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THE EFFECT OF NON-SPECIFICALLY ACTING TRANSFER FACTOR COMPONENT ON ACNITIS TYPE OF LUPUS MILIARIS FACIEI

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Abstract. A chromatographically purified component of human dialysable transfer factor, which was shown previously to cause a non-specific stimulation of cell-mediated immunity, was used in treatment of a patient with the acnitis type of lupus miliaris faciei and a negative skin reaction to 100 TU of PPD. After the treatment, skin reaction was positive with 10 TU of PPD, but no change was seen in the blast transformation test to PPD. The skin eruption started to heal after 2 weeks' therapy and disappeared completely in 3 months.

Key words: Transfer factor; Papular tuberculide; Lupus miliaris faciei; Delayed hypersensitivity; Immune stimulation

Human dialysable transfer factor (dTF) has been successfully used as a therapeutic agent in conditions where a defective cellular immune response may have been causally related to the disease (3).

We have previously isolated from dTF a component which seems to represent its major therapeutic principle (chromatographically purified transfer factor, dTFc) (6). Characteristically, dTFc induced or enhanced a missing or a weak skin reaction to various natural antigens, such as PPD, without any effect on lymphocyte stimulation in vitro. The chemical nature of dTFc is still unknown, but it contains several heterocyclic structures (6).

In the present work we report data concerning in vivo and in vitro reactions as a measure of cellular immunity in a patient suffering from the acnitis type of lupus miliaris faciei. This patient demonstrates a defective immune response both in vivo and in vitro. After the treatment with dTFc, a change in the skin reactivity is seen to coincide with a definitive clinical improvement.

MATERIAL AND METHODS

Preparation of dTFc. The preparation of dTFc from dialysable transfer factor by gel filtration on a Sephadex G-10 column has been described earlier (5, 6). The active fraction was freeze-dried, diluted in physiological saline, sterilized through a Millipore 0.22 μm filter and divided into 1 ml doses, each containing 15 μg of dTFc. Doses of 1 ml were given subcutaneously on the upper arm.

Skin testing. Skin testing was performed one week before and in conjunction with the administration of dTFc and was checked occasionally later on. Tuberculin (PPD, State Bacteriological Laboratory, Copenhagen, Denmark) was used in concentrations of 0.1, 1, 10 and 100 TU and oidiomycin (OM, Dermatophytin "O", Hollister-Stier, Spokane, Wa., USA) in dilutions of 1:50 and 1:500. 0.1 ml of test antigen was injected intradermally on volar forearm sites. The reactions were read after 24, 48 and 72 hours, and erythema and induration of more than 5×5 mm in diameter was regarded as a positive reaction.

Lymphocyte stimulation. In vitro blast transformation responses were measured before and after the administration of dTFc using PHA (Phytohemagglutinin P, Difco Laboratories, Detroit, Mich., USA), PPD, and OM as antigens as described earlier (5, 6).

Kveim test. In order to exclude the possibility of cutaneous sarcoidosis, the Kveim test was performed on the patient and on a proven sarcoid patient simultaneously. Histological investigations of the injection sites were made one month later. As an sarcoid test antigen, we used type i, lot 8, L. E. Siltzbach, Mt Sinai Hospital, N.Y.

Evaluation of the clinical effect of dTFc. dTFc was injected five times at weekly intervals and thereafter three times every alternate week. Skin biopsies were taken before the therapy and 4 months later. The responsible dermatologist examined the patient twice a month. No other therapy was given.

RESULTS

Case history. The patient is a 23-year-old previously healthy man. Three months before hospitalization the first papules appeared on his forehead, spreading rapidly all over the face. No effect was obtained with tetracycline, erythromycin or lymecycline and the patient was admitted to the

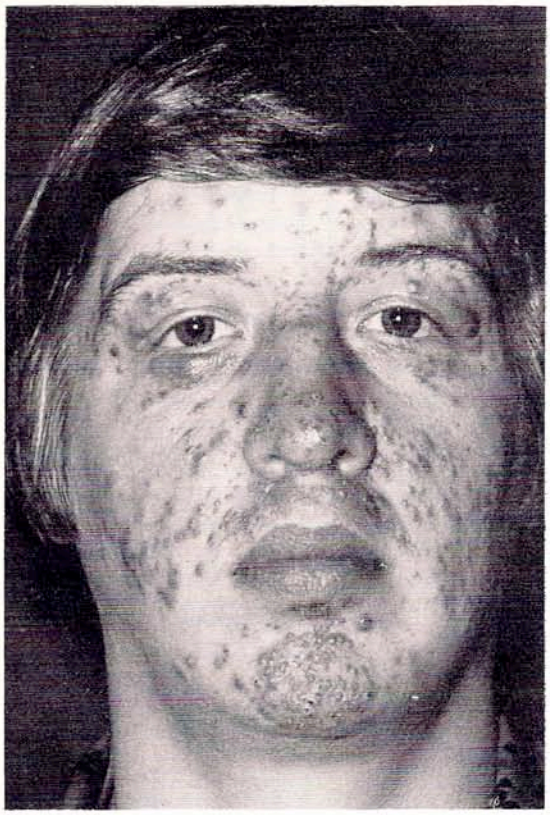

Fig. 1. Profuse eruption of acnitis type of lupus miliaris faciei in a 23-year-old man.

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On admission, the disseminated eruption consisting of bluish-red papules and pustules 3–6 mm in diameter was seen all over the facial skin, on the lips, earlobes and scalp (Fig. 1). Some papules were molluscum-like in size and shape, some were covered with crust (Fig. 2). In diascopy the colour was yellow-brown. Both lips and eyelids were swollen; caries and gingivitis were also found. The submandibular lymph nodes were markedly enlarged.

Histology. A biopsy sample was taken from the skin of the chin. Granulomas containing areas of caseous necrosis, epithelioid cells and Langhans giant cells were seen, similar to cutaneous tuberculide. No acid-fast bacilli were seen in the lesions.

Laboratory examinations. Routine laboratory tests were made prior to the therapy in order to reveal possible etiological factors. Haemoglobin and white blood cell counts were normal, Cardiolipin test was negative. AST, ASTA, Latex, Waaler-Rose, cryoprecipitins, and cold agglutinins were all within normal ranges. Serum protein electrophoresis and immunoglobulins were normal. Mycobacterium tuberculosis was not found in cultures from sputum and skin biopsy.

Immunological findings. Before the administration of dTFc skin tests with 100 TU of PPD and OM in 1:50 were negative. After the first injection of dTFc the PPD test became positive to 10 TU, but the oidiomycin reactivity was unaltered (Table I). Stimulation of lymphocyte cultures with PHA gave only a weak response, and responses to PPD and OM were negative. After the administration of dTFc no significant changes were noticed.

The patient had a negative Kveim test, while the sarcoid control patient showed a positive response.

Clinical effect of dTFc. After the first two injections of dTFc the oedema of the lips and eye-

Fig. 2. Molluscum-like bluish-red papules and pustules, before treatment.

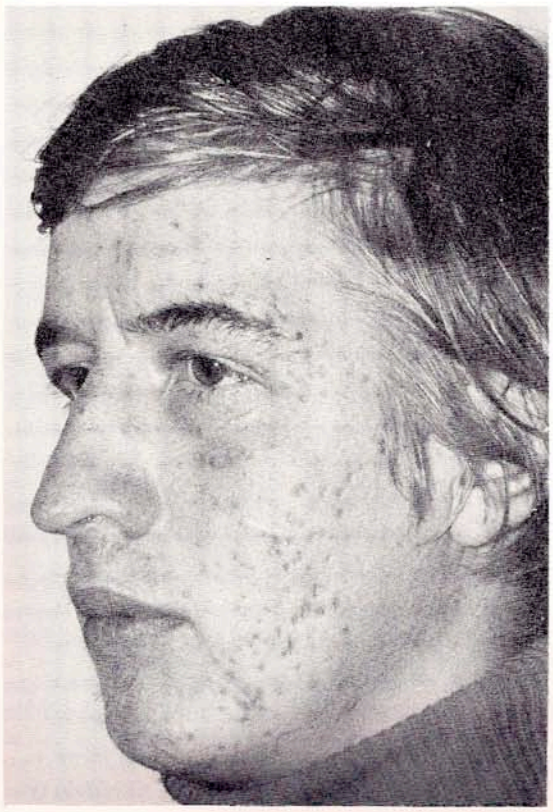

Fig. 3. Pitted scars on facial skin after 3 months' treatment with dTFc.

lids disappeared, and no new papules were noted. The papules began to turn bluish and to shrink and diminish in size, forming scaling plaques. After 3 months' therapy only light-coloured pitted scars were seen on the facial skin (Fig. 3).

Examination of a biopsy sample from the skin of the chin taken 4 months after the beginning of the therapy revealed only residues of granulomatous changes, without caseous necrosis.

DISCUSSION

The present report provides us with a new disease in the vast group of conditions, where administration of Lawrence's transfer factor or some of its components have shown beneficial effects on the clinical history of a recipient. Our patient presented a typical clinical picture of the acnitis type of lupus miliaris faciei, a rare disease of unknown etiology. It is generally believed that this disease is not caused by infection with mycobacteria and the only similarity with genuine tuberculosis is its histology (1, 2, 7, 8).

It is evident that decreased or abnormal immunological reactions could be of pathogenetic significance for the production of this type of granulomatous lesion. Indeed, our studies show that the present patient had a profound defect in his cellular immunity, which was demonstrable both in vivo and in vitro. His blast transformation reactions both to a nonspecific and to a specific mitogen were low, and he had negative skin reactions to oidiomycin and tuberculin. The anergy was not due to the lack of contact with the test antigen, as he had received BCG vaccination in early childhood. It is not certain whether the strengthening of skin test reactivity with PPD was caused by the booster effect of repeated skin testing in this case, but in healthy persons the repeating of skin tests did not cause any significant changes; the reactivity of only one of fourteen subjects was altered, when tested with PPD, and none with OM (4). The skin test sensitivity to OM was not affected, possibly due to the lack of any previous contact with the antigen, or due to the lack of stronger dilutions of the antigen in skin testing.

In evaluation of the therapeutical effect of dTFc the natural course of the lupus miliaris faciei must be considered. The disease is generally self-limiting, and spontaneous resolution takes place

Table I. *The effect of adiministration of dTFc on skin testing and lymphocyte stimulation*
Normal response to PHA more than 55% and positive response to PPD and OM more than twice the control

	Skin testing		Lymphocyte stimulation (blast %)				
	PPD	OM	C_1[a]	PHA	C_2[a]	PPD	OM
Before	100 TU−	1:50−	4.3	42.0	4.5	3.2	4.9
After	10 TU+	1:50−	0.0	49.2	0.4	0.6	0.6

[a] C_1=3-day control culture, C_2=6-day control culture without antigen.

in 1–2 years (1, 8). At the beginning of the therapy our patient had only a month history of the disease, which was in an active and progressive phase.

In view of the known natural history of the disease the improvement in the patient's clinical condition was rapid, and it can therefore be suspected that the observed improvement was due to the action of dTFc.

The mechanism of action of dTF, as well as that of dTFc, is not known, but it seems to be associated with a partial normalization of the immune response of the recipient.

The findings in our present case, with reappearance of skin reactivity to PPD, and without any simultaneous alteration in the in vitro reactions, are characteristic of dTFc. Theoretically, it is possible that dTFc affects the population of lymphocytes responsible for lymphokine production, but the defect in the present case as well as in others, where dTF therapy has proved effective, might equally well be in the cells of the monocyte–macrophage cell line, leading to the unresponsiveness to the lymphokines.

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