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Peptide T: a New Treatment for Psoriasis?

A review of our experiences

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Peptide T (Ala-Ser-Thr-Thr-Thr-Asn-Tyr-Thr) is a ligand of the CD4 receptor. It was discovered as part of the HIV envelope protein gp 120 (1). Synthetic Peptide T inhibits both the binding of HIV envelope to rat brain membranes and HIV infection of human T-cells (2). When used to treat an HIV-infected patient who has concomitant psoriasis, the skin disease disappeared. This prompted us to further treat a few HIV-negative psoriasis patients, with promising results (3, 4, 5, 6).

In the following we describe and discuss our further experience with this new treatment.

MATERIALS AND METHODS

Nine HIV-negative psoriasis patients with longstanding and recalcitrant psoriasis were included (2 females and 7 males). Their median age was 55 years (range 36–67). All the topical and systemic therapies were withheld 2 weeks prior to administration of Peptide T except for one patient (no. 6) who stopped etritinate and PUVA therapy one week before. The median dose of Peptide T/kilogram body weight was 26 μg (range 22–34). Only indifferent emollients were permitted during the entire period. Two milligrams of Peptide T were given intravenously in 500 ml saline for 28 consecutive days. All patients were hospitalized during the first week and thereafter treated as out-patients. The follow-up period lasted for another 3 months.

PASI score was employed (7) to evaluate the treatment effect. Biopsies from psoriasis lesions were taken before, weekly during the first 4 weeks and 4 weeks after discontinuing therapy. For the processing of the biopsies, see the appropriate papers (8, 9). The length of the epidermal rete lists was measured in the microscope from the tip of the rete lists, along the axial length to the junction between the epithelium and stratum comeum on haematoxylin eosin-stained histological sections.

RESULTS AND DISCUSSION

The clinical results are shown in Fig. 1. As can be seen the condition of all the patients except one had improved after 28

Fig. 1a

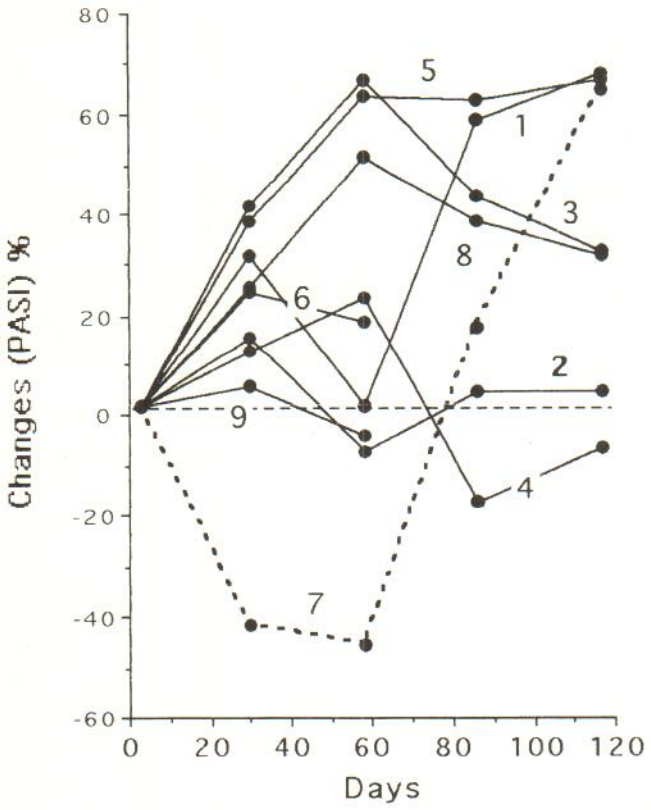

Fig. 1a. The clinical course is illustrated as a percentage of the pretreatment PASI score (zero level) during and after Peptide T treatment (2 mg/day from day 1 to 28). Increases denote improvements and decreases deteriorations. Figures on the graph stand for patient numbers. Patient no. 7 is denoted by a dashed line.

Fig. 1b

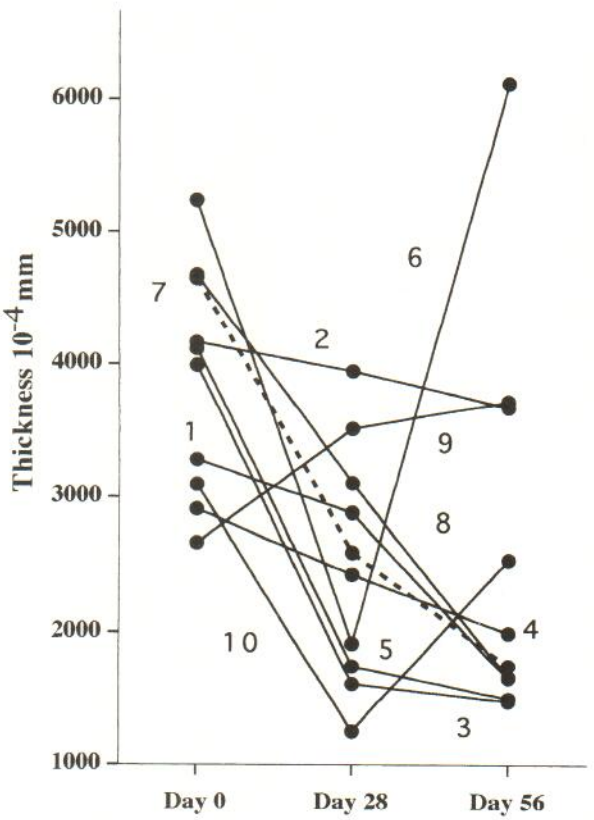

Fig. 1b. This graph shows the changes in the length of the epidermal rete lists (10^{-4} mm) for each patient during and after the Peptide T treatment. The figures correspond to those of Fig. 1. A 10th patient, shown in (*a*),is also included. Patient no. 7 is denoted by a dashed line.

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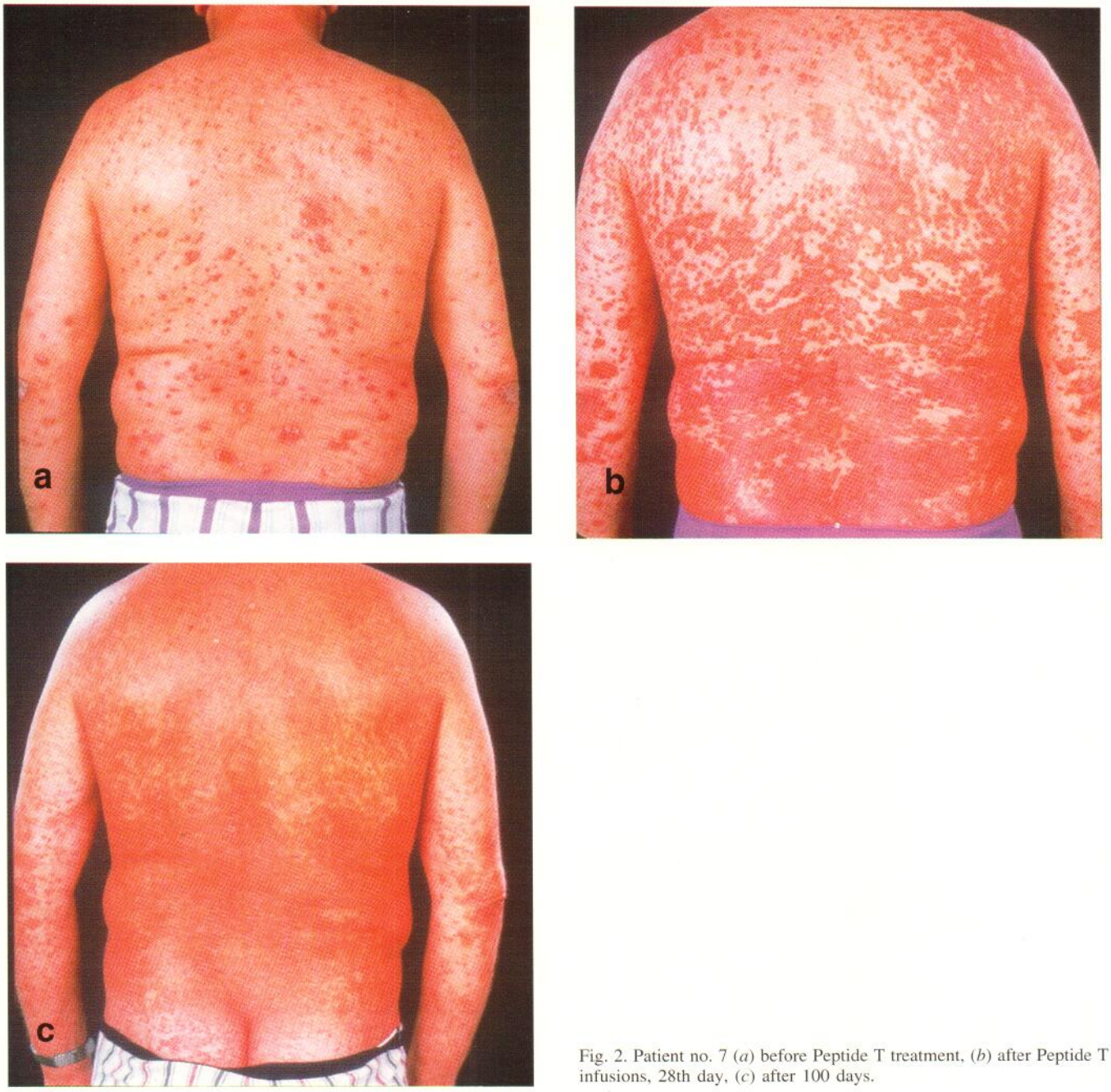
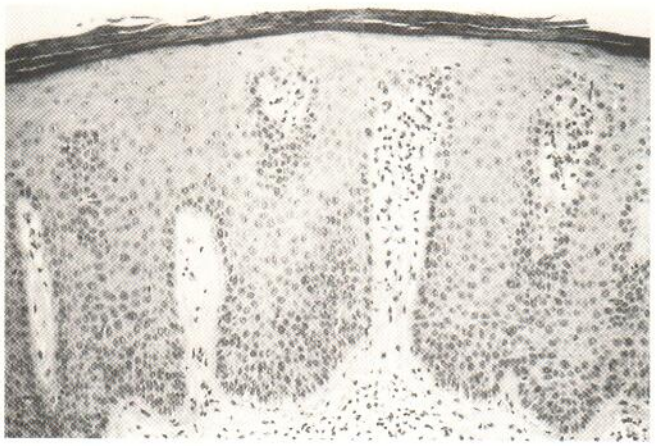
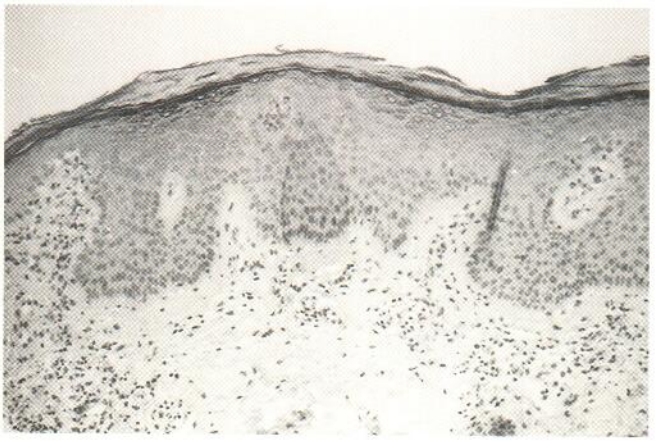


Fig. 2. Patient no. 7 (*a*) before Peptide T treatment, (*b*) after Peptide T infusions, 28th day, (*c*) after 100 days.

days, e.g. at the end of the time during which they were receiving Peptide T. The patients were followed for another 3-month period and an improvement of over 50% was noted in 5 patients. Interestingly, most of the conspicuous clinical improvements were seen after cessation of therapy. With regard to the histological improvement it can clearly be seen that epidermal thickness was reduced in all but one patient at the end of therapy (Fig. 1b) and increased thickness during the post-treatment period was observed in 2. We have previously presented data on other patients (4, 5, 6) showing continuous improvement throughout the observation period and we want to take this opportunity to describe one patient (no. 7) with an unusual pattern of response. Clinically he showed a severe deterioration at the beginning of the treatment which lasted till about day 60 (Fig. 2a, b). The deterioration measured by the PASI score was due to the increased area of involvement and the increased intensity of the redness. Then a pronounced clinical improvement was seen (Figs. 1a, 2a, b, c). During the worst period the affected areas were intensively red and glossy, with minimal scaling and induration. The recovery was seen during the follow-up period when no active treatment was given. With regard to the histological events it can be clearly seen that there was a continuous thinning of the epidermis (Figs. 1b, 3a, b, c). Farber et al. have also reported a positive clearance effect on psoriasis in a well designed controlled study (10). Thus we believe that Peptide T has a unique effect and that a placebo response is less likely, as has been suggested (11, 12).

The mechanisms of action of Peptide T are obscure. We have





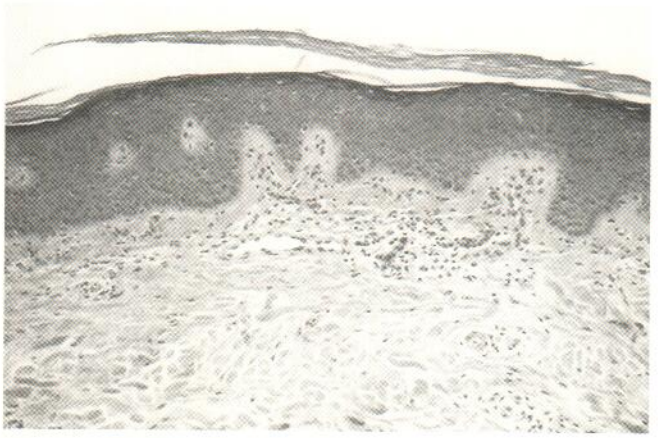


Fig. 3a. Pronounced psoriasiform acanthosis with agranulosis prior to Peptide T in patient no. 7.

Fig. 3b. During treatment, gradually decreasing epidermal thickness and normalization of the granular and corneal layers in patient no. 7 after 4 weeks.

Fig. 3c. Histological picture of lesional skin of patient no. 7 after 8 weeks.

analysed our serial biopsies from various aspects preferentially focused on the neuropeptides. One peptide, namely somatostatin, was found to be associated with dynamic changes in our biopsies. We have observed somatostatin-loaded dendritic cells in the dermis and a change in their numbers during therapy. In many instances the number is high initially or increases during the treatment and then decreases. We do not know exactly how to interpret our findings. Could it represent endogenously produced and released somatostatin, or are we observing migration of somatostatin-loaded dendritic cells? In view of the reported results from treatment with somatostatin, we believe that our findings are relevant (8) and that Peptide T may affect the synthesis of somatostatin. The true nature of these cells is at present unknown. Do they represent Langerhans cells or other cutaneous dendritic cells? With regard to epidermal Langerhans cells, they also show changes in number. At the beginning of therapy they are very few and during the course of treatment they increase in those who responded to Peptide T. We therefore believe that the Langerhans cells play an active role in the clearing of psoriasis. The possible relation and interaction between somatostatin, epidermal growth factor and vasoactive intestinal peptide has also been extensively discussed (9).

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