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Serum Levels of Interferons and TNF-α Are Not Correlated to Psoriasis Activity and Therapy

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Sera from 52 patients with psoriasis and 106 controls were tested for IFN-τ, IFN-α2 and TNF-α in ELISA and for total IFN activity using an infectivity inhibition micromethod. Psoriasis patients had lower serum levels of IFN-τ than had the controls: median 0.10 ng/ml vs. 0.16 ng/ml ($p = 0.01$). The highest median serum INF-τ levels were in patients with peripherally spreading psoriasis, 0.10 ng/ml, and acute guttate psoriasis, 0.09 ng/ml. Patients with stable plaque psoriasis had lower serum IFN-τ levels (median 0.0) than those with other forms of psoriasis, or blood donors. The serum levels of IFN-α2, total IFN activity and TNF-α did not differ between the psoriasis and control group. Treatment with cyclosporin, acitretin and the Goeckerman regimen increased the total IFN activity, but did not affect the levels of IFNs nor TNF-α. *Key words: IFN-τ; IFN-α2; cyclosporin; acitretin; Goeckerman.*

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Psoriasis is a papulosquamous disease of unknown etiology. An infiltrate consisting mainly of activated CD4+ T lymphocytes and macrophages is regularly present in early and fully developed lesions (1, 2). Early in the disease process, T lymphocytes pass into the epidermis. The epidermal T lymphocytes are mainly of the CD8 phenotype and could react with autoantigens or foreign antigens (3). We have previously detected antiviral activity consistent with the presence of interferon (IFN) both in serum and in suction blister fluid from skin lesions in psoriasis patients (4). Both IFN-τ and IFN-α could be implicated. Another cytokine of interest in psoriasis is the tumour necrosis factor (TNF) which is synthesized by macrophages (5) and keratinocytes (6). TNF is cytotoxic for neoplastic cells and stimulates a variety of cells involved in immune responses.

The present study was undertaken to clarify whether the serum levels of IFNs and TNF-α are correlated to disease activity and therapy in psoriasis. We have examined IFN-τ, IFN-α2, total IFN activity and TNF-α in sera from patients with different clinical types of psoriasis, before and during treatment with cyclosporin, acitretin and Goeckerman regimen.

MATERIAL AND METHODS

The material consisted of 16 patients with stable, plaque-type psoriasis (A0) (age, mean 50.0 years, range 24–85), 22 patients with highly active psoriasis (A1) (age, mean 47.7 years, range 27–76) and 14 patients with acute guttate psoriasis (A2) (age, mean 31.3 years, range 18–49). None of the patients received local nor systemic anti-psoriatic therapy prior to the study. Eigth patients were treated with acitretin 0.5 mg/kg/day and 5 patients with cyclosporin 3–7 mg/kg/day. Nine patients received Goeckerman therapy (UVB radiation and 3% coal tar ointment) 3–6 times weekly. The serum samples were stored at -20°C until examination. Sera from 106 healthy blood donors (age, mean 36.6 years, range 19–65) were used as normal controls.

IFN-τ, IFN-α2 and TNF were measured using an ELISA method based on MoAbs developed at F.Hoffmann-La Roche Laboratories.

Total IFN activity was detected by an infectivity inhibition micromethod employing human embryonic lung fibroblast cells, in their fifth to fifteenth passage, and vesicular stomatitis virus as the challenge virus (7).

RESULTS

Psoriasis patients had lower serum levels of IFN-τ detected by ELISA than had the controls: median 0.10 ng/ml vs. 0.16 ng/ml ($p = 0.01$). The highest median serum IFN-τ levels were in patients with peripherally spreading psoriasis (A1), 0.10 ng/ml, and lowest in patients with stable, plaque psoriasis (A0), median 0.0 ng/ml. However, the differences between IFN-τ in the psoriasis groups were not statistically significant. On the other hand, there were significantly lower serum levels of IFN-τ in psoriasis patient groups A2 and A0 than in the healthy controls (Table I).

The serum IFN-τ levels did not change following therapy with cyclosporin, acitretin (Table II), or Goeckerman regimen (Table III).

The serum levels of IFN-α2 did not differ between the psoriasis (positive 2/33) and control groups (positive 7/34).

Nor was there any difference in serum levels of TNF-α between patients with psoriasis (positive 10/41) and controls (positive 7/40) (Table IV).

The serum levels of IFN-α2 and TNF-α did not change following therapy with the cyclosporin, acitretin and Goeckerman (Table IV).

Total IFN activity in serum increased following therapy with cyclosporin, acitretin and Goeckerman (Table IV). However, the number of sera tested was low and the increase was not statistically significant.

Table I. *Serum IFN-τ levels in patients with psoriasis*

Disease activity	No. of samples	IFN-τ (ng/ml)		
		Median	Mean±SD	Range
A2	14	0.09[a]	0.12±0.14	0–0.40
A1	22	0.10	0.44±0.75	0–2.90
A0	16	0.00[b]	0.05±0.09	0–0.30
Psoriasis total	52	0.10[c]	0.23±0.52	0–2.90
Controls	106	0.16	0.30±0.43	0–2.50

Statistically significant difference from controls at [a]$p = 0.01$, [b]$p = 0.0003$, [c]$p = 0.002$ using Mann-Whitney's test.

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Table II. *Acitretin therapy: Serum IFN-τ levels*

Weeks treated	Patients' initials							
	OL	HS	KH	GK	OV	RJ	AS	LB
Before	0.15	0	0	0.50	0	0	0.10	0
2	0.00	0	0	0.60	0		0.10	0
4	0.15	0	0	0.45	0	0	0.10	0
6	0.20	0	0	0.50	0	0	0.10	0
8	0.15	0	0	0.50		0	0	0
10	0.15	0	0	0.50				0
12	0.20	0	0					0
14	0.15	0	0	0.60				

Table III. *Goeckerman therapy: Serum IFN-τ levels*

Treatment no.	Patients' initials							
	DR	MN	AR	AT	MN	SS	HL	MK
Before	0.40	0.65	0.10	0	0	0	0.50	0
5	0.40	0.60	0.30	0	0	0	0.45	0
10	0.40	0.80	0.30	0	0	0	0.50	0
15	0.50	0.50	0.30	0	0	0	0.50	0
20	0.40	0.50	0.30		1.00	0.10		
25	0.50	0.50	0.30		0.10	0.10		
30			0.60		0	0.10		

DISCUSSION

In the present study the serum IFN-τ levels were higher in patients with the most active psoriasis than in patients with stable plaque psoriasis. However, the difference was not statistically significant. Taken together, the psoriasis patients had significantly lower serum IFN-τ levels than the healthy controls. There were no detectable differences in serum levels of IFN-α2 and TNF-α between the three psoriasis groups, nor compared with the controls.

IFN-τ produced by infiltrating activated T lymphocytes would induce KC in the psoriatic lesion to express HLA-DR antigens and intercellular adhesion molecule 1 (ICAM-1). TNF-α induces ICAM-1, but not HLA-DR. In psoriatic lesions the ICAM-1 expression (8) is more pronounced than the often weak HLA-DR expression (3,8). The reason might be that the infiltrating immune cells produce more TNF-α than IFN-τ. However, Takematsu et al. (9) reported the absence of TNF-α in suction blister fluids and stratum corneum from patients with psoriasis. On the other hand, there are data indicating production of IFN-τ in psoriatic lesions. IFN can be detected in suction blister fluid from psoriatic lesions (4) and in situ by staining with anti-IFN MoAbs (10). The normal TNF-α serum levels in patients with psoriasis contrast with the elevated levels we recently found in patients with systemic sclerosis (11).

Ultraviolet irradiation is a potent inducer of cytokine release from epidermal cells (12). The results were consistent with an increase in total IFN activity in serum in most patients following Goeckerman therapy, similar to what we have found earlier in sera and suction blister fluids (13). Diezel et al. (14) reported increased IFN activity after PUVA therapy. Measured by the infectivity inhibition method, we found an apparent increase in the anti-viral activity also after cyclosporin and acitretin treatment. There was no change in serum levels of IFN-τ, IFN-α2 and TNF-α measured by ELISA during therapy with Goeckerman regimen, acitretin, or cyclosporin. Konnikov et al. (15) reported elevated levels of plasma interleukin-1 (IL-1) in patients with psoriasis following UVB therapy for psoriasis, while Kowalzick et al. (16) found no change in serum levels of soluble IL-2 during PUVA therapy.

There are several possible explanations for the differing IFN results obtained with the infectivity inhibition method and the immunological assay. First, there may be other IFNs not detected by the ELISA: IFN-α subtypes, including acid-labile IFN-α and IFN-β. We have previously concluded that there are elevated levels of acid-labile IFN-α in sera from patients with psoriasis (17). Second, IFN-antibodies are inhibitors in the ELISA, but not in the virological IFN assay. Third, keratinocytes produce a variety of cytokines. Among these, IL-6 (IFN-β2) have a slight anti-viral activity such that we cannot exclude interference with the infectivity inhibition assay for IFN activity (18).

Table IV. *Effect of treatments for psoriasis on IFN and TNF. No. of positive sera*

No. pats treated	Treatment with		
	Goeckerman 9	Acitretin 8	Cyclosporin 5
Total IFN			
before	2	1	2
after	5	4	3
IFN-α2			
before	0	0	2
after	0	0	3
TNF-α			
before	1	1	2
after	1	1	2

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REFERENCES

1. Bjerke JR, Krogh HK, Matre R. Characterization of mononuclear cell infiltrates in psoriatic lesions. J Invest Dermatol 1978; 71: 340–343.
2. Bjerke JR. Subpopulations of mononuclear cells in lesions of psoriasis, lichen planus and discoid lupus erythematosus studied using monoclonal antibodies. Acta Derm Venereol (Stockh) 1982; 62: 93–100.
3. Bjerke JR, Matre R. Demonstration of Ia-like antigens on T-lymphocytes in lesions of psoriasis, lichen planus and discoid lupus erythematosus. Acta Derm Venereol (Stockh) 1983; 63: 103–107.

4. Bjerke JR, Livden JK, Degré M, Matre R. Interferon in suction blister fluid psoriatic lesions. Br J Dermatol 1983; 108: 295–259.
5. Männel DN, Moore RN, Mergenhagen SE. Macrophages as a source of tumoricidal activity (tumor-necrotizing factor). Infect Immunol 1980; 30: 523–530.
6. Sauder DN, Wang D, Mackenzie R, et al. The pluripotent keratinocyte: Molecular characterization of epidermal cytokines. J Invest Dermatol 1988; 90: 605 (Ab).
7. Dahl H, Degré M. A micro assay for mouse and human interferon. Acta Path Microbiol Scand [B]. 1972; 80: 863–870.
8. Griffiths CE, Voorhees JJ, Nickoloff BJ. Characterization of intercellular adhesion molecule-1 and HLA-DR expression in normal and inflamed skin: modulation by recombinant gamma interferon and tumour necrosis factor. J Am Acad Dermatol 1989; 20: 617–629.
9. Takematsu H, Ohta H, Tagami H. Absence of tumor necrosis factor-α in suction blister fluids and stratum corneum from patients with psoriasis. Arch Dermatol Res 1989; 281: 398–400.
10. Livden JK, Nilsen R, Bjerke JR, Matre R. In situ localization of interferons in psoriatic lesions. Arch Dermatol Res 1989; 281: 392–397.
11. Bjerke JR, Tigalonova M, Gallati H, Degré M, Jablonska S. TNF-α and IFN-α and -τ in sera from patients with scleroderma. Nordic Dermatologic Congress, Reykjavik, June 1993, Abstracts p. 43.
12. Schwarz T, Luger TA. Effect of UV irradiation on epidermal cell cytokine production. J Photochem Photobiol, B: Biology 1989; 4: 1–13.
13. Livden JK, Bjerke JR, Degré M, Matre R. The effect of Goeckerman therapy on interferon in serum and suction blister fluid from patients with psoriasis. Br J Dermatol 1986; 114, 217–225.
14. Diezel W, Waschke SR, Sönnichsen N. Detection of interferon in the sera of patients with psoriasis, and its enhancement by PUVA treatment. Br J Dermatol 1983; 109: 549–552.
15. Konnikov N, Picus SH, Dinarello CA. Elevated plasma interleukin-1 levels in humans following ultraviolet light therapy for psoriasis. J Invest Dermatol 1989; 92: 235–239.
16. Kowalzick L, Köhler I, Meissner K. Influence of PUVA-treatment on serum levels of soluble interleukin-2 receptor in patients with cutaneous T-cell lymphoma (Mycosis fungoides) and psoriasis. Eur J Dermatol 1993; 3: 219–22.
17. Bjerke JR, Haukenes G, Livden JK, Matre R, Degré M. Acid-labile alpha interferon. N Engl J Med 1984; 310: 922–923.
18. Billiau A. Interferon β2 as a promoter of growth and differention of B cells. Immunol Today 1987; 8: 84–87.