The Characteristic of the Immune Status at Hiv-Infected Children with Acute Rhinosinusitis

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ABSTRACT.

The immune status has been studied at 25 HIV-infected of children with ARS. The control group of comparison consisted from 14 practically healthy faces. At a HIV-infected of patients with ARS has revealed deep infringements of the immune status, especially from the T-link of immunity and its subpopulations, and also frustration humoral an immunity link, suppression of proinflammatory cytokine IL-10 and increase proinflammatory IFN-γ. Under the influence of the spent treatment have not revealed certain changes from the immune status at patients. It is possible to ascertain only positive changes of maintenance IL-10 and parallel decrease IFN-γ in dynamics of treatment.

KEY WORDS: *The immune status, a HIV-infection, acute rhinosinusitis, cellular immunity, humoral immunity, an immunodeficiency, cytokines***.**

HIV/AIDS is the retrovirus infection characterized by epidemic distribution of global scale, amazing exclusively T-helpers [1-3].

Last two decades the defining reason of a secondary immunodeficiency (SID) at children beca-me a HIV-infection which pandemic continues to accrue. Defeat of immune system at a HIV-infection has system character, being shown deep suppression T- and B-links of cellular immunity [1, 3, 4].

One of the first symptoms of AIDS quite often are diseases of LOR-organs. Acute rhinosinusi-tis (ARS) often comes to light at children with a HIV-infection, disease of it at children's age fluc-tuates within 60-75%, and lethality makes 0,01-0,2% from the diseased [1, 6,9].

According to a number of authors, at a HIV-infected of children ARS meet more often, than at children normal immune system [1, 4, 5].

Aims *of the study* – To study parameters of the immune system at a HIV-infected of children with ARS.

Material and Methods

We investigated 25 children at the age from to 3 till 14 years of a HIV-infected with ARS, were on hospitalization in LOR-BRANCH of the Bukhara regional children's versatile medical centre. Boys have made 56.6%, girls – 43.4%. Unilateral defeat of sine was observed at 57.8%, bilateral - at 42.2%. Except inflammation signs the general anxiety, a bad dream, refusal of a chest food, headaches was marked. Besides traditional inspection (the general analysis of blood, urine, bacteriological and bio-chemical researches) all patients have passed LOR-survey, under indications - sine sounding (26.5%), X-ray additional bosoms of a nose (9.6%). In the basic group there were 25 HIV-infected with ARS pa-tients, and in a control - almost healthy 14 children of similar age who did not have in anamnesis ARS and a HIV. All 25 HIV-infected children consisted on the account in the Bukhara regional AIDS-cen-tre. Patients received antiretroviral therapy, antibacterial, anti-inflammatory and local therapy in the conditions of a hospital.

The HIV diagnosis was based on revealing of specific antibodies in standard serological tests (ELISA, immune bloating in updating Western-bloat) and comparisons epidemiological and serological data.

Immunologic studies were carried out in conjuction with the the Institute of Immunology NA RUz (Tashkent). In researches included patients from a HIV-infection and ARS which parents have given the informed consent to participation in the given researches (work has been executed according to the Helsinki declaration and it is approved by ethical committee of Bukhara State Medical Institute).

Phenotyping lymphocyte carried out indirect by immune fluorescent method with the help mo-

noclonal antibodies to CDs-receptors «Sorbent Ltd» (Russia). Defined T-lymphocytes (total set - CD3); T-helpers (subset of Th - CD4); T-suppressors (subset of Ts - CD8); B-lymphocytes (subset CD19).

Calculated an immunoregulatory index (IRI) – the ratio of CD4/CD8. Concentration serum antibodies (Ig) A, M and G defined a method of radial immune diffusion[7]. Level cytokines (IFN-γ, IL-10) in whey of peripheral blood was studied a method of the immune enzyme analysis with use of test sys-tems by firms "Vectors-best" (Russia). Parameters of the immune status studied twice: before and 1 month after treatment.

The obtained data was exposed to statistical processing with use of computer program Micro-soft of Excel 2003 on LG-Pentium IV. Significance of differences when comparing the mean values were determined by Student´s ***t*** test. Data are presented as of M ± m. Differences were considered significant at $P<0.05$.

Results of research and their discussion

The retrospective analysis of studying of the immune status at a HIV-infected of children with ARS has shown that in terms before carrying out before treatment at them essential infringements have been revealed from their immune system (tab. 1). At a HIV-infected with ARS patients observed 0.7-fold fall of absolute value of leukocytes and the relative contence lymphocyte, double decrease in the absolute values of lymphocyte. Such decrease was reflected in statistically significant decrease from 2 to 3 times of absolute values of the total pool T (CD3) - and B (CD19)- lymphocyte (tab. 1).

At a HIV-infected patients with ARS children showed profound suppression T-cell immunity in their relative expression, namely, 0.6-fold reduction in T-cells with the phenotype (CD3), even more si-gnificant suppression T-share helpers cells - Th (CD4) – up to 13.8 ± 2.3% (in the control group 34.2 ± 1.6%; $P<0.001$), while the content of subset of T-cells - T (CD8)-cytotoxic exceeded the background va-lues in the control group moderate ($P>0.05$).

In this connection in the given group there is an inversion an immune regulatory index (IRI) – the ratio of CD4/CD8, - that leads to serious changes in immune system of patients with HIV-infec-tion, combined with the ARS. Thus, we find out a disbalance of T-cell subset with a decrease in the proportion of helpers Th(CD4) and increase suppression parts - Ts(CD8) (tab. 1). Reduction IRI regis-tered by us at HIV-infected with ARS children testifies to functional insufficiency of cages with a phe-notype of Ts(CD8), and it is a sign of the profound immunodeficiency which has developed at patients. At a HIV-infected of patients with ARS have revealed small activation of subset of T-killers - Tk (CD16) that, possibly, is also *pathognomonic* at this pathology.

In respect of B-cell component of the immune system can be said that moderate decrease occurred, which was statistically is possible to tell that there was a moderate decrease that statistically confirmed ($P>0.05$). Decrease B(CD19) lymphocytes was reflected in the spectrum of serum

immuno-globulin (SI) content of two classes - IgA and IgG, and quantity IgM, on the contrary, increased (tab. 1).

The data obtained by us testifies to profound infringements in the functioning of the immune sy-stem in children of patients with a HIV-infection and ARS, which were reflected a spectrum cellular and humoral immunity factors. These disorders appear to be quite possible as a fact that plays an important in the pathogenesis of this mixed-pathology in children. The decrease of the relative quantitative propeties of Th(CD4) - this aggravating factor, and an unfavorable forecast criterion.

The spent treatment did not lead to appreciable changes of parameters of immune system at a HIV-infected of children with ARS. We observed a tendency in moderate increase of separate links of cellular immunity and humoral immunity, however restoration of key parameters of the immune status (tab. 1). Besides, at patients with chronic processes saved pressure of the humoral component of sys-tem of immunity remained at P>0.05. In a HIV-infected of patients with ARS have found out weak increase T(CD3) and B(CD19) in their relative and absolute values, and also moderate increase of production of Tk(CD16), Ts(CD8), the concentration of IgA (tab. 1).

Spectrum studying cytokines at a HIV-infected of children with ARS has shown that at them presence *of significant* differences between values of the basic group with control group was marked. So, for example, if at healthy children level IFN-γ made 23.70 ± 5.38 pg/ml, at a HIV-infected of children with ARS the similar parameter was in 3/5 times above and there was at level 82.84 ± 21.17 g/ml (tab. 2). So, high level IFN-γ at a HIV-infected of children with ARS testified to expressiveness of degree of inflammatory reaction.

It is known that as a source IFN-γ serve activated T-lymphocytes and natural killers. Among T-lymphocytes producers IFN-γ are both the cytotoxic Ts (CD8), and Th (CD4) cells, however at a differ-rentiation of the last on Th1 and Th2 ability to develop IFN-γ keep only Th1-cells. The major function IFN-γ is its participation in medium interrelations between lymphocytes and macrophages, and also in regulation of a parity cellular and humoral components of the immune response. Being the basic pro-

duct Th1-клеток, IFN-γ reduces secretor activity Th2-cells. Thus, IFN-γ *enhances* the development of cellular immunity and suppresses displays humoral immunity. Hence, IFN-γ plays an important role in immune regulation, being key by the cytokine cellular immune response and inhibitor of the humoral immune response [8].

Table 1. Parameters of immune system at a HIV-infected of children with ARS in dynamics Of treatment.

Indicator	**Healthy** (n=14)	**Patients** (n=25)
Leukocytes, num./mklt	6123 ± 162	4251 ± 321***
		4437± 234***
Lymphocytes, %	29.6 ± 1.7	21.4 ± 2.15**
		22.7 ± 2.4*
Lymphocytes, abs.	1812.4 ± 35.7	931.5 ± 97.2***
		1003.6 ± 47.5***
T(CD3), %	58.3 ± 2.5	38.4 ± 3.2***
		41.2 ± 2.7***
T(CD3), abs.	1058.2 ± 72.2	362.5 ± 43.6***
		425 ± 51,4***
Th(CD4), %	34.4 ± 1.6	13.8 ± 2.3***
		12.4 ± 2.7***

Ts(CD8), %	22.7 ± 1.2	24.2 ± 2.8
		26.5 ± 3.1
IRI (CD4/CD 8)	1.5 ± 0.14	0.58 ± 0.31**
		0.49 ± 0,36**
Tk(CD16), %	15.4 ± 0.9	16,2 ± 2,5
		18,4 ± 3,2
B(CD19), %	24.3 ± 1.22	19,62 ± 4,4
		22.5 ± 2.6
CD19, abs.	351.6 ± 29.4	182.1 ± 20.5***
		228.7 ± 34.9**
IgA, mg%	129.2 ± 10.8	84.4 ± 7.8**
		101.9 ± 13.6
IgM, mg%	86.7 ± 8.9	140.4 ± 13.1***
		136.3 ± 16.5**
IgG, mg%	1047.3 ± 33.4	888.7 ± 42.7**
		761.4 ± 54.6***
The note: in numerator the data before treatment, in a denominator - after treatment; * - P <0.05; ** - P <0.01; *** - P <0.001 - in comparison with control group.		

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Table 2. The maintenance pro- and anti-inflammatory cytokines at HIV-infected of children in a combination with ARS in dynamics of treatment.

Indicator	Control group	The basic group
IFN-γ, pg/ml	23.70 ± 5,38	82.84 ± 21.17**
		21.93 ± 7.42
IL-10, pg/ml	10.95 ± 3.63	86.08 ± 19.43***
		52.04 ± 12.06**
The note: in numerator the data before treatment, in a denominator - after treatment; * - P <0.05; ** - P <0.01; *** - P <0.001 - in comparison with control group.		

Level IL-10 in group at a HIV-infected of children with ARS approximately in 8 times *higher* than those values of the control group. It is known that IL-10 it is described as the factor stimulating B-lymphocytes as it causes proliferation B-cells. The main producers IL-10 are Th2 cells. IL-10 inhibits functions of macrophages and secretion by them IL-1, FNO and IL-6, having thus anti-inflammatory an effect. IL-10 causes proliferation and a differentiation B - and T-lymphocytes, influences development hematopoietic cells, on macrophages, natural killers, basophiles, being the functional antagonist cyto-kines, produced Th1 cells. IL-10 promotes development of allergic reactions, possesses the expressed anti-inflammatory action [8].

The comparative analysis has shown that the parity IFN-γ/IL-10 (proinflammatory/anti-inflammatory cytokines or Th1/Th2) at healthy children equaled 2.2. In the presence of the expressed inflammatory process, that is at children of the basic group, this indicator made 0.96. The expressed disbalance in functioning of the core regulator cytokines which was expressed by acute lifting of level anti-inflammatory cytokines and suppression proinflammatory cytokines, acute inflammatory condi-tions being the basic regulators is revealed.

Thus, the HIV-infected of children with ARS have an expressed stimulation of production both proinflammatory, and anti-inflammatory cytokines. Such processes can as a necessary condition for

protection against the infectious agent and system damaging action of high concentration proinflammatory cytokines [8].

After treatment carrying out in group of a HIV-infected of children with ARS level IFN-γ has come nearer to control values, and level IL-10 in dynamics of treatment if decreased, but nevertheless remained at high level, in 5.5 exceeding those parameters at children of control group.

The parity IFN-γ/IL-10 in the basic group tended to even bigger to decrease, making 0.42.

Thus, at a HIV-infected of children with ARS deep deficiency of most of the parameters of the immune status is observed. One of the major disorders of the immune status is a significant suppression of Th (CD4)-lymphocytes and inversion of the IRI with an increase in functional activity of Ts (CD8)-lymphocytes, which is unfavorable clinical criteria. The given patients did not have positive dy-namics of changes of the immune status after treatment carrying out. Under the influence of treatment there was a suppression proinflammatory of cytokine IFN-γ. However, it should highlight that the dete-cted change in the level of IL-10 and a violation of the proportion of pro- and anti-inflammatory cyto-kines indicates the presence of preexisting immune deficiency, which, apparently, and was manifes- ted in the form of complications associated with HIVinfection.

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