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Evaluation of Subpopulation of T Lymphocytes and Expression of P53 on T Lymphocytes in Peripheral Blood of Human Psoriasis

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Abstract: There is a great deal of information suggesting that T cells play a major role in the pathogenesis of psoriasis. Whether the T cells causing psoriasis belong principally to the CD4+ or CD8+ T cell subset is uncertain. P53 as a tumor suppressor gene regulates apoptosis, cell cycle and oncogenesis. To explore the role of p53 and T cell in autoimmune disease like psoriasis, we analyzed the subpopulation of T lymphocytes and p53 expression in peripheral blood in patients with psoriasis and those in the control group. Fifty patients with psoriasis and forty normal controls were enrolled. Peripheral blood samples were obtained from the patients and the normal group. The cell analysis was performed through flow cytometry. A significant decrease was observed in the percentage of the CD4+ and CD8+ T cells in patients in comparison with the controls ($p < 0.05$). P53 expression in lymphocytic gate (total lymphocytes) in the patients was significantly lower than that of the controls ($p < 0.03$). T lymphocytes and p53 appear to be among the most important factors in the pathogenesis of psoriasis.

Key words: Lymphocyte · Psoriasis · P53 · Oncogene Expression · Skin Disease · Tumor Suppressor Protein

INTRODUCTION

The ethiopathogenesis of psoriasis is not fully understood. However, it has become increasingly clear that T cell plays a crucial role in the induction and maintenance of psoriatic lesions [1]. The disease is characterized by epidermal hyper proliferation and inflammation, which lead to the disease [2]. Psoriasis may not be a simple inflammatory skin disease with local T cell activation, but may be a disorder associated with systemic T cell activation [3].

In some studies, the T cell lines isolated and cultured from both psoriatic lesions and from peripheral blood to study their phenotypes. The presence of abnormalities in the peripheral blood lymphocytes of psoriatic patients remains controversial [4].

It is possible that circulating lymphocytes could share some activation markers with skin-infiltrating lymphocytes [4]. Whether the T cells causing psoriasis belong principally to the CD4+ or CD8+ T cell subsets remain controversial.

Despite intense investigation of p53, the physiological and pathological roles of p53 *in vivo* still are not well understood. The first publication to discuss p53 and psoriasis appeared in 1989, when Tadini *et al* reported p53 nuclear expressions in psoriatic skin [5]. P53 is important in cell growth control, DNA repair,

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angiogenesis and apoptosis. Inactivation of this protein (e.g. by mutation) produce an abnormal protein with loss of regulation of cell cycle leading to uncontrolled cell proliferation [6].

It is likely that increased expression of p53 in psoriatic skin is a physiological reaction indicating the attempt to counteract the proliferation and to repair DNA errors [7, 8]. The aim of this study was to analyze the subpopulations of T lymphocytes with p53 expression in peripheral blood in patients with psoriasis and control group.

MATERIALS AND METHODS

This analytic case control study was conducted on fifty patients (male: 36) with plaque type psoriasis and forty normal persons (male: 23) in Tehran from 2010-2011. These patients had received no topical treatment for at least two weeks prior to the study. None of the patients had been exposed to photo chemotherapy or any other systemic antipsoriatic treatment for at least one month. All patients were diagnosed by a dermatologist at Razi university hospital, Tehran, Iran. After collecting peripheral blood samples from the patients and the controls, surface and cytoplasmic staining in each case were performed on fresh cells on the day of sample collection,using combination of fluorescein isothyocyanate conjugated CD4 monoclonal antibody (anti CD4-FITC), phycoerythrin conjugated CD8 monoclonal antibody (anti CD8-RPE), fluorescein isothyocyanate conjugated P53 monoclonal antibody (anti P53-FITC), phycoerythrin conjugated CD4 monoclonal antibody (anti CD4-RPE) and phycoerythrin-CY5 conjugated CD3 monoclonal antibody (anti CD3-RPE,CY5). All of conjugated monoclonal antibodies were obtained from Dako Company (Denmark). The cell surface analysis was performed by means of Becton Dikinson FACScan flow cytometer and events were analyzed by WinMDI software. This study was approved by the Ethics committee of the school of Public Health affiliated to Tehran University and informed written consent was obtained from all the patients.

RESULT AND DISCUSSION

The results are reported as percentage and expression of CD4+ and CD8+ T cells and p53 expression in subpopulation of T lymphocytes. A significant decrease was observed in the percentage of the CD4+ and CD8+ T cells in patients in comparison with the controls ($p < 0.05$) (Table 1). P53 expression in lymphocytic gate (total lymphocytes) in patients was significantly lower than that of the controls ($p < 0.03$). P53 expression also decreased in R2 (T lymphocytic gate) and R3 (CD4+T lymphocytic gate) and R4 (CD8+T lymphocytic gate), but it was statistically insignificant (Table 2). Male patients had significantly lower p53 expression in subpopulation of Tcells (CD4+, CD8+) compared to the controls and the female patients ($p < 0.04$ in CD4+ T cells and $p < 0.01$ in CD8+Tcells), But the tendency of decreased expression of p53 in subpopulation of T cells was statistically insignificant in female patients. CD4-MFI (Mean Fluorescence Intensity) and CD8-MFI decreased in patients in comparison with the controls. P53-MFI also decreased in R1 (total lymphocytic gate) but it was statistically insignificant.

Table 1: Comparison of parameters between psoriatic patients and controls

Variables	Group	Mean	P-value
CD4	Control	53.90	0.05
	Case	49.90	
CD4-MFI*	Control	1217.15	0.01
	Case	952.16	
CD8	Control	43.61	0.02
	Case	37.54	
CD8-MFI	Control	991.28	0.00
	Case	719.76	

*Mean Fluorescence Intensity

Table 2: Comparison of parameters between psoriatic patients and controls

Lymphocyte Gates	Group	Mean	P-value
R1	Control	59.01	0.03
	Case	42.48	
R1-MFI*	Control	654.43	0.52
	Case	582.15	
R2	Control	65.71	0.97
	Case	65.46	
R2-MFI	Control	972.15	0.51
	Case	1081.50	
R3	Control	71.20	0.38
	Case	65.60	
R3-MFI	Control	486.10	0.11
	Case	384.63	
R4	Control	61.87	0.18
	Case	51.18	
R4-MFI	Control	253.00	0.73
	Case	282.37	

* Mean Fluorescence Intensity
R1: P53 expression in lymphocytic gate
R2: P53 expression in T lymphocyte gate
R3: P53 expression in TCD4+lymphocytic gate
R4: P53 expression in TCD8+lymphocytic gate

There is increasing evidences to indicate that T lymphocytes are the central feature of the pathogenesis of psoriasis. Chang *et al*, found that CD8+Tcells are clonally expanded in the psoriatic lesions [9]. Changes in percentage and expression of subpopulation of T cells in peripheral blood patients suggest that systemic activation of immune system. Lecewicz *et al*, showed percentage of the CD4+Tcells and CD8+Tcells have decreased in peripheral blood of the psoriatic patients in comparison with the controls [10]. And also in our study, CD4+Tcells and CD8+Tcells percentage decreased significantly in patients in comparison with the controls which be either due to decrease of production or transmission of these cells from the blood to the skin and higher rate of apoptosis. It might also be owing to a deficiency in T-regulatory cells in the peripheral blood.

The P53 gene is expressed in response to infiltration and genotoxic stimulation as a protective mechanism to induce cell cycle arrest and apoptosis. Continued oxidative stress can eventually cause mutation in various genes, including P53, which supports cell for survival. Yamanishi Y *et al*, showed suppression of P53 function in human synoviocytes increases proliferation and invasiveness and mutant cells that arise in the RA joint could contribute to increased cytokine production [11].

P53 also play important roles in inflammatory disorders and many studies indicate that P53 gene mutation may exacerbate arthritis by enhancing the production of inflammatory cytokines [12]. P53 mediated gene repression in inflammatory cells plays a decisive role in the development of autoimmune diseases. P53 dysfunction causing the enhancement of the autoimmune response (Rheumathoid Arthritis, Multiple Scleoris…). Our study revealed a decrease P53 expression in peripheral blood lymphocytes in the patients. The abnormal P53 expression can disturb cell cycle regulation leading to abnormal proliferation of auto reactive lymphocytes that perpetuate the inflammatory response [12]. We wonder why male patients in our study had lower expression of P53 than female ones.

The present study also confirms the importance of T lymphocyte and P53 expression in pathogenesis of psoriasis and provides selective immunotherapeutic intervention in this disease.

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