANSFER FACTOR ON CYSTIC ACNE

Pentti Gröhn, Kirsti Kuokkanen and Kai Krohn

The Institute of Biomedical Sciences, School of Medicine, University of Tampere, and Department of Dermatology, Central Hospital of Tampere, Tampere, Finland

Abstract. A chromatographically purified component of human dialysable transfer factor, previously described as causing a non-specific stimulation of cell-mediated immunity, was used as a therapeutic agent in three cases of stage IV cystic acne. The treatment caused a marked strengthening of skin test responses and had a promising effect on skin eruption in each case.

Key words: Transfer factor; Acne; Delayed hypersensitivity

Acne in its various forms is a common problem in everyday medical practice, especially in dermatology. Its existence can be said to be universal in early adulthood. The question concerning the etiology of acne is still open; theories based on anatomical changes in sebaceous glands and ducts, on hormonal background and heredity have been presented. Consequently the therapy is always symptom-based, consisting of antibiotics, hormones, local antiseborrhoeic treatment, cryotherapy, UV-light, etc. (7).

In the worst cases, infection of the sebaceous follicles followed by scar formation is a prominent feature. In fact, the resistance of the patient to infections may stand in relation to the duration and severity of the disease. It has been noticed previously that delayed hypersensitivity responses are often diminished in acne patients, but this has been believed to be a secondary effect of the widespread inflammation (7).

We have previously described a chromatographically purified component of human dialysable transfer factor (dTf), which is effective in stimulating decreased skin reactivity non-specifically (6). In this pilot study we have examined the state of cell-mediated immunity of 3 patients with severe cystic acne. They were all resistant to conventional therapy. Their skin reactivity to common recall

antigens, tuberculin and oidiomycin, was markedly decreased. The patients were treated with dTf, and this enhanced the skin reactivity and had a beneficial effect on the skin eruption in each case.

MATERIAL AND METHODS

Description of the patients

Patient 1, a 30-year-old woman, has suffered since puberty from stage IV cystic acne on the face, back and shoulders. She has always had a pronounced tendency to scar formation. She has received local therapy (retinoic acid, cryotherapy, corticosteroids) and prolonged treatment with tetracycline and lincomycin, but these all have been ineffective. Her leukocyte count and immunoglobulins have always been normal.

Patient 2, a 16-year-old boy, has suffered from stage IV cystic acne for 4 years. In May, 1975, he had a septic fever, which was supposed to originate from the inflammatory state of his acne. He has received both cephalosporin and tetracycline treatment, with only temporary effect. The state of humoral immunity has been normal.

Patient 3, a 30-year-old woman, has suffered from stage IV cystic acne since the age of 15 years. She has received numerous antimicrobial treatments and local treatment with antiseborrhoeic agents and cryotherapy. She has had a pronounced tendency to scar formation on the facial skin. The eruption has been very resistant to any kind of therapy. The state of her humoral immunity has been normal.

Controls

Healthy adults served as controls in immunological tests. Their immunological state has been described in a previous paper (3).

Preparation of a non-specifically acting transfer factor component

Dialysable transfer factor (dTf) was prepared from pooled buffy coat cells obtained from healthy donors (Finnish Red Cross Transfusion Service, Helsinki, Finland) according to a modification of Lawrence's method. The dialysate was further fractionated on a Sephadex

Table I. The skin test results of three acne patients before and after the administration of dTFc

Grading of the skin tests: PPD: 100 TU- = 0, 100 TU+ = 1, 10 TU+ = 2, 1 TU+ = 3. OM: 1:50- = 0, 1:50+ = 1, 1:500+ = 2

Patient	PPD responses		OM responses	
	Before	After	Before	After
1	0	2	1	2
2	1	2	0	1
3	0	1	0	2
Controls	3.1 ± 0.8		1.1 ± 0.7	

G-10 column, as previously described (6). Fraction VIa, designed by us as a chromatographically purified transfer factor (dTFc), eluting after the total volume of the column was pooled, lyophilized and weighed. It was redissolved in physiological saline at a concentration of 15 µg/ml and sterilized by Millipore filtration. Aliquots of 1 ml were stored at -20°C until use.

In vivo and in vitro tests

a) *Skin testing.* Skin tests were performed by using tuberculin (PPD, State Bacteriological Laboratory, Copenhagen, Denmark) and oidiomycin (OM, Dermatophytin "O", Hollister Stier, Spokane, Wa., USA) as antigens in serial concentrations. The skin testing was started with weak concentrations and repeated at one-week intervals until either the positive reaction was noted or the highest concentration of the test antigen was reached. An erythema and induration of more than 5 × 5 mm in diameter was regarded as a positive reaction (3). Grading of the skin test responses is given in Table I.

b) *Lymphocyte stimulation.* Phytohemagglutinin (PHA, Phytohemagglutinin P, Difco Laboratories, Detroit, Mich., USA) and PPD were used as test antigens. The blast transformation tests were performed with a method described earlier (3). After the culturing of the leukocytes the cell preparations were made and stained for visual counting.

General outline of the study

The state of cell-mediated immunity (CMI) was estimated by in vivo and in vitro methods at the beginning of the trial. Thereafter, dTFc injections were given subcutaneously twice with a one-week interval, then twice with a fortnight's interval and finally once a month. The test panel was repeated after the first injection and sometimes during the follow-up period. The clinical condition of the patients was checked by the dermatologist in charge.

RESULTS

The state of CMI of the patients before and after the administration of dTFc. In vivo, all the patients showed a diminished reactivity to PPD and OM

before the administration of dTFc. Injection of a single dose of dTFc caused a marked strengthening of the skin test responses in each case. After the treatment the skin test values were regarded as normal when they were compared with the skin test responses of the controls (Table I).

In blast transformation tests the results in PHA stimulation were normal both before and after the injection of dTFc (blast responses more than 55 %). By contrast, responses to PPD were negative. The administration of dTFc did not cause any significant change in the blast transformation responses (Table II).

Clinical effects of dTFc. Patient 1 received the first injection of dTFc in September, 1975. After the third injection the skin eruption began to disappear, and after the sixth injection, in January, 1976, not a single pustule remained in the previously affected area. Even the cheloid scars seemed to be smaller and lighter than earlier. The patient has been free of acne now for 10 months and has not received any kind of treatment.

Patient 2 received the first injection of dTFc in June, 1975. A month later he got the second dose. After this, new cystic pustules no longer formed. In September, a month after the fourth injection of dTFc, the skin eruption had disappeared entirely. The remission lasted without any therapy until July 1976, when new pustules began to break out.

Patient 3 received her first injection of dTFc in August, 1975. After 3 months' therapy, consisting of seven doses of dTFc, the formation of new pustules stopped. In December, 1975, the acne had disappeared, leaving severe scarring all over her face. The total number of injections was now 11. The remission lasted for 8 months. In July, 1976, cystic pustules reappeared on the face. Skin testing showed then that the patient was negative to 100 TU of PPD of OM again, but her blast responses

Table II. Blast transformation responses to PHA and PPD of three acne patients before and after the administration of dTFc

Patient	PPD (blast, %)		PHA (blast, %)	
	Before	After	Before	After
1	0.0	0.0	90.8	90.0
2	0.0	0.0	66.0	88.1
3	0.0	0.0	64.5	86.7
Controls	8.8 ± 5.4		64.0 ± 5.0	

were unaltered. The treatment was started again. Tuberculin skin reaction turned positive to 100 TU of PPD and 1:50 dilution of OM in September after 9 more injections of dTFc, with consequent healing of the eruption. Bacterial specimens were taken from the pustules, but they proved negative.

DISCUSSION

The present report describes 3 cases of severe acne, resistant to conventional therapy, and all of them in stage IV. In common, they showed skin anergy to PPD and OM, but their blast responses to PHA were normal and negative to PPD. After the administration of dTFc the skin reactivity was markedly strengthened, though without any significant changes in blast transformation responses. The skin eruption was observed to disappear in each case during the transfer factor therapy. The effect of the dTFc therapy was seen to last for more than 8 months without any kind of other treatment.

The transfer factor preparation used in this study has been shown to consist of aromatic or heterocyclic material of low molecular weight—less than 700 daltons (6). The mode of action of dTFc is unknown, but because of its chemical character, it is supposed to act immunologically nonspecifically. The targets of the action have been thought to be either those T cells which liberate lymphokines, or monocytes, which become able to transform themselves into tissue macrophages.

Transfer factor has been shown to be an effective therapy in many clinical conditions where a decreased CMI response is demonstrable, such as in chronic infections and perhaps in neoplastic diseases (5). However, the best clinical effects of transfer factor therapy are seen in a great variety of diseases which affect the skin and mucous membranes, such as chronic mucocutaneous candidiasis (2), lupus miliaris (4) and lepra (1). It is possible that most T cell activity is situated in the skin and mucous lining of the body, and the T cell mediated cellular immunity, rather than the B cell mediated humoral immunity, constitutes the outermost im-

munological shield against infectious agents. The good clinical results with transfer factor therapy seen in dermatological cases could be based on this great T cell activity in skin and mucous membranes.

The results of this preliminary study are encouraging in the treatment of severe acne. We recommend determination of the skin reactivity of acne patients and treatment of the most anergic cases with transfer factor preparations.

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P. Gröhn, M.D.
Radiotherapy Clinic
Helsinki University Central Hospital
Haartmaninkatu 4
SF-00290 Helsinki 29
Finland