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The Problem of Anti-Cytokine Therapy in Psoriasis Patients

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Abstract

All forms of psoriasis show an increase in the presence of certain cytokines, including, IL-2, IL-6, IL-8 and TNF-alpha, with the last one revealing direct participation in the pathogenesis of dermatosis as modern biological therapeutic agents act directly on the activation of this cytokine. A study of the cytokine profile shows Th1-type immune response in the psoriasis patients, the severity of which depends upon the clinical form of the dermatosis. In this study, 104 patients with psoriasis were treated using the immunomodulating preparation, polyoxidonium, in a complex therapy. In these patients, the regress of the PASI index was noted, which concurred with the normalization of the known parameters of the cytokines, and primarily, with a reduction in the TNF-alpha level, which clearly demonstrated the therapeutic efficacy of polyoxidonium, the preparation used. IJBM 2012; 2(3):201-203.
Key words: *psoriasis, clinical picture, cytokines, treatment.*

Introduction

Psoriasis is one of the common skin diseases occurring all over the world, affecting 1-2% of population, in various countries [1, 2]. Recently, psoriasis has been recognized as being not merely an isolated skin disease but as a specific systemic "psoriatic disease" with predominant skin manifestations. This is confirmed by data on the systemic immune changes that are genetic in nature and the frequent involvement of the locomotor system in the pathological process [1-3].

A disorder of the immune system is one of the main pathogenic chains visible in psoriasis, characterized by the presence of a noted deviation of the cytokine profile of the Th1-type, besides an increase in the level of the interleukins IL-1, IL-2, IL-6, IL-8 and IFN-γ. Also, a rise in the level of the tumor necrosis factor-α plays an important role [4, 5].

The tumor necrosis factor alpha (TNF-α) is the anti-inflammatory cytokine involved in several biological processes. This cytokine is involved in the regulation of cellular and tissue homeostasis by stimulating cell apoptosis. TNF-alpha is the primary mediator of inflammation, responsible for the involvement of the leucocytes into the foci of inflammation, inducing an increase in the expressions of the adhesive molecules on the endotheliocytes and keratinocytes. The TNF-alpha secretion interacts with cells such as the macrophages, T-lymphocytes, neutrophils, and keratinocytes and stimulates their production of TNF-alpha. The high levels of TNF-alpha above their normal limits in the non-affected skin correlating with the index of severity and area of the psoriatic lesions (PASI) is revealed in the psoriatic plaques and synovial fluid of the affected joints. Tissue inflammation is caused by the activation of the pro-inflammatory cytokines, which reflects the effect of TNF-alpha on the formation of psoriatic skin lesions. The discovery of the significant role played by TNF-alpha in the pathogenesis of immuno-inflammatory diseases resulted in the preparation of monoclonal antibodies directed to inhibit this cytokine; however, some complications and insufficient availability of these preparations have arisen, which consequently, limit their use (3, 5-8]. As a result, further development of the currently available immuno-modulating agents with a potential pathogenic effect on the cytokine system in psoriasis patients appears to be gaining great significance.

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Materials and Methods

In this study, 104 psoriasis patients between 20 and 55 years were observed. In light of the focus of this study, the initial examination of the patients included the general clinical methods of investigation, dermatological examination and evaluation of the PASI index, determination of biochemical blood parameters, and evaluation of the cytokine status before and after therapy. The clinical examination included a collection of patient history, including risk factors (bad habits, dietary regimens, familial diseases), and a thorough complex physical investigation.

The patients were divided into the following groups: group I (55 patients) with general psoriasis; group II (28 patients) with the exudative type; group III (21 patients) with the palmoplantar form of psoriasis. The common form of psoriasis was evident by the presence of small- and large-plaque rashes, accompanied by desquamation of various localizations, including the hair part of the head. The exudative form of psoriasis was also characterized by widely-disseminated rashes with the formation of corticated squamules. The latter were more marked on the rashes located in the area of the large skin folds and head hair sites, which were accompanied, as a rule, by subjective sensations, sometimes very intensive. In patients with palmoplantar psoriasis, marked hyperkeratosis and large-laminar desquamation with the formation of deep and painful fissures were noted. In this type of psoriasis, rashes rarely occurred on the other skin sites. In all cases of palmoplantar psoriasis, the nail plates of the hands and plantars were involved in the pathological process, resulting in onychogryphosis, onycholysis and subungual hyperkeratosis. The concentration of cytokines in serum were determined by ELISA method using Human test-system. All of the data was processed according to the statistics method using the software Microsoft Office Excel 2007.

The results of investigation of the cytokine status are presented in Table 1.

The complex therapy employing the pathogenically confirmed immuno-modulating drug (polyoxidonium) in patients with all the clinical forms of psoriasis resulted in a reliable and substantial reduction in the PASI index simultaneously, with significant changes in the parameters of the cytokine status, the dynamics of which are given in Table 2.

A comparison of the parameters of the cytokine levels in the different types of psoriasis revealed that in all patients, despite the clinical signs of dermatosis, a normalization of some of the cytokine levels (IL-2,4,6, and 8) was noted. Incidentally, TNF-α, the cytokine most associated with psoriasis, was also noted to reduce substantially; however, in patients with the exudative type, the parameters before and after treatment significantly exceeded the analog parameter noted in the subjects of the control group: 40.7+ 2.8 pg/ml and 34.5+1.7 pg/ml, respectively, in $p<0.05$.

Discussion

Antipsoriatic agents related to the highly technological biological preparations that have been produced over the recent years, are tumor necrosis factor-α monoclonal antibodies [6,8]. Infliximab appears to be the most clinically studied, which is IgG1 chimeric monoclonal antibody (human protein – 75%, murine – 25%) and international experience has confirmed the clinical effect of Infliximab in a standard dose of 5 mg/kg in the second and sixth week, following maintainance of therapy every eight weeks. Infliximab has a few contraindications, which limit its use; for example, acute infections, tuberculosis, heart failure and others. Presently, other TNF-α inhibitors are gaining recognition, for example, etanercept (adalimumab), containing fully humanized monoclonal antibodies as well as other T-cellular modulators (alefacept, abatacept and others). According to the investigations performed [3,7] biological preparations are necessary in severe forms of psoriasis (psoriatic erythroderma, psoriatic arthritis), while in cases of moderate to severe clinical course and only skin manifestations of dermatosis, the dermatologist must prescribe only preparations with an immuno-modulating

Table 1
Parameters of the cytokine status in the blood serum of patients with the different types of psoriasis

Cytokines (pg/mL) (n=22)	Psoriasis forms			Control
	Vulgaris	Exudative	Palmoplantar	
IL 2	9.7±1.1*	11.1±2.7*	6.1±1.9	5.2±1.1
IL 4	42.2±2.8*	48.9±2.7*	55.1±4.1*	38.1±2.2
IL 6	29.9±1.1*	27.9±3.1*	22.1±2.6*	19.1±2.5
IL 8	66.1±5.3*	77.1±2.5*	58.1±3.5*	42.1±5.2
INF-γ	42.5±2.2*	37.2±5.1*	40.5±4.5*	28.1±3.7
TNF-α	57.1±2.7*	65.2±3.3*	48.1±2.9*	34.5±1.7

Note: *the differences were statistically significant when compared with the indicators of the control: * - $p<0.05$*

Table 2
Dynamics of cytokine status parameters in the patients with various forms of psoriasis

Cytokines (pg/mL)		Psoriasis forms			Control (n=22)
		Vulgaris	Exudative	Palmoplantar	
IL 2	before treatment	9.7±1.1	11.1±2.7	6.1±1.9	5.2±1.1
	after treatment	5.3±0.7*	5.5±0.8*	5.0±0.8	
IL 4	before treatment	42.2±2.8	48.9±2.7	55.1±4.1	38.1±2.2
	after treatment	33.5±1.7*	35.3±1.7*	31.3±2.3*	
IL 6	before treatment	29.9±1.1	27.9±3.1	22.1±2.6	19.1±2.5
	after treatment	21.3± 2.8*	20.3± 1.1*	19.5±1.1*	
IL 8	before treatment	66.1±5.3	77.1±2.5	58.1±3.5	42.1±5.2
	after treatment	42.3±5.5*	51.4±3.8*	43.2±2.3*	
IFN-gamma	before treatment	42.5±2.2	37.2±5.1	40.5±4.5	28.1±3.7
	after treatment	30.7±1.9*	30.5±2.3*	26.3±1.9*	
4/5FNO-alpha	before treatment	57.1±2.7	65.2±3.3	48.1±2.9	34.5±1.7
	after treatment	36.2±1.9*	40.7±2.8*	34.5±5.3*	

Note: * - *significant difference in the parameters before and after treatment in p<0.05*

capacity which will act directly upon the cytokine status, as was demonstrated in the present investigation. Inclusion of the drug polyoxidonium resulted in normalization of the cytokine levels, particularly that of TNF-α, which is a confirmation of the pathogenic basis of the method of treatment developed for the treatment of the different types of psoriasis.

Conclusions

- The significant imbalance in the cytokine production connected with the clinical manifestations of the disease has been demonstrated in patients with psoriasis.
- Inclusion of the immuno-modulating preparation (polyoxidonium) into the complex therapy of psoriasis patients allows a simultaneous increase in the therapeutic efficacy and normalization of the cytokine parameters, including TNF-α in the majority cases.
- Pathogenically confirmed therapy allows a two- to three-fold increase in the period of clinical remission of the psoriatic process.

References

1. Khairutdinov VR, Samtsov AV, Moshkalov AV. The current notions about immune mechanisms of psoriasis development. Vestn Dermatol Venerol 2007; 1:3-6.
2. Elberg E. Psoriasis vulgaris. Tartu1997.
3. Badokin VV. Anticytokine therapy of psoriatic arthritis. Russian Medical Journal 2006; 14(8):605-609.
4. Boniface K, Blom B, Liu YI. From interleukin-23 to T-helper 17 cells differentiation revisited. Immunol Res 2008; 226:132-146.
5. Rousaki-Schulze AV, Koukoukis C, Petinaki E. Evaluation of cytokine serum levels in patients with plaque-type psoriasis. Int J Clin Pharmacol Res 2005; 25(4):169-173.
6. Hohler TA, Kruger A, Schneider PM. TNF-alpha promoter polymorphism is associated with juvenile onset psoriasis and psoriatic arthritis. JInvestDermatol1997; 109(4):562-565.
7. Nishibu A, Oyama N, Nakamura K. Lack of association of TNF-238A and-308A in Japanese patients with psoriasis vulgaris, psoriatic arthritis and generalized pustular psoriasis. J Dermatol Sci 2002; 29 (3):181-184.
8. Qiu S, Zhang J, Liu J. Effect of liangxue huoxue tang on serum of TNF-alpha, IFN-gamma and IL-6 in psoriasis of blood-heat type. J Tradit Clin Med 2005; 25(4):292-295.