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.

Keywords: The immune status, a HIV-infection, acute rhinosinusitis, cellular immunity, hu-moral immunity, an immunodeficiency, cytokines.

1. INTRODUCTION:

The defeat of the immune system with HIV infection is systemic character, manifesting by deep supremacy of T and B-links of cellular immunity. During the development of this infection, natural changes in the hypersensitivity of immediate and slow motion, humoral immunity and factors of nonspecific protection, functional activity of lymphocytes and monocytes are taken (1,8).

In the last two decades, the determining cause of secondary immunodeficiency in children has been HIV infection, the pandemic of which continues to grow. HIV / AIDS is a kind of viral infection, the first in the history of medicine acquired immunodeficiency associated with a specific causative agent and a characteristic epidemic race-space. The first epidemic human disease caused by retroviruses, which exclusively amaze the T-helpers. The problem of infection caused by the human immunodeficiency virus (HIV infection), in otorolanryngology in our country has been studied since the early 90's(11).

The diseases that are the indicator of the acquired immunodeficiency syndrome (AIDS) are studied and described, the symptomatology of the ear, throat and nose in AIDS and HIV-infected patients were studied. In connection with the significant increase in the number of HIV-infection, the probability of contact of the idolo-amrologist with HIV-infected patients increases. At HIV infection, there are often rapid manifestations of the disease with the defeat of ENT bodies. Otorinolary-logs, as, however, other specialists already have to take an active part in the diagnosis, treatment of HIV-infected patients, preventive work, which will certainly require knowledge of the features of the pathology of the ear, throat and nose in HIV infection (AIDS). The diversity of clinical manifestations of HIV infection is due to the accession of opportunistic infections, among which the fungal, bacterial and viral infections are most important. The classical manifestation of HIV infection, with which the otorolagologist may face, is the development of acute rinosinusite (9,10).

HIV/AIDS is the retrovirus infection characterized by epidemic distribution of global scale, amazing exclusively T-helpers (2, 3, 4).

Last two decades the defining reason of a secondary immunodeficiency (SID) at children became 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. One of the first symptoms of AIDS quite often are diseases of ENT-organs. Acute rhino sinusitis (ARS) often comes to light at children with a HIV-infection, disease of it at children's age fluctuates within 60-75 %, and lethality makes 0,01-0,2 % from the diseased (5,8).

According to a number of authors, at a HIV-infected of children ARS meet more often, than at children normal immune system. One of serious complications ARS at a HIV-infected of children of infantile age is brain defeat. Thus the risk of development minengoencephalopathical the complications leading to a failure of the basic disease sharply increases(7).

In connection with the aforesaid in medicine questions of studying of immune system at children with ARS and a HIV are actual. Classical display of a HIV-infection which can face to the otolaryngologist is development ARS against a HIV. It had been dictated necessity of the present researsh (6).

Researsh objective – To study parameters of the immune system at a HIV-infected of children with acute rhinosinusitis .

2. 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 ENT -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 ENT -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 patients, 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-centre. 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 monoclonal antibodies to CD+s-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 systems 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 $P<0.05$.

3. 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 im-portant in the pathogenesis of this mixed-pathology in children. The decrease of the relative quanti-tative 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 .

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.		

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 proinflam-matory 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.

4. CONCLUSION.

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 dynamics 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 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 immune deficiency, which, apparently, and was manifested in the form of complications associated with HIVinfection.

5. REFERENCES

[1] Bessarab T.P .Aspects of a HIV-infection and AIDS in otolaryngology. //The Attending Physician. - 2014. - № 1. - P. 26-30.
[2] Bessarab T.P, Jushuk N.D, Anjutin R.G, et all. A HIV-infection in otolaryngological practice. //The Attending Physician. - 2015. - № 3. – P. 12-7.
[3] The defeat of the LOR-organs of HIV infection in children. // Medical portal EUROLAB. / C. 1-4.
[4] Rakhmanova A.G. Pediatric aspects of HIV infection. Preventing HIV infection in newborns. SPb. : Institute of Epidemiology and mikrobiology nm. Pasteur, 2012. - 80 p.
[5] Mofenson L.M, Korelitz J, Pelton S, et all. Sinusitis in children infected with human immu-nodeficiency virus: clinical characteristics, risk factors, and prophylaxis. Clin. Infect. Dis. 21 (2015), 1175-81.
[6] Chen A.Y, Ohlms L.A, Stewart M.G & Kline MW Otolaryngologic disease progression in children with human immunodeficiency virus infection. Arch. Otolaryngol. Head Neck Surg. 122 (2016), 1360–3.
[7] Mancini G., Carbonara A.O., Heremans J.F. Immunochemical quantitation of antigens by single ra-dial immunodiffusion. Immunochemistry, 2013; 2: 235-54.
[8] Simbirtsev A.S. Cytokines - a new system of regulation of defense reactions. //Cytokines and inflam-mation. - 2012. - № 1. - P. 9-17.
[9] Narzullaev N.U. FarGALS efficiency in complex treatment of HIV-infected children with acute purulent sinusitis//European Science Review. - Austria, 2017. - No.1-2. - pp.86-88.
[10] 10 Narzullaev N.U. The Incidence of exudative otitis media in HIV-infected children//International Journal BIOMEDICINE (IJBM) USA. – 2012. -No.1. -pp.211-213.
[11] Narzullaev N.U. Immune Status of HIV-positive Children with Acute Rhinosinusitis//International Journal of Public Health Science (IJPHS) USA. – 2013. - Vol. 2, No.3. - pp. 83-88.