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SIGNIFICANCE OF CYTOKINE SPECTRUM AND ITS CHANGES IN PRIMARY AND RECURRENT LARYNGOTRACHEITIS IN CHILDREN

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Abstract
The peculiarity of the immune status in recurrent SLT is manifested by a long-standing selective deficiency of IgA, including in combination with high levels of IgE, decreased phagocytosis indices, and increased concentrations. OSLT in children is characterized by increased levels of B-lymphocytes and hyperproduction of IgA, IgG and IgE, as well as IL-4. The levels of cytokines in the oral secretion, IL1β, TNF-α and IL-4, are dramatically elevated in children with RSLT.

Keywords: Acute stenotic laryngotracheitis, cytokines, children, immunoglobulin

Introduction
The study of the role of cytokines in acute stenotic laryngotracheitis (OSLT) in children is one of the fundamental points for understanding the pathogenesis of viral infections and the nature of virus pathogenicity. For clinical practice it is difficult to overestimate the study of cytokine status because it reflects the individual primary reaction to a viral agent, allows to assess the nature of the course of the process and predict the outcome of the disease in many viral infections, as well as allows to objectively assess the effectiveness of therapy.

Research Objective:
Study of the role of cytokines in the pathogenesis of acute stenotic laryngotracheitis.

Material and Methods:
The study was based on clinical and laboratory examination of 275 children with acute stenotic laryngotracheitis, who were admitted to the City Infectious Diseases Hospital No.3. All examined children were divided into 2 groups according to the forms of acute stenotic laryngotracheitis according to Yu.V. Mitin classification: Group 1 - 122

children with primary stenotic laryngotracheitis, Group 2 - 153 children with recurrent stenotic laryngotracheitis.

All immunological indices, including interferon α and γ: levels of antiviral (α-IFN) and proinflammatory (γ-IFN) interferons in peripheral blood serum were studied by enzyme immunoassay using "Vector-Best" test systems (Novosibirsk, Russia).

To determine the role of cytokine link in the pathogenesis of acute and recurrent course of OSLT in children we determined the level of interferon IFN-α and IFN-γ, the level of IL-4 and the level of proinflammatory cytokines: IL-1β, IL-6. Our data demonstrate a significant dependence of the concentration of proinflammatory cytokines in the blood serum on the form of OSLT. Particularly pronounced abnormalities were noted in children with RSLT. The revealed changes differed significantly from the values obtained in the PSLT group of children.

Thus, while in RSLT the serum TNF-α level in the examined children was significantly elevated (243.5±23.9 pg/ml compared to the control group children - 82.4±7.0 pg/ml, P<0.001), in PSLT there was only a moderate increase in this cytokine (118.7±9.3 pg/ml, P<0.05 compared to control).

Analysis of serum IL-1β levels in children with PSLT revealed an almost 10-fold increase in its level compared to controls, 346.7±36.6 pg/ml versus 35.8±3.9 pg/ml (P<0.001).

Children with PSLT showed more than a 3-fold increase in IL-1β levels compared with controls, 110.4±8.3 pg/ml (P<0.001).

As is known, IFN-γ is produced by activated Th1 cells and NK cells. In our studies, we observed a decreased IFN-γ level compared to the control group of children. Moreover, this decrease was observed in OSLT: in RSLT - 74.3±4.9 pg/ml (P<0.001), in PSLT - 78.5±7.3 pg/ml (P<0.001). The level of INF-γ, meanwhile, was 131.7±11.0 pg/ml in the control group of children. When analyzing the levels of a number of inflammatory cytokines in the serum of children with OSLT compared to controls, we noted a significant significant significant increase in TNFα and IL-1β in RSLT and a moderate increase in their serum levels in PSLT.

Serum levels of IFN-γ in OSLT were significantly lower than in the control group and did not depend on its form.

Studying the serum IL-4 level in children revealed a similar pattern: the highest IL-4 level was found in children with PSLT (15,1±0,63 pg/ml), which was significantly (P<0,001) higher than that in children with PSLT (12,0±0,38 pg/ml).

In contrast to peripheral blood, in a smear taken from the area closest to the center of inflammation the IL-4 level was significantly (P<0.001) higher in children with PSLT (310.0±13.5 pg/ml) than in children with RSLT (76.0±3.6 pg/ml).

We studied the cytokine profile of oral secretions in children with OSLT in projection to the severity and stage of the disease (activation-remission). We analyzed the content of three cytokines - IL-1β, TNFα and IL-4.

In the healthy children group, IL-1β content in saliva was 21.8±1.80 pg/ml. The following results were obtained for the patient groups: Group 2 - 196.0±20.76 pg/ml, Group 1 - 128.0±14.04 pg/ml (for all parameters P<0.001). Differences between groups are significant (P<0.01) В контрольной группе содержание TNFα в слюне составило - 27,3±2,55 пг/мл. По группам больных получены следующие результаты: 2 группа - 95,7±9,16 пг/мл, 1 группа - 54,6±4,56 пг/мл, (для всех показателей P<0,001).

In healthy children, IL-4 content in saliva was 6.2±0.41 pg/ml. The following results were obtained for the groups of patients: Group 2 - 19.5±1.79 pg/ml, Group 1 - 12.7±1.02 pg/ml (for all parameters P<0.001).

The obtained data develop the idea that the state of real homeostasis can be an indicator of distant pathological processes [2, p.104], including allergic inflammation. In the present study, this was evident in the study of the cytokine profile (IL-1β, TNFα and IL-4) of the oral secretion in children with OSLT. It was found that in the acute phase of the disease, the content of all three cytokines increased significantly. The most significant and constant increase was noted for IL-1β. In patients with a severe course the indexes were higher than in moderate and mild forms of the disease; for the latter two groups no significant differences were found. This was observed for all three cytokines. The difference is that mild forms of the disease usually do not cause an increase in serum IL-1α and TNFα.

We found it interesting to perform a correlation study between the concentrations of these cytokines depending on the form of OSLT.

Our correlation analysis revealed a direct relationship between the serum content of IFN-γ and IL-1β. We found that the strength of this relationship has an inverse correlation with the form of OSLT. Thus, while in the control group the correlation coefficient was close to one (r=0.95), in groups 1 and 2, the correlation coefficient values were 0.59 and 0.37, respectively. No significant correlation coefficients between other pairs of cytokine content parameters were obtained in either group.

Conclusions:

Our results show a significant dependence of the concentration of proinflammatory cytokines in the blood serum on the form of OSLD. The results of the study confirm the relationship between the concentrations of IFN-γ and IL-1β, and this relationship

is direct and decreases depending on the form of OSLD, indicating impaired immunoregulatory mechanisms.

Thus, our results indicate impaired metabolic processes and pronounced immunological shifts, which contribute to the development of complications of this disease.

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