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Immune Status of HIV – Positive Children with Acute Rhinosinusitis

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ABSTRACT

The immune status of 25 HIV-positive children with Acute Rhinosinusitis (ARS) has been studied in comparison with the control group of 14 practically healthy children of the same age. HIV-infected patients with ARS have shown deep infringements of the immune status, especially of T-cells and its subpopulations, and impairments of the humoral immunity, suppression of anti-inflammatory cytokine IL-10 and increase of pro-inflammatory IFN-γ. After conducted treatment we have not seen any certain changes of the immune status in HIV positive patients, even in the cases with clinical improvement. It is possible to ascertain only positive changes of IL-10 maintenance and parallel decrease of IFN-γ in the dynamics of treatment.

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1. INTRODUCTION

HIV is a retroviral infection characterized by epidemic distribution at the global scale, affecting exceptionally T-helpers [1]-[3].In the last two decades the defining reason of a secondary immunodeficiency (SID) on children became a HIV-infection, this pandemic continues to accrue. Defeat of immune system at a HIV-infection has system character, appearing as deep suppression in T- and B-links of cellular immunity [1];[3];[4]. One of the first symptoms of AIDS is quite often availability of diseases of ENT organs. Acute rhinosinusitis (ARS) is often revealed at children with a HIV-infection, incidence rate of it in children's age fluctuates within 60-75%, and lethality makes 0,01-0,2% of the sick [1];[6]. According to the data of a number of authors, ARS is met more often at HIV-infected children than at children who have normal immune system [1];[4];[5].

The aim *of the current research is* to identify parameters of the immune system in HIV-infected children with ARS.

2. RESEARCH METHOD

We examined 25 HIV- positive children at the age from 3 till 14 years with ARS, who were hospitalized in the otolaryngology department of the Bukhara Regional Children's Multi-profile Medical Center. Boys have made 56.6%, girls – 43.4%. Unilateral defeat of sine was observed in 57.8%, bilateral - in 42.2% of patients. Besides the inflammatory symptoms, children suffered anxiety, insomnia, refusal of a breast feeding and headaches. Clinical examination tests were conducted (the blood formula, urine test) and

bacteriological and biochemical tests as well, all patients also passed ENT-examination, under indications - sine sounding (26.5%), X-ray of additional bosoms of a nose (9.6%).

In the study group there were 25 HIV-positive pediatric patients with ARS, and in the control group there were – 14 healthy children of similar age who did not have ARS and HIV in anamnesis. All 25 HIV-infected children were enrolled in the Bukhara Regional AIDS-Center. The patients received antiretroviral therapy, antibacterial, anti-inflammatory and local therapy in the inpatient department.

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

While having carried out the immunologic studies we were affiliated with the Institute of Immunology at Science Academy of Uzbek Republic (Tashkent). Patients with a HIV-infection and ARS were included whose parents had given the informed consent to participate in the study (the work had been executed according to the Helsinki Declaration and it is approved by ethical committee of Bukhara State Medical Institute).

Phenotyping of lymphocytes were carried out by indirect immune fluorescent method with the help of monoclonal antibodies to CD-receptors made by «Sorbent Ltd» (Russia). T-lymphocytes (total set - CD3); T-helpers (subset of Th - CD4); T-suppressors (subset of Ts - CD8); B-lymphocytes (subset CD19) were defined. The immune regulatory index (IRI) – the ratio of CD4/CD8 was calculated.

Concentration of serum antibodies (Ig) A, M and G was defined by the method of radial immune diffusion [7].

Level of cytokines (IFN-γ, IL-10) in the serum of peripheral blood was studied by the method of the immune enzyme analysis using the test systems of the firm "Vector-Best" (Russia).

Parameters of the immune status were studied twice: before and one month after treatment. We proceed an obtained data in Microsoft Excel 2003 on LG-Pentium IV. Reliability of differences in comparing of the means was determined by Student´s t test. Data was presented in the form M ± m. Differences were considered reliable at $p<0.05$.

3. RESULTS AND ANALYSIS

The retrospective analysis of studying of the immune status of HIV-infected children with ARS has shown that before the treatment essential infringements have been revealed in their immune system (tab. 1).

HIV-positive pediatric patients with ARS had shown a 0.7-fold fall of absolute quantity of leukocytes and the relative content of lymphocytes, double decrease in the absolute size of lymphocytes. Such decrease was reflected in statistically reliable decrease from 2 to 3 times of absolute values of the total pool T (CD3) - and B (CD19)- lymphocytes (tab. 1).

Our patients had profound suppression of T-cell immunity in their relative expression, namely, 0.6-fold reduction in T-cells with the phenotype (CD3), some more marked suppression of T-cell helpers - 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 lymphocytes exceeded the background essence in the control group in moderate level ($P>0.05$).

Due to it in the given group an inversion of an immune regulatory index (IRI) occurs – the ratio of CD4/CD8 that leads to serious changes in immune system of patients with HIV-infection combined with the ARS. Thus, we found a misbalance of T-cell subset with a decrease in the proportion of their helpers' portion Th (CD4) and increasing of suppression parts - Ts(CD8) (tab. 1). IRI reduction being registered by us at HIV-infected with ARS children testifies to functional insufficiency of cells with a phenotype Th(CD8), and it is a sign of the profound immunodeficiency which has developed at patients. At HIV-infected patients with ARS we revealed a slight activation of subset of T-killers - Tk (CD16) that, possibly, is also *pathognomonic* at this pathology.

Concerning to B-cell component of the immune system it can be said that moderate decrease occurred, which was not statistically confirmed ($P>0.05$). Decrease of B(CD19) lymphocytes was reflected in the spectrum of serum immunoglobulin (IC) content of two classes - IgA and IgG, and quantity of IgM, on the contrary, increased (tab. 1).

The study data has revealed profound infringements in the functioning of the immune system of children with a HIV-infection and ARS, which were reflected on a spectrum of cellular and humoral immunity factors. Decrease of the relative quantity of Th(CD4) - is an aggravating factor, and an unfavorable prognostic criterion.

The conducted treatment did not lead to appreciable changes of parameters of immune system of HIV-infected children with ARS. We observed a tendency in moderate increase of separate links of cellular immunity and humoral immunity, however, recovery of basic parameters of the immune status has occurred

(tab. 1). Besides, patients with chronic processes pressure of the humoral component of immunity system remained at P>0.05. In HIV-infected patients with ARS we observed a slight increase of 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).

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

It is known that activated T-lymphocytes and natural killers serve as a source of IFN-γ. Among T-lymphocytes producers of IFN-γ are both: the cytotoxic Ts (CD8), and Th (CD4) cells, however, while differentiation of the last to Th1 and Th2 only Th1-cells keep the ability to develop IFN-γ. The major function of IFN-γ is its participation in medium interrelations between lymphocytes and macrophages, and also in regulation of correlation of cellular and humoral components of the immune response. Being the basic product of Th1-cells, IFN-γ reduces secretor activity of Th2-cells. Thus, IFN-γ *enhances* the development of cellular immunity and suppresses display of humoral immunity. Hence, IFN-γ plays an important role in immune regulation, being key cytokine cellular immune response and inhibitor of the humoral immune response [8].

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

Indicator	The Sound (n=14)	Patients (n=25)
Leukocytes, kl/mkl	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.

Table 2. Pro- and anti-inflammatory cytokines at HIV-infected children in combination with ARS in dynamics of treatment

Indicator	Control group	The basic group
IFN-γ, pg/ml	23.70 ± 5,3	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 of IL-10 in group at HIV-infected children with ARS approximately in 8 times is *higher* than those values of the control group. It is known that IL-10 is described as the factor stimulating B-lymphocytes as it causes proliferation of B-cells. The main producers of IL-10 are Th2-cells. IL-10 inhibits functions of macrophages and IL-1, FNO and IL-6secretion by them, having thus anti-inflammatory effect. IL-10 causes

proliferation and differentiation of B- and T-lymphocytes, influences on the development of hematopoietic cells, macrophages, natural killers, basophiles, being the functional antagonist of cytokines, produced by Th1-cells. IL-10 promotes the development of allergic reactions, possesses the expressed anti-inflammatory action [8].

The comparative analysis has shown that the correlation between IFN-γ/IL-10 (pro-inflammatory/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 composed 0.96. The expressed disbalance is revealed in the functioning of the core regulatory cytokines which was expressed by acute lifting of the level of anti-inflammatory cytokines and suppression of pro-inflammatory cytokines, which are the basic regulators of acute inflammatory states.

Thus, the HIV-infected children with ARS have an expressed stimulation of production both pro-inflammatory, and anti-inflammatory cytokines. Such processes could be as a necessary condition for protection against the infectious agent and system damaging action of high concentrations of pro-inflammatory cytokines [8].

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

Correlation between IFN-γ/IL-10 in the basic group tended to even more decrease, composing 0.42.

4. CONCLUSION

Thus, in HIV-infected children with ARS a deep deficiency of main parameters of the immune status was observed. One of the major disorders of the immune status was a significant suppression of Th(CD4)-lymphocytes and inversion of the IRI with an increase of functional activity of Ts (CD8)-lymphocytes, which is an unfavorable clinical criterion. The given patients did not had a positive dynamics of changes of the immune status after conducting the treatment. Under the influence of treatment there occurred a suppression of pro-inflammatory IFN-γ cytokine. However, it should be highlighted that the detected change in the level of IL-10 and a violation of the proportion of pro- and anti-inflammatory cytokines indicates the presence of preexisting of immune deficiency condition, which, and apparently, was manifested in the form of complications on the background of HIV infection.

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