Peptide T a New Treatment for Psoriasis?

A Study of Nine Patients

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Nine patients with recalcitrant and long-standing psoriasis were treated over a period of 28 days with 2 mg Peptide T iv, once daily (22–34 µg/kg body weight). Eight of them showed an improvement of less than 50% by day 28 and one deteriorated. The patients were evaluated for a further 3 months when no topical or systemic treatment was given. Five patients recovered by more than 50%, during the months following termination of the therapy. Two patterns of healing were noted: firstly, a steady clearance beginning immediately with the Peptide T infusions; secondly, a clearance pattern preceded by deterioration. No serious side effects were noted.

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Peptide T is a synthetic octapeptide (Ala-Ser-Thr-Thr-Asn-Tyr-Thr) which has a sequence homologous with the envelope glycoprotein 120 of human immunodeficiency virus (HIV) (1). Glycoprotein 120 is essential for attachment of the virus to the CD4 receptor of T helper cells (2). This receptor also appears on other cells, such as Langerhans cells of the skin (3) and cells of the nervous system (1). Peptide T was designed to block the CD4 receptor, and so prevent binding of the HIV virus and its penetration into the CD4-positive cell (1).

In 1987, Wetterberg et al. reported an improvement of psoriasis in one AIDS patient treated with Peptide T (4). This prompted us to test this compound on 3 HIV-negative psoriasis patients (5,6). In 2 of them all the lesions responded immediately and in one a severe deterioration preceded clearance 2 months after discontinuing the Peptide T therapy. During the ensuing 12 months, remission was striking and suggested that Peptide T might have a unique effect on psoriasis. We therefore designed an open study, taking into consideration these aspects of the effect of Peptide T on psoriasis and aiming to ascertain the optimal dose.

MATERIAL AND METHODS

Patients

Nine HIV-negative patients with long-standing psoriasis participated. Eight of them were healthy, except for the skin disease. Patient no. 8 had hypertension. Patient characteristics are given in Table 1. All the topical and systemic therapies for psoriasis had been discontinued 2 weeks previously, except in patient no. 6 who had been unsuccessfully treated with PUVA and etretinate until one week before. Only indifferent emollients were permitted during the entire period.

Peptide T treatment

All patients were given intravenously 2 mg Peptide T in 500 ml saline once daily for 28 consecutive days. All were hospitalized for the first week and thereafter treated as out-patients. Patient no. 6 was an in-patient for the first 4 weeks because of severe arthritis. The patients were studied from November 1989 to June 1990.

Laboratory investigations

Laboratory tests were carried out on days 0, 14 and 28.

Blood. ESR, hemoglobin, white blood cell count (WBC), differential count, thrombocytes, potassium, sodium, aspartate aminotransferase, alanine aminotransferase, bilirubin, alkaline phosphatase, gamma glutamyltransferase, blood glucose, creatinine, urea and glomerular filtration rate.

Urine. Protein, glucose, hemoglobin.

PPD. Intracutaneous tests were made on days 29–35 with PPD (Purified Protein Derivative of tuberculin, State Serum Institute, Copenhagen, Denmark) to evaluate in vivo the presence of a delayed type of immunity.

Evaluation

The following procedures were used to document the course of psoriasis.

1. Psoriasis area and severity index (PASI), as described by Fredriksson & Pettersson (7).
2. Since the PASI score might have missed details during the course, we also evaluated three target lesions. When possible, we chose sites of these lesions on the upper and lower extremities and the trunk. Erythema, desqua-
Table I. Patient characteristics.

<table>
<thead>
<tr>
<th>Patient’s no.</th>
<th>Age</th>
<th>Initial PASI</th>
<th>Peptide T (µg/kg body w.)</th>
<th>Psoriasis type</th>
<th>Duration of psoriasis (years)</th>
<th>Body area affected (%)</th>
<th>PPD</th>
<th>Previous treatment/Remarks</th>
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</thead>
<tbody>
<tr>
<td>1/F</td>
<td>52</td>
<td>6.1</td>
<td>31</td>
<td>P1</td>
<td>33</td>
<td>4.0</td>
<td>Pos</td>
<td>Bet</td>
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<tr>
<td>2/M</td>
<td>59</td>
<td>6.6</td>
<td>22</td>
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<td>25</td>
<td>4.1</td>
<td>Neg</td>
<td>Tar</td>
</tr>
<tr>
<td>3/M</td>
<td>37</td>
<td>7.8</td>
<td>24</td>
<td>P1</td>
<td>7</td>
<td>5.8</td>
<td>Pos</td>
<td>UVB</td>
</tr>
<tr>
<td>4/F</td>
<td>55</td>
<td>3.7</td>
<td>25</td>
<td>Chr g</td>
<td>35</td>
<td>2.4</td>
<td>Pos</td>
<td>Bet</td>
</tr>
<tr>
<td>5/M</td>
<td>36</td>
<td>7.6</td>
<td>27</td>
<td>N</td>
<td>11</td>
<td>7.8</td>
<td>Neg</td>
<td>Bet</td>
</tr>
<tr>
<td>6/M</td>
<td>40</td>
<td>13.6</td>
<td>31</td>
<td>PIAcArth</td>
<td>10</td>
<td>9.8</td>
<td>Pos</td>
<td>PUVA + Et</td>
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<tr>
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<td>43</td>
<td>6.4</td>
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<td>N</td>
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<td>Pos</td>
<td>Ud</td>
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<tr>
<td>8/M</td>
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<td>5.4</td>
<td>26</td>
<td>N</td>
<td>30</td>
<td>1.9</td>
<td>Pos</td>
<td>Bet + UVB</td>
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<tr>
<td>9/M</td>
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<td>18.1</td>
<td>34</td>
<td>P1 La</td>
<td>26</td>
<td>32.0</td>
<td>Pos</td>
<td>Ht</td>
</tr>
</tbody>
</table>

Pl = plaque psoriasis; Chr g = chronic guttate psoriasis; N = nummular psoriasis; Ac = acral psoriasis; Arth = arthritis; PIAcArth = large plaque psoriasis; Bet = Betamethasone valerate cream; Et = Etretinate; Mtx = methotrexate; Ud = Urapidil; Ht = Hypertension.

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3. Since Peptide T induced new skin lesions besides the initial ones in one of our first 3 patients, the body area affected was estimated at regular intervals using the area of an average palm as a 1% reference.

Patients were examined on day zero, once weekly during the first 8 weeks and ever second week for the remaining 8 weeks over a total observation period of 16 weeks.

Course
To simplify the interpretation of therapeutic efficacy, PASI scores were used to calculate the percentage improvement or deterioration as follows:

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P(t) - P_0 \times 100 \]

where \(P(t)\) represents the initial PASI value and \(P_0\) the actual scores on days 0, 28, 56, 84, and 115 (Fig. 1).

RESULTS
The clinical course in each individual is summarized in Fig. 1. During the treatment period (the first 28 days) 5 patients improved by more than 20%, 3 showed a positive tendency, while one deteriorated. During the interval up to about day 60, 4 became worse and 4 continued to improve, of which 3 reached the 50% improvement level. About day 85, 2 of the latter 3 worsened and one remained improved while a 4th patient reached the 50% level. By day 120 a 5th patient crossed the 50% level.

Three individual patients representing various types of responses will be described in relation to detailed graphs showing that only the use of PASI score will hide valuable information. Patient no. 5 (Fig. 2a) showed a steady clinical improvement with regard to all parameters studied. Patients 7 and 1 (Fig. 2b,c) represent an improvement preceded by deterioration. In case no 1 the worsening came after discontinuing the therapy and in case 7 within the first week of therapy. The area of involved skin increased and the surface became intensely red and glossy. Despite that, a steady thinning of the target lesions in both patients was registered and could not be seen in the PASI score.

Patient no. 6 had arthritis in his knee, fingers and toe joints as well as saccroitis. No positive effect on the joint lesions was observed. He was excluded from the study after day 60 because of severe deterioration. Another interesting notion was made in patient no 7. After the observation period he exposed himself to sunshine and the remaining skin lesions cleared up rapidly. He had never previously improved after UVB, PUVA or sunbathing. All the patients reported less desquamation and a reduced need for emollients during the treatment.

Side effects
Laboratory tests. Hemoglobin and creatinine values decreased from a mean of 147–139 g/l to 85–77 µmol/l (p<0.05). A decrease in the WBC from 3.8 × 10^9/l to 2.2 × 10^9/l (reference value 3.0–9.0 × 10^9) was noted in patient no. 4, 2 weeks after the institution.

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Fig. 1. Percentage change in PASI score during and after Peptide T treatment (2 mg/day from day 1 to day 28). Starting levels are designated as zero. Increases denote improvements and decreases deteriorations. Figures on the lines stand for patient number.

of treatment and 2.5 10^9/l at the end of the period. From day 1 to 28, a relative lymphocytosis (about 66% on the differential count) was noted. Three weeks after the last dose the WBC and differential count had normalized. No such hematological derangements were seen in the other patients.

Blood pressure. Both systolic and diastolic blood pressure values were significantly decreased, mean 140/82 to 125/79 (p < 0.05).

Subjective symptoms. Three patients complained of headache, 2 of fatigue and lethargy, 2 of dizziness, 2 of flatulence, and 3 of euphoria. Three reported no side effects. During the post-treatment period, no

Fig. 2a, b, c. Clinical changes in subjects 5 (a), 7 (b) and 1(c). The Y-axis represents the PASI values; the mean value of two parameters (erythema and induration) of the target lesions and the percentage of body area affected. The X-axis represents the observation time in days. Peptide T was given on days 1 to 28.
side effects developed. There was no increase in susceptibility to infections.

Skin test

Intracutaneous tests were made with PPD immediately after day 28; seven of them proved positive and two (patients 2 and 5) were negative (Table 1). Patient no. 2 had previously shown a negative response. We have no information about the previous PPD reactivity of patient no. 5.

DISCUSSION

The psoriasis in all the 9 psoriatic patients benefitted from the treatment, but only 5 of these 9 improved by 50% or more during the follow-up. Peptide T gave immediate clinical relief and, in addition, a delayed effect after cessation of therapy. The reason for this is not clear but we believe that Peptide T may intervene at a crucial step in the pathogenetic process initially, and what we observe as a late effect may reflect the time needed for the epidermis to recover.

In some patients there was a period of deterioration before ultimate improvement. Patient no. 7 for example (Fig. 2b) deteriorated seriously during the first 28 days and remained in poor condition for 2 months until the process of clearance began. He had been treated with potent topical steroids before Peptide T and it is plausible that we recorded a rebound phenomenon after the withdrawal of topical steroid therapy, but the Peptide T effect was obviously strong enough to promote healing. In case no. 1 (Fig. 2c) there was a deterioration on day 60 which brought the patient to zero level and then came a sudden accelerated improvement. This we believe to be a unique effect of Peptide T rather than a rebound phenomenon due to the long time that had elapsed between the discontinuation of previous therapy and the start of deterioration.

Why did not all the patients respond? The simplest answer may be that the doses were too small. Our small patient sample, however, precluded the establishment of a dose-effect relationship. Since AIDS patients have tolerated higher doses, there is evidently a broad therapeutic margin (8, 9, 10, 11, 12). Therefore, an important issue for future trials is to determine the optimal dose. Another interesting point is that what we call psoriasis may in fact be a reaction pattern of the skin with various etiologies in certain genetically predisposed subjects. Only one of the causes may be amenable to treatment with Peptide T. Further clinical experience will clarify this.

In a previous case report we described a patient with oligoarthritis and psoriasis, both of which responded satisfactorily to Peptide T (5). In this series, however, no positive effect on the severe arthritis of patient no. 6 was noted.

The subjective side effects were considered to be minimal and none of the patients wished to discontinue the treatment. None of the deviations in the laboratory parameters was of any clinical significance, except for the decrease in WBC in patient no. 4. Whether this decrease was caused by Peptide T or other circumstances unrelated to Peptide T remains to be investigated. The significant lowering of the blood pressure should be kept in mind when treating patients with cardiovascular disease and psoriasis. This could be a vasoactive intestinal peptide (VIP) effect on the small blood vessels, since in some experiments Peptide T has been shown to have a VIP mimetic effect (13).

The mechanism by which Peptide T affects psoriasis is still unknown. One suggestion is a blocking effect, similar to that suggested for HIV, on a putative psoriasis-causing virus (14); another possibility is a functional alteration of CD4 positive cells.

Finally, Peptide T mimics vasoactive intestinal peptide and both compete with the HIV envelope protein glycoprotein 120 for binding to the CD4 receptor. Whether vasoactive intestinal peptide plays a role in the psoriasis process is not known.

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REFERENCES


