Iranian J Publ Health, Vol. 36, No.2, 2007, pp.87-91

Original Articles

Th1/Th2 Cytokines in Psoriasis

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(Received 30 Sep 2006; accepted 10 Apr 2007)

Abstract

Background: The aim of this study was to determine the Th1 and Th2 serum cytokines, in patients with psoriasis and to compare their cytokine levels with those of normal control subjects.
Methods: Serum levels of Interferon-gamma (IFN-γ), Interleukin-2 (IL-2), Interleukin-4 (IL-4), and Interleukin-10 (IL-10) were measured by enzyme linked immunosorbent assay in 40 patients with psoriasis and in 40 normal controls.
Results: Compared with control subjects, patients with psoriasis had elevated levels of IFN-γ and IL-2 (P<0.001). In addition a positive correlation was found between the levels of IFN-γ, IL-2 and disease severity.
Conclusion: Th1 secreting inflammatory cytokines may contribute to the pathogenesis of psoriasis.

Keywords: *Psoriasis, Cytokines, T Cell*

Introduction

Psoriasis is a chronic inflammatory skin disorder, afflicting approximately 2-3% of the world's population, and characterized by altered proliferation and differentiation of keratinocytes (1, 2). Although the exact nature of the triggering agent (s), and the series of events leading to psoriasis are not fully understood, it is well established that genetic, environmental, and immunological factors contribute to the pathogenesis of psoriasis (1-5).

A considerable body of investigation has now verified that the clinical manifestations of psoriasis following T-cell activation and distorted local and systemic cytokine production (6).

Cytokines are potent mediator and communication molecules capable of regulating a broad spectrum of biologic functions, including immune responses (7). Whereas the role of cytokines in the pathogenesis of human diseases is not yet understood, assays for cytokines have become a common feature in research and medical laboratory.

Although there remains some debate (8, 9), a number of investigators are thought that altered balance between T helper type 1 and 2 (Th1 and Th2) cells, may play an imperative role in the pathogenesis of psoriasis (10, 11).

The aim of this study was (i) to determine whether there was a difference in cytokine levels between psoriasis patients and healthy controls, (ii) to evaluate the balance shift in Th1/Th2 cytokines in patients and (iii) assessment the relationship between mentioned cytokines and disease severity.

Materials and Methods

Sera from 40 patients with psoriasis (22 men, 18 women) were collected in dermatology clinics. of Imam Khomeini general hospital affiliated to Tehran University of Medical Sciences. The mean age of the patients in this study was 38.33±14.34 yr (men, 37.09±15.32 yr; women, 39.83±13.32 yr). The patients were diagnosed by consultant dermatologists at a teaching hospital affiliated to Tehran University of Medical Sciences. This popu-

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lation was classified with the following subtypes: guttate (n= 11), plaque (n= 21), erythrodermic (n= 6), and scalp psoriasis (n= 2). Patients were characterized with respect to the presence of associated autoimmune disorders: 33 had no family history of autoimmune disease or any other disorders; 7 had a family history of autoimmune disorder but had no other disease. Autoimmune diseases were alopecia areata (n= 1), vitiligo (n= 2), insulin dependent diabetes mellitus (n= 1) and psoriasis (n= 3). The mean duration of psoriasis was 11.38± 8.48 yr (men 11.73±9.43 yr; women 10.94±7.39 yr). Sera from 40 healthy individuals (22 men, 18 women), with no history of either psoriasis or of any autoimmune disorders such as hashimoto's thyroiditis (HT), graves' disease(GD), insulin-dependent diabetes mellitus (IDDM), vitiligo, psoriasis or alopecia areata(AA) were used as controls. The mean age of the healthy controls was 38.85±11.77 yr (men, 39.64±11.62 yr; women, 38.83±11.63 yr). All sera were kept frozen at -70 ºC until use.

Psoriasis Area and Severity Index A measure of clinical severity of psoriasis is the Psoriasis Area and Severity Index (PASI). This index is evaluated by the quantative assessment of the skin surface area involved, desquamation, induration and erythema of plaques. The PASI scores were calculated by means of the formula as described in the literature (12) and ranges from 0 to 72. The indices of disease severity were accomplished by the same physician.

ELISA The serum concentrations of IL-2, IFN-γ, IL-4 and IL-10 were quantified by ELISA using a commercial kit (Euroclone, Italy) according to manufacturer's guidelines. Assay sensitivities were less than 10 pg/ml for IL-2, 5 pg/ml for IFN-γ, 2 pg/ml for IL-4 and IL-10.

Statistical analysis Statistical difference in two groups was analyzed by Student's *t* test. Correlations between different parameters were calculated by Pearson test. *P*-values lower than 0.05 were considered statistically significant. Data are reported as means±SD.

Results

Forty patients with psoriasis and forty normal controls were included in the study. Serum concentrations of IL-2 and IFN-γ in patients and the healthy controls are summarized in Table1. Statistical analysis of these cytokines showed that there were significant differences among patients and control subjects ($P< 0.001$). The mean values of IL-2 and IFN-γ were 12.88±9.29 pg/ml and 17.50±9.19 pg/ml, for patients and 2.90± 1.92 pg/ml and 6.88±3.91 pg/ml for controls respectively. In contrast there were no significant differences between groups for the levels of IL-10 (Fig.1). IL-4 was not detectable in the serum of any patients and controls.

The Th1 cytokines (IL-2 and IFN-γ) correlated well with each other (r= 0.79, $P<0.001$). A mean value of PASI scores was 6.26±6.23, and there was a significant correlation between disease severity and serum IFN-γ (r= 0.88, $P< 0.001$) and IL-2 (r= 0.52, $P<0.001$) levels. In addition the correlation between the levels of IL-2, IFN-γ and disease severity was analyzed in different categories of patients. It was found out that a significant correlation existed between IFN-γ and disease severity in plaque psoriasis (r= 0.90, $P< 0.001$).

Table 1: The features and laboratory results of patients with psoriasis and controls

	Patients	Controls	Statistical significance
Age (yr)	38.33±14.34	38.85±11.77	NS
Sex (female/male)	22/18	22/18	
Interleukin-2 (pg/ml)	12.88±9.29	2.90±1.92	S
Interferon-γ	17.50±9.19	6.88±3.91	S
Interleukin-10(pg/ml)	0.90±2.56	0.14±0.58	NS

NS=not significant, S=significant

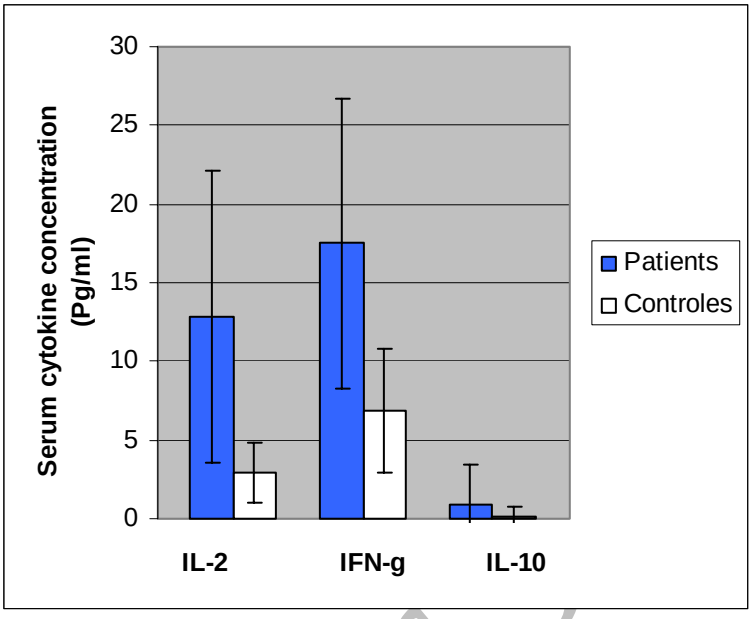

Fig. 1: Serum cytokine levels of psoriatic patients and controls

Discussion

The etiology of psoriasis is not clearly understood and it seems various causative factors implicate in the pathogenesis of disease. At present, a new integrated theory, cytokine network model, is proposed concerning the psoriasis pathophysicology, which incorporate the confederacy of cell types and the great number of mediators (13). In this model, an external or internal stimulus was suggested as triggering of a plethora of cellular events by stimulating a cascade of cytokines.

The cytokines are diverse molecules, having a pivotal role in initiating and coordinating inflammatory and immune reactions. These mediators are produced by different cell types including T cells. In addition, several studies demonstrating that T cells are involved in the disease process (6) and it seems aberrant T-cell involvement in generating the symptoms of psoriasis. As a result, one of the primary questions addressed by researchers was whether a polarized Th1- versus Th2-type cytokine production profile would be valid to psoriasis.

T cell could be divided according to their cytokine profile into Th1 cells, which mainly secrete IFN-γ, IL-2, and TNF-α, and support cellular immunity. In contrast, Th2 cells produce primarily IL-4, IL-5, and IL-10, and responsible for B cell proliferation and production of antibodies (14).

An imbalance between Th1 and Th2 subtypes may lead to the development of different autoimmune disorders such as IDDM, rheumatoid arthritis (RA), HT, and GD. In GD the balance is typically skewed toward expression of Th2 cytokines, and in RA, IDDM, or HT, the balance is deviated toward Th1 cytokines (15-17).

In this study we measured a panel of cytokines in sera of 40 patients with psoriasis and in 40 matched healthy subjects. We found that IFN-γ and IL-2 were increased in the patients compared with controls ($P< 0.001$). In addition there was no significant difference in serum IL-10 levels between patients and control subjects ($P> 0.05$) and IL-4 were not detected in any group. IL-4 may have been present at levels below the detectable range. Moreover, when IFN-γ and IL-2 were compared with disease severity, it showed positive correlation ($P< 0.001$). When a similar comparison was done in different categories of patients, a significant correlation was found between the level of IFN-γ and disease severity

in plaque psoriasis ($P< 0.001$). These results demonstrate reasonable correlation with formerly available data which show elevated concentrations of IFN-γ in psoriatic sera (10, 11).

No significant differences observed between disease severity and the levels of Th1 cytokines in other categories of patients. This could be as a result of small sample size in each group and we suggest the quantification of serum Th1 cytokine levels in a higher number of different subtypes of patients.

The importance of cytokine network has been reported by several investigators (9, 13). Some authors have found high levels of some cytokines in psoriatic patients, where as others have not (18-24). It seems that the pathogenesis of psoriasis is a multistep process, and an array of cytokines has an impressive role in these processes (9). IL-2 and IFN-γ are two important cytokines, which secreted upon Th1 activation. These cytokines activate different signal transducers and augment transcription of a large group of immune related genes and may contribute to the overall pathogenic process (5).

Our data indicated that Th1 cytokines (IL-2 and IFN-γ) were elevated in the sera of psoriatic patients and support the hypothesis that Th1 cells may play a role in the pathogenesis of disease.

Acknowledgements

We are grateful to the psoriasis patients for their generous participation. This work was supported by Tehran University of Medical Sciences, Iran.

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