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SHORT COMMUNICATION

Comparison of Cytokine Levels in Sera of Patients with Autoimmune Endocrinopathies

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Summary

Autoimmune endocrinopathies can be divided according to the presence of organ specific autoantibodies and according to the clinical manifestations into isolated autoimmune endocrinopathies, autoimmune polyglandular syndromes (APS) and polyglandular activation of autoimmunity (PAA). Many factors take part in the development of the autoimmune disease: predominantly a genetic predisposition, environmental etiologic causes and dysregulation in the microenvironment of the target organ. Until now it is not completely clear, if manifestations of the clinical disease depend primarily upon external factors and the degree of regulation mechanism disorder (e.g. in Th1/Th2 regulation) or upon the different genetic predisposition. In this work we compared the levels of Th1 and Th2 lymphocyte cytokines in peripheral blood in three groups of patients: group A of 30 patients with autoimmune thyroiditis, group B of 25 patients with PAA, and group C of 10 patients with APS type II. From group of Th1 cytokines IL-2 and IFN-γ were detected, whereas from group of Th2 cytokines IL-4 and IL-10 were determined by ELISA kit. We did not find any differences in the concentrations of IL-2, IFN-γ, IL-4 and IL-10 among the groups of patients with autoimmune endocrinopathies.

Key words

Autoimmune thyroiditis • APS type II • Polyglandular activation of autoimmunity • Cytokines

Autoimmune endocrinopathies are organ specific autoimmune diseases. Autoimmune impairment could be targeted not only specifically at a single organ, but it also involves an association of endocrinopathies in autoimmune polyglandular syndromes (APS). APS is divided into 3 types: the APS type I, APS type II and APS type III (Muir *et al.* 1994). In isolated autoimmune endocrinopathies, we found a concomitant presence of autoantibodies against other endocrine glands, which did not exhibit functional impairment. We called this group polyglandular activation of autoimmunity (PAA). In patients with autoimmune thyroiditis, the most frequent finding was the presence of antibodies against the adrenal cortex in combination with antibodies against the ovary (Šterzl *et al.* 1999). Evidence of autoantibodies may precede clinical manifestations of the disease by several years (Moncayo *et al.* 1993). Many factors take part in the development of the autoimmune disease: environmental etiologic causes, dysregulation in the microenvironment of the target organ and a genetic predisposition. The most important genetic factor seems to be the polymorphism of the HLA system

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(Wucherpfennig *et al*. 1995). One of the very important factors is the involvement of Th1/Th2 lymphocyte subpopulations with different, in some cases even contradictory functions concerning the autodestructive part of the T cytotoxic lymphocytes activated by the products (cytokines) of the Th1 lymphocyte subpopulation. This is in contrast to the autoantibody activity mediated by the cytokines of Th2 subpopulation enabling the protection of the target antigen against destruction (Šterzl 1999). It is not clear yet what contributes to the different clinical manifestations of autoimmune endocrinopathies. Until now, it could not be proven if clinical disease manifestations depend primarily on external factors and the degree of regulation mechanism disorder (e.g. in Th1/Th2 regulation) or on a different genetic predisposition. In this study, we compared the groups of autoimmune endocrinopathies according to the levels of Th1 and Th2 lymphocyte cytokines in the peripheral blood. IL-2 and IFN-γ were selected from Th1 lymphocyte cytokines and IL-4 and IL-10 were selected from Th2 lymphocyte cytokines.

We selected three groups from patients of Institute of Endocrinology based on the detection of organ specific autoantibodies: group A of 30 patients with autoimmune thyroiditis, group B of 25 patients with PAA, group C of 10 patients with APS type II. Group D consisted of 9 healthy individuals without any autoimmune disorders. The levels of the cytokines IL-2, INF-γ, IL-4 and IL-10 were determined from patient sera by the ELISA method (Bender MedSystems, Vienna, Austria). For the statistical evaluation of the differences in cytokine levels and their ratios among particular groups, Kruskal Wallis One-way ANOVA on ranks and the Kruskal Wallis multiple comparison Z-value test were used.

Cytokine concentrations of IL-2, INF-γ, IL-4 and IL-10 in particular groups are shown in Table 1. Group D had a significantly higher concentration of IL-4 when compared with groups A, B and C ($p<0.001$). In the Th2/Th1 cytokine ratios, we found a significant difference in the ratio of IL4/IL2, where the ratio was significantly higher in group D when compared with groups B and C ($p<0.05$). We did not find any significant difference among groups A, B and C in either particular cytokines or Th2/Th1 cytokine ratios.

Table 1. Cytokine concentrations (pg/ml) in particular groups of patients

	IL-10			**IL-2**			**IL-4**			**IFN-γ**		
Group	Median	Q_L*	Q_U*	Median	Q_L	Q_U	Median	Q_L	Q_U	Median	Q_L	Q_U
A	0.71	0.08	2.28	3.14	1.34	4.93	0.00	0.00	0.11	0.31	0.08	0.95
B	1.02	0.71	1.65	5.38	1.79	6.72	0.00	0.00	0.00	0.34	0.05	0.86
C	1.34	0.78	2.84	3.14	2.12	5.83	0.00	0.00	0.11	0.20	0.03	0.51
D	0.39	0.00	0.39	4.03	1.79	6.27	0.71	0.57	1.84	0.56	0.27	0.64

**Q_L and Q_U denote lower and upper quartiles, respectively.*

In this work we did not find any differences in the Th1 lymphocyte cytokine (IL-2, IFN-γ) and Th2 lymphocyte cytokine (IL-4, IL-10) concentrations in the peripheral blood among particular groups of patients. Peripheral cytokines probably do not play a role in the different manifestation of autoimmune endocrinopathies. These results indicate that the determination of cytokines in peripheral blood does not provide relevant information; an open question still remains if the local cytokine concentrations could provide this. We are preparing samples of the thyroid gland by *in situ* hybridization – the results are not available yet. Our preliminary results of autoimmune polyglandularity in the region of HLA antigen expression show a possibility of different genetic association in APS type II and PAA (Hrdá *et al*. 2001).

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Reprint requests

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