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Interferon-α Therapy in Atopic Dermatitis

ANTONIO TORRELO[1], ANTONIO HARTO[1], ENRIQUE SENDAGORTA[2], BEATE M. CZARNETZKI[3] and ANTONIO LEDO[1]

[1]Department of Dermatology, Hospital "Ramón y Cajal", Madrid, Spain, [2]Department of Clinical Research (Dermatology), F. Hoffmann – La Roche Ltd., Basel, Switzerland, and [3]Department of Dermatology, Rudolf Virchow Clinic, Freie Universität Berlin, Berlin, Germany

Thirteen patients with a severe adult form of atopic dermatitis (AD) received 3.0×10^6 IU of recombinant interferon-α2a (rIFN-α2a) 3 times a week. A satisfactory response was obtained in 5 of them. Serum IgE levels in all 13 patients remained unchanged throughout the study. Flu-like symptoms were common, but clinical or laboratory adverse effects were otherwise slight. The moderately beneficial therapeutic effects observed in this study support a possible role for IFN-α in controlling immunologic deficiencies in atopic dermatitis.

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A. Ledo, Department of Dermatology, Hospital "Ramón y Cajal", Apartado 37, E-28034-Madrid, Spain.

It is well known that several immunologic abnormalities are present in patients with atopic dermatitis (AD), although it is not known whether they represent a primary defect in the disease. Modulation of the immune system is an attractive approach for therapy of patients with AD, and diverse results have been obtained with levamisole (1), transfer factor (2), thymopentin pentapeptide (TP-5) (3), and cyclosporin A (4, 5). Recombinant interferon-α2a (rIFN-α2a) is a biological response modifier which has been effective in the treatment of diverse dermatologic diseases, such as Behçet's disease (6), cutaneous lupus erythematosus (7), and some cutaneous tumours (8). IFN-τ has been effective in pilot trials of AD patients (9, 10), and rIFN-α was effective in a hyper-IgE patient with eczema (11) and ineffective in 2 AD patients (12). In the present study, the results of a pilot study of rIFN-α2a therapy in 13 patients with AD are reported.

PATIENTS AND METHODS

Patients

Thirteen patients (9 men, 4 women, age 18–31 years), with severe AD for more than 4 years participated in the study. All patients fulfilled diagnostic criteria for AD (13) but were otherwise healthy, and pregnancy was excluded in women.

Treatment

The patients received 3.0×10^6 IU of intramuscular rIFN-α2a, 3 times a week, for 4 weeks. This dosage could be doubled for another 4 weeks, if no response was observed at that time, or otherwise continued at the same dosage.

Evaluation criteria

Evaluation of the response to the therapy was made by the same investigator on the basis of clinical examination. We employed the score system proposed by Costa et al. (14), measuring intensity and extension of AD and obtaining a total score. The intensity was assessed using values from 0 to 7 for the following parameters: erythema, oedema, vesicles, crusts, excoriations, scales, lichenifications, pigmentation/depigmentation, pruritus, and loss of sleep, with a maximal score of 70. The extension was assessed by division of the body surface in 10 areas: feet, popliteal fold, remaining legs, hands, arms, buttocks, back, anterior chest and abdomen, face, and scalp. A score of 0 to 3 was assigned for each region regarding the extension of AD, up to a maximum of 30. Thus, a total sum of 100 would mean the highest score of severity. Dermatological examinations were repeated every 2 weeks. At the end of the study, an evaluation of the global therapeutic effect was made by the patient and the investigator using the following scale: no improvement, slight response, moderate response or satisfactory response. Clinical evaluation of adverse effects was made twice a week.

Laboratory tests

Complete blood cell count, biochemical parameters, urinalysis, and clotting studies were performed before and 3 times a week during the first 2 weeks of therapy, and every week thereafter in order to detect any adverse effects promptly. Total serum IgE was measured by radioimmunoassay (RIA) every week. Two weeks after withdrawal of therapy, these determinations were repeated, together with electrocardiogram and thorax roentgenograms. During the assay, only emollient baths were permitted. Oral paracetamol 500 mg was administered together with rIFN-α2a prophylactically to minimize flu-like reactions. In patient no. 10, low potency topical corticosteroids were applied to the most severely affected areas.

RESULTS

The values of scoring prior to therapy and at 2, 4, 6, and 8 weeks are summarized in Table I. All patients completed the 4-week therapeutic trial, while in 6 patients therapy was prolonged for 4 weeks more. No patient had to discontinue therapy due to adverse reactions.

At 4 weeks of therapy a satisfactory response was registered both by the patients and the investigator in patients nos. 1–5, while in the other 8 patients a slight response or no improvement was achieved. Of the 5 patients who improved markedly at 4 weeks, nos. 1, 2 and 3 experienced a prolonged remission without any treatment. Patient no. 4 suffered a new attack of AD when rIFN-α2a was interrupted at 8 weeks, which could be controlled with the same medication at identical dosage; however, a later bout of lesions appeared while he was on rIFN-α2a treatment, which could not be controlled with this medication (score 42). Patient no. 5 worsened at 8 weeks despite continued rIFN-α2a treatment. The treatment was prolonged for patients nos. 10, 11 and 12 at a double dosage and at the same dosage in patient no. 13. None of them improved. Serum IgE levels remained high and unchanged throughout the trial, in both responsive and non-responsive patients. Adverse effects are shown in Table II. All of them subsided during the trial or shortly after finishing.

Table I. *Scoring of severity of atopic dermatitis*

No	Prior to therapy	2nd week	4th week	6th week	Follow-up (8th week)
Responsive patients:					
1	44	27	10		
2	51	6	9		
3	46	9	7		
4	59	41	19	13	25
5	35	39	17	28	40
Unresponsive patients:					
6	56	40	36		
7	61	42	52		
8	59	47	68		
9	60	41	60		
10	61	35	51	52	58
11	51	50	47	56	55
12	63	53	52	49	45
13	50	48	38	41	52

DISCUSSION

In the present study, 5 out of 13 patients improved markedly after 4 weeks of therapy with rIFN-α2a, while therapy failed or induced only a slight improvement in the other 8 cases.

Strannegard & Strannegard (15) observed a defective capacity to generate interferons in response to viral antigens in AD. Furthermore, peripheral blood mononuclear cells from a significant proportion of patients with AD have an impaired capacity to generate IFN-τ after PHA stimulation in vitro (16, 17). Moreover, small quantities of IFN-τ inhibit the ability of IL-4 to stimulate B-cell growth, enhance IgG1 and IgE production, and induce the expression of low affinity receptors for Fc fragments of IgE ($Fc_\varepsilon R_L$/CD23) on B cells (18). IFN-α decreases IL-4 induced IgE synthesis as well (11). Lately, both IFN-α and -τ have been shown to block spontaneous IgE production by mononuclear cells of allergic patients in vitro (11). In view of these and additional studies (19), it has been suggested that a decreased production of IFN and an increased production of IL-4 could lead to some primary or secondary immunologic abnormalities in AD.

Previously, Souillet et al. (11) described a patient with hyper-IgE syndrome and eczema in whom treatment with IFN-α resulted in clinical improvement and a gradual decrease of the serum IgE levels. In contrast, MacKie found no benefit from treating 2 AD patients with rIFN-α (12). Parkin et al. (20) reported on 2 AIDS patients with atopic symptoms who improved strikingly after IFN-τ therapy, and two reports noted strikingly beneficial effects with IFN-τ in AD patients (9, 10). The number of patients treated with rIFN-α was too small to draw any conclusions.

The presented data indicate some possible beneficial effect of rIFN-α treatment in AD patients. A placebo group was not considered in our study due to its pilot nature and the resistance of our patients to conventional therapy.

Table II. *Adverse effects*

Effect	No. of patients
Flu-like syndrome	12
Increased serum triglycerides	4
Increased serum transaminases	4
Hair loss	1
Peripheral oedema	1
Decreased prothrombin time	1

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