The production of some cytokines in primary APS-associated glomerulonephritis

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Продукция некоторых цитокинов при первичном АФС-ассоциированном гломерулонефрите

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Abstract: *there was held the clinical and immunological examination of 76 patients with primary nephropathy with APS, and without it. In the I group there were 52 patients with primary nephropathy without APS (control group); In the II group were 24 patients with primary nephropathy combined with APS (main group). The control group consisted of 23 healthy people of comparable age. It was found that in patients with primary nephropathy associated with APS increased production of pro-inflammatory cytokines (IL-1.beta, IFN-gamma), and anti-inflammatory cytokines (IL-4).*

Аннотация: *проведено клинико-иммунологическое обследование 76 больных первичной нефропатией как с АФС, так и без АФС: I группа - 52 больных первичной нефропатией без АФС (группа сравнения); II группа – 24 больных первичной нефропатией в сочетании с АФС (основная группа). Контрольную группу составили 23 практически здоровых человека сопоставимого возраста. Выявлено, что у больных первичной нефропатией, ассоциированной АФС, повышены продукции как провоспалительных (ИЛ-1β, ИФН-γ), так и противовоспалительных цитокинов (ИЛ-4).*

Keywords: *antiphospholipid syndrome (APS), APS-associated nephropathy (APSN), glomerulonephritis, cytokines.*
Ключевые слова: *антифосфолипидный синдром (АФС), АФС-ассоциированная нефропатия (АФСН), гломерулонефрит, цитокины.*

In 1999 year D Nochy et al. published the first clinical and morphological study on renal disease in 16 patients with primary APS, which describe a kind of vascular damage to the kidneys, characteristic of APS, analyzed the morphological characteristics and proposed to name the term "APS-associated nephropathy" (APSN). According to modern concepts, APSN - vaso-occlusive lesion intrarenal vessels (glomerular capillaries, arterioles, arteries) leading to renal ischemia and progressive renal failure due to nephrosclerosis [2, 4, 7, 8, 9, 10].

The violation of immunity with the formation of an autoimmune component is the central pathogenetic link, determining the fact of developing the disease [1, 4, 7, 9, 10]. From this perspective, it was interesting to explore the nature and significance of pathogenetic disturbances cytokine status in patients with primary kidney disease, combined with APS and without it.

We have been studied and and evaluated the pathogenetic significance of cytokine level changes (IL-1β, IL-4, and γ-IFN) in the blood serum of 76 patients with primary nephropathy as the APS, and without APS, which have been divided into two representative groups: the I group - 52 patients with primary nephropathy without APS (control group); the II group - 24 patients with primary nephropathy combined with APS (main group). The control group consisted of 23 practically healthy people of comparable age.

Cytokines were determined in the blood serum of patients by ELISA.

An important thing for characterizing of the state of immunity, including cytokine profile of patients with APSN, is the investigation of the main pro- and anti-inflammatory cytokine, which is carried out via intercellular regulation of organism functions.

Analysis of the cytokine profile in patients with primary nephropathy with APS and without it showed increased production of the basic cytokines of the blood serum - IL-1β, IL-4 and IFN-γ in patients of both groups.

The IL-1β production in healthy individuals ranged from 21 to 32 pg/mL, and the average was 26,6±0,93 pg/ml. Thus, the levels of pro-inflammatory cytokine IL-1β were significantly elevated in patients in both treatment groups ($P<0,001$ and $P<0,001$); and averaged 338,1±3,58 pg/ml - in patients with primary nephropathy without APS and 490,6±23,69 pg/ml - in patients with APSN. The ratio of increase of cytokine concentration relative to control values in patients with primary nephropathy in 12,7 times in patients exceed this figure APSN 18,4 times compared with the control. These data suggest the presence of a certain concentration dependence of IL-1β on the nature of the pathological process, as evidenced by a very high level secretion in both groups, particularly in patients with APSN.

During the investigation of this cytokines' concentration in blood serum of healthy persons, it ranged from 17 to 32 pg/ml and averaged 24,1±0,82 pg/ml. Study of IL-4 production showed its increase in 1,9-2,0 times in patients without nephropathy primary APS (45,7±1,19 pg/ml, $P<0.001$), and patients APSN (48,7±1,45 pg/ml, $P<0,001$) as compared with the control group, indicating to the cytokine network operation failures.

We found that the level of IFN-γ production in healthy individuals is on average 12,2±0,60 pg/ml. In patients with primary nephropathy without APS the concentration of this cytokine is increased in 24,8 times relative to the

control and is 302,5±4,07 pg/ml (P<0.001), while the average value of this indicator in patients with APSN was 365.7±1,67 pg/mL, and 30 times higher than in the control group values (P<0,001), which once again reflects the degree of infringement of IP functions in APSN.

On the basis of detected values of the serum concentrations of these cytokines have been studied factors, showing the state of immunity in healthy individuals studied, patients with primary nephropathy without APS and APSN.

The study found that the rate of IL-1β/IL-4 ratio in healthy individuals is equal to 1,1; in patients with primary nephropathy without APS – 7,4; and in patients with APSN the figure is 10,1. The correlation coefficient against IFN-γ / IL-4, the following results were obtained: Healthy – 0,5; primary nephropathy patients without APS – 6,6 and patients with APSN – 7,5.

As it is seen, when APSN have higher coefficients of correlation of pro- and anti-inflammatory cytokines compared with patients nephropathy primary without APS, which indicates the superiority of the pro-inflammatory cytokines (IL-1β, IFN-γ) on the anti-inflammatory (IL-4), which increased activity It has a weighty significance in immunopathogenetic exposure in APSN.

Thus, cytokine profile of patients with APSN characterized by increased production of both pro-inflammatory (IL-1β, IFN-γ), or anti-inflammatory cytokines (IL-4), indicating that the imbalance in the cytokine network in this disease. The above feature of cytokine production plays a pathogenetic role in the maintenance of the autoimmune process both immunological and clinical manifestations of APSN.

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