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Short Communication
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Increased Serum Levels of TNF- A and IL-6 are not Related to HLA-Cw6 in Psoriasis Patients Correlation of Cytokine with HLA Cw6

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Abstract

Psoriasis is a T cell mediated inflammatory skin disease. Complex network of cytokine induces and maintain the psoriatic lesion. Study was performed to evaluate the correlation between the level of TNF- α and IL-6, in the psoriasis patients with HLA-Cw6. Cytokine levels were assayed by sandwich ELISA and HLA-Cw6 typing was done by microcytoxicity method. Serum TNF-α and IL-6 were significantly (p=<0.001 in both) expressed in psoriasis patients. TNF-α had significant positive correlation with IL-6 (p=0.56, p=<0.001). We can conclude that TNF-α and IL-6 are found elevated in serum in psoriasis patients, compared to the control group. Proinflammatory cytokine such as TNF-α and IL-6 may cause inflammatory changes in microenvironment of psoriasis lesion. Gender of patient and age on onset of disease does not influence the expression of these cytokine in psoriasis cases. Results suggest that HLA- Cw6 did not influence these cytokines secretion.

Keywords: Psoriasis, TNF-α, IL-6, HLA-Cw6

Introduction

Psoriasis is characterized by two primary events hyper proliferation of keratinocyte and inflammatory dermal infiltration of mononuclear cells [1]. Previous studies had confirmed that altered T cells regulation along with complex network of cytokines are the main factors for induction and maintenance of various pathological stages of psoriasis [2-4]. Studies also demonstrated that proinflammatory cytokines TNF-α and IL-6 were markedly increased in the serum of psoriasis patients [5-9]. HLA antigen positive and negative individual differ in their ability to produce cytokines [10,11] or cytokines induce the expression of HLA antigen [12]. So present study was performed to evaluate correlation between the level of TNF- α and IL-6, in the psoriasis patients with HLA-Cw6.

Methods and Methods

In total of 60 psoriasis patients and 60 healthy controls were enrolled in this study. Neither patients nor control had present or past history of any skin disease or systemic or present history of infectious disease. Psoriasis patients who had not received any prior local or systemic treatment within three months were included in the study and were in active state of their disease.

About 5 ml of venous blood sample were collected from patients and controls in plain sterilized vials and 5 ml in heparinized vial for HLA-Cw6 typing. Serum sample was stored at -70°C until processed. Serum TNF-α and IL-6 were assayed using sandwich ELISA of Beckman Coulter, France. Typing for HLA-Cw6 antigen was performed by microcytotoxicity method of Terasaki and McCleland as described in detail by Mehra [13]. Antisera used for HLA-Cw6 typing was of BAG Company, Germany. The study was approved by ethical committee of the institution and informed consent was taken from all patients enrolled in the study.

Statistical Analysis

All data was analyzed using SPSS 14.0 (SPSS Inc., Chicago, IL, USA) computer statistics programme. Values were given as mean ± Standard deviation (SD). Student t test used to compare mean, Pearson *Chi-square* used for comparing frequency and Pearson correlation was used to analysis of correlation. p values less than 0.05 were considered significant.

Results

A total of 120 subjects were enrolled in the study comprise of 60 psoriasis patients (median age 35 years) and 60 controls (median age 28 years). In patient group 35 males and 25 females were included and in control group 37 males and 23 females were included. Disease duration ranged from 0.5-30 years with the mean of 6.37 ± 6.35 years and age of onset ranged from 4- 69 years with the mean age of 30.48 ± 9.03 years. HLA-Cw6 was found positive in 20 cases (33.3%) of psoriasis while only six cases (10.0%) in control group. HLA-Cw6 was significantly expressed in patients with psoriasis as compared to control group with p value 0.002.

In controls mean value of serum TNF-α was 7.58±4.19 pg/ml (range 2-15 pg/ml) while in psoriasis TNF-α was markedly increased (29.73 ± 17.31 pg/ml, range 9-74 pg/ml). Rise of TNF-α was highly significant (p<0.001). Similarly serum IL-6 was markedly raised in psoriasis (36.88 ± 26.61 pg/ml, range 5-98 pg/ml) as compared to healthy control (5.56 ± 2.29 pg/ml, range 2-11 pg/ml) which was statically significant (Figures 1 and 2). In patients univariate analysis showed that serum TNF-α correlated significantly with IL-6 (r=0.26, p=0.024). HLA Cw6 showed positive correlation with family history (r=0.35, p=0.003) suggesting that HLA Cw6 was expressed in patients with positive family history psoriasis. No correlation was found among the cytokines and HLA Cw6 (Tables 1 and 2).

Discussion

Cytokines are essential for various pathological changes in the development of psoriasis. Cytokines form a complex and multidimensional network in psoriasis pathobiology, none of which alone can be considered to involve in disease causative mechanism [2].

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They influence keratinocyte proliferation, induce neutrophil and T cell chemotaxis, keep T cells in type 1 differentiation, enhance angiogenesis and upregulate adhesion molecules on endothelial cells, and stimulate the release of other chemokines. We found IL-6 and TNF-α to be elevated in our patient's group than in control group. Elevated serum levels of these cytokines were reported by most of the investigators [14-17]. TNF-α is produced by Langerhans cells, macrophages, monocytes, T cells and keratinocytes [18]. TNF-α is a proinflammatory cytokine and increases proliferation of keretinocytes [19]. TNF-α also induces keratinocyte to produce IL-1, IL-6, IL-8 and adhesion molecules [6,20-22] all of which have proinflammatory properties. Autoantibody against TNF-α had also been reported in psoriasis patients [2]. Anti TNF-α therapy causes regression of the psoriatic lesions [4,19,23]. IL-6 is another proinflammatory cytokine which was included in our study. It is produced by keratinocytes, fibroblasts, endothelial cells and Th2 cells [24]. IL-6 is a major mediator of the host response to injury and infection. Some investigators reported that IL-6 enhances the activation, proliferation and chemotaxis of T lymphocytes in dermal infiltrate and also enhances proliferation and activation of B cells and macrophages [2,24]. Psoriatic keratinocyte are more sensitive to the growth-promoting effect of IL-6 than normal ones [2]. Increased level of IL-6 was also reported in psoriatic skin lesions [25,26]. It is speculated that the koebner phenomenon is likely to result from the increased activity of IL-6 and its receptor in psoriasis [27]. Antipsoriatic therapy including phottherapy, systemic and tropical steroid reduced the increased level of IL-6 [1,25]. Elevated levels of TNF-α and IL-6 in psoriasis patients supports that they may cause inflammatory changes in microenvironment of psortiatic lesions and anti TNF therapy as well as anti-IL-6 therapy may be useful for treatment of psoriasis along with other drugs. TNF-α and IL-6 were positively correlated to each other suggesting that they influence the secretion of each other in psoriasis. Our results showed that TNF-α and IL-6 did not correlate with age of onset of psoriasis, gender, family history and HLA-Cw6. Our study for the first time correlated these parameters with cytokines in patients with psoriasis. Our results suggested that secretion of these cytokines are not age or gender biased. Association of HLA-Cw6 with psoriasis is well established. HLA-Cw6 expressing cells might affect the cytokine milieu in psoriasis and constitute an immune pathway important in psoriasis pathogenesis [28]. No correlation was found between elevated TNF-α and IL-6 with HLA-Cw6 antigen in our study suggests that HLA-Cw6 did not influence these cytokines secretion. Thus our study concludes that HLA-Cw6 may not influence the level of TNF-α and IL-6 in psoriasis patients. There may be some other factor(s) which elevation of these cytokines in psoriasis patients [29].

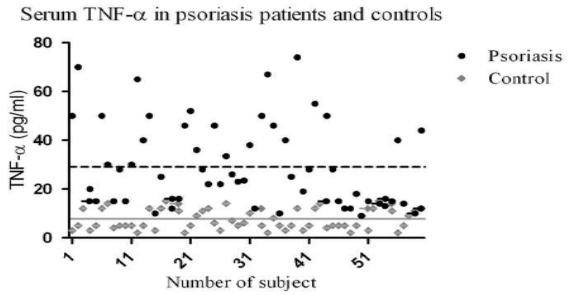

Figure 1: Showing serum TNF-α level in psoriasis patients and controls. Mean of TNF-α in psoriasis group and mean of TNF-α in control group.

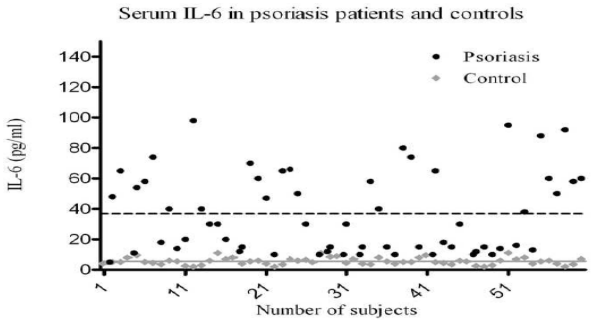

Figure 2: Showing serum IL-6 level in psoriasis patients and controls. Mean of TNF-α in psoriasis group and mean of TNF-α in control group.

Cytokine	Group	Range (pg/ml)	Mean ± SD (pg/ml)	p	CI (95%)	
					Lower	Higher
TNF-α	Psoriasis	9-74	29.75 ± 17.31	<0.001*	16.96	26.07
	Control	2-15	7.58 ± 4.19			
IL-6	Psoriasis	5-98	36.88 ± 26.61	<0.001*	24.50	38.15
	Control	2-11	5.56 ± 2.29			
*- significant (p <0.05)						

Table 1: Serum level of TNF-α and IL-6 in patients of psoriasis and controls.

		TNF α	IL- 6	HLA-Cw6	Age of onset	Gender	Family History
TNF α	r	1	0.26	-0.41	0.05	-0.01	-0.03
	p		0.024*	0.377	0.362	0.467	0.399
IL- 6	r		1	0.11	-0.184	-0.23	-0.14
	p			0.211	0.080	0.042	0.144
HLA-Cw6	r			1	0.05	0.10	0.35
	p				0.356	0.234	0.003*
Age of onset	r				1	-0.004	0.09
	p					0.489	0.247
Gender	r					1	0.015
	p						0.467
*- significant (p <0.05)							

Table 2: Correlation of cytokines with HLA-Cw6, age of onset, gender and family history.

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