International Journal of Psychosocial Rehabilitation, Vol. 24, Special Issue 1, 2020
ISSN: 1475-7192

Pathogenetic Value of Cytokine Production in HIV Infection

[1]Allabergen Bayjdanov, [2]Sokhiba Utegenova

Abstract--*Against the background of the progression of HIV infection, there is an imbalance in the production of cytokines, characterized by the switching of the TV-1 response to TV-2. As the disease progresses, the prevalence of anti-inflammatory cytokines produced by Th-2 cells is observed, which shows the aggravation of immunosuppression and the development of opportunistic diseases. It was revealed that IL-2, IL-4 and IL-10 might have a multidirectional action depending on local conditions. Thus, cytokines can serve as markers for predicting the progression of HIV infection.*

Keywords--*cytokines, interleukin-2, interleukin-10, HIV infection, CD4+ lymphocytes.*

I. INTRODUCTION

HIV infection, in addition to damaging the T-cell immunity link and polyclonal activation of the immunity humoral link, leads to the disruption of the normal balance of cytokines and the functioning of the cytokine network [2].

In the pathogenesis of HIV infection, the imbalance of cytokines produced by TV-1 and TV-2 lymphocytes and monocytes is central, influencing the strength of the immune system's response to specific human immunodeficiency virus (HIV) antigens [5].

All cytokine receptors are transmembrane glycoproteins in which the extracellular part is responsible for cytokine binding. As a rule, these receptors consist of more than one subunit, and high-affinity binding is a consequence of interaction with different subunits, each of which is capable of binding the corresponding cytokine itself, but with lower affinity. The cytokine network is involved in almost all stages of interaction of the virus-cell, the spread of HIV in the human body, the formation of immunodeficiency of the body and the development of opportunistic diseases. At the early stage of HIV infection there is an increase in the level of proinflammatory cytokines, which, according to most authors, act as cofactors of immunodeficiency virus activation. There is enough convincing data on the role of switching indicators of pro-inflammatory and anti-inflammatory cytokines to the development of HIV-associated diseases. The imbalance of cytokines contributes to the defeat of the CD4+ lymphocyte virus, leading to the progression of immunodeficiency (immunosuppression) and the subsequent development of opportunistic diseases [10].

IL-2 interacts with specific membrane receptors expressed on T- and B-lymphocytes, NK-cells and monocytes/macrophages. Currently, it is believed that the receptor complex of IL-2 consists of 3 subunits, which are polypeptides of different sizes, designated as α-, β- and γ-chains, each of which is encoded by its gene. In vitro

[1]*Chief doctor of Samarkand Regional Clinical Infectious Disease Hospital, Samarkand*
[2]*Research Institute of Virology the Ministry of Health Tashkent, Uzbekistan, E-mail:dr.utegenova@gmail.com*

DOI: 10.37200/IJPR/V24SP1/PR201222
Received: 18 Jan 2020 | Revised: 07 Feb 2020 | Accepted: 27 Feb 2020

studies, it was found that the culture of monocytic cells of healthy donors in HIV-infection corresponded to an increase in the production of IL-4, TNF-α and INF-γ, while the levels of IL-8, IL-1RA and INF-α and an increase in the level of IL-8 [9, 10].

The highest level of circulating TNF-α is most clearly associated with the rapid progression of the disease. A soluble TNF receptor of type II seems to have a similar significance, and sTNFR-75 is considered to be an early marker of the intensity of HIV infection, in contrast to neopterin, which is a marker of prognosis of late stages of disease and death [7].

The concentration of TNF-β and APO-1/Fas in blood serum also correlates with the intensity of antigen-dependent cytolysis and the rapid rate of HIV progression [6].

The data of a number of scientists demonstrate the connection between the progression of HIV infection not only with the level of TNF-α, but also with the concentration of IL-10, with a decrease in the IL-10/TNF-α coefficient being observed during the progression of HIV infection, which indicates a change in the healthy balance of these regulators [5].

At the same time, it is known about the in vitro inhibitory effect of IL-10 on the production of TNF-α, as well as on the production of another cytokine stimulating HIV replication - IL-6, which may indicate a possible protective role of IL-10 in the development of the terminal clinical stage of HIV infection [8].

IL-10 is a key regulator of immune response. IL-10 produced by T-cells (Th2) can be considered as an antagonist of a number of cytokines. Thus, IL-10 suppresses the production of interferon by Th1-cells. It also inhibits the proliferative response of t cells to antigens and mitogens and inhibits the secretion of activated IL-6 monocytes. At the same time, IL-10 stimulates IgE secretion. In its inhibitory effect on cellular immunity, IL-10 is synergistic with IL-4. Stimulation of lymphocyte maturation by influencing dendritic cells. Inhibition of the maturation of dendritic cells that activate Th2, their expression of class II molecules of the main histocompatibility complex and co-stimulating molecules and, as a consequence, the suppression of Th2 activation. Anti-inflammatory cytokines: IL-4, IL-10. IL-13, TGF-b, receptor antagonist IL-1 are able to reduce HIV replication by inhibiting the production of proinflammatory cytokines IL-1b, IL-6 and TNF-α. Didion S.P. and co-authors (2009) note that high levels of TGF-β in HIV-infected plasma are combined with low viral load of HIV, although in contrast to the unambiguously blocking effect of IFN-α, IFN-β, and IL-16 on the replication of the virus, INF-γ, IL-2, IL-4, IL-10, and TGF-β may have a multidirectional effect depending on local conditions [3].

With the progression of the disease and its transition to the IV-clinical stage (AIDS stage), a shift towards the prevalence of anti-inflammatory cytokines produced by Th-2 cells is observed. It is known that the decrease in the stimulated production of Th-1 lymphocytes INF-γ and IL-12 is associated with an increase in the expression of the virus [1].

It has been established that HIV-infected patients at different stages of the disease experience a change in the level of cytokine INF-γ, which reflects the functional activity of type 1 T-helpers and is a regulator of immune inflammation, the main activator of NK cells and macrophages. Thus, at the initial and asymptomatic stages of HIV

DOI: 10.37200/IJPR/V24SP1/PR201222
Received: 18 Jan 2020 | Revised: 07 Feb 2020 | Accepted: 27 Feb 2020

infection, the average concentration of INF-γ was the highest and amounted to 597.5 pg/ml; during the transition to the stage of generalized lymphadenopathy, a tendency to reduce interferons - INF was revealed, and in the stage of secondary diseases, accompanied by the growth of opportunistic infections, the level of INF-γ was even lower - 425 pg/ml was noted in the final stage of HIV infection [2].

These data testify to the suppression of the interferon system, which aggravates with the progression of the disease and is one of the pathogenetic mechanisms for the formation of generalization of viral infections. However, there is an opinion that the progression of HIV infection is mainly accompanied by a decrease in the content of type 2 T-lymphocytes [6].

The biological effect of IL-4 is the immunological deflection of CD4+ T-lymphocyte differentiation towards Th-2, regulation of B-cell immunity activation [2].

It has been shown that the IL-4 inhibits the expression of coreceptors for the immunodeficiency virus on the surface of T-lymphocytes, reducing the possibility of the virus's introduction, but at the same time strengthening the replication of the virus in the already infected cells [4].

The increase in the IL-4 level contributes to changes in the HIV phenotype from non-sintium to syncytium, thus changing the degree of progression of the disease. A change in the migration activity of leukocytes has been found as a result of the induction of IL-4, which increases with the progression of the disease [8].

As for endogenous IL-2, its role, as well as that of IL-4, is ambiguous in terms of HIV replication control. On the one hand, IL-2 can stimulate HIV replication in activated and proliferating T-lymphocytes. High-affinity interaction of IL-2 with its receptor requires the participation of all three subunits that perform different functions in the receptor complex [9].

II. CONCLUSION

However, it should be noted that IL-2 does not cause replication of the immunodeficiency virus in the absence of T-cell proliferation. On the other hand, IL-2 reduces the expression of receptors on antigen-presenting cells, thus reducing the rate of their infection with the virus. In addition, IL-2 reduces apoptosis of T-lymphocytes and increases their survival rate. Also essential factors in suppressing HIV replication are the destruction of the virus of infected immune cells by activated cytotoxic T-lymphocytes and NK-cells as a result of IL-2 stimulation. Due to this deterrent mechanism, the virus does not actively replicate during the first years of the disease [3].

Thus, the pathogenesis of HIV infection is characterized by chronic immunological dysfunction, which results in hyperproduction of proinflammatory cytokines. During the infectious process of HIV are influenced by a fairly large number of factors: virulence of the pathogen, the characteristics of the patient's genotype and the conditions and mechanisms of the immune response. Objective assessment of the set of parameters characterizing the effectiveness of counteraction to the body's immune system and control of HIV replication can determine with a certain degree of reliability the individual prognosis of the disease at the early asymptomatic stages and initiate intensive preventive therapy in persons with an adverse prognosis.

DOI: 10.37200/IJPR/V24SP1/PR201222
Received: 18 Jan 2020 | Revised: 07 Feb 2020 | Accepted: 27 Feb 2020

REFERENCES

1. Asadulla C., Sterri V., Volk H.D. Interleikin-10 therapeutic review of the new approach / Pharmacological reviews. - 2003. - Volume 55, Volume 2. - P. 241-269.
2. Choi E.S., Panayi G.S. Cytokine pathways and joint inflammation / New England Journal of Medicine. - 2001. - Vol. 344, Vol. 12. - P. 907-916.
3. L.YAMUNA M.E. Communication Systems, K. Ramakrishnan College of Engineering, and Trichy. "High Performance Dual-band Printed Doublet Design Loaded with Split Resonator Structures." International Journal of Communication and Computer Technologies 2 (2014), 64-67. doi:10.31838/ijccts/02.01.10
4. Didion S.P., Kintsenbau D.A., Schrader L.I. and others. Inhibits angiotensin II-induced vascular/hypertension. - 2009. - Vol. 54, Vol. 3. - P. 619-624.
5. Kelsall B. Interleukin-10 in inflammatory bowel disease / N. Ingl. - 2009. - Vol. 361, Vol. 21. - P. 2091-2093.
6. Lan R.Y., Ansari A.A., Lian Z-X. et al. Regulating T-cells: development, function and role in autoimmunity / Autoimmune. Rev. - 2005. - Vol. 4, Vol. 6. - P. 351-363.
7. Rohit Kalra, Pallavi Shetty, Srinivas Mutalik, Usha Y. Nayak, M. Sreenivasa Reddy, Udupa N.. "Pharmaceutical Applications of Radio-Frequency Identification." Systematic Reviews in Pharmacy 3.1 (2012), 24-30. Print. doi:10.4103/0975-8453.107134
8. Medrano F.J., Leal M., Arienti D. AIDS Res. Hum. Retroviruses. 1998. Vol. 1. Iss. 14:10. P. 835.
9. Tinsley J.H., South S., Chiasson V.L., et al. Interleukin-10 reduces inflammation, endothelial dysfunction, and blood pressure in hypertensive pregnant rats / Am. J. Physiol. Regul. Integr. Comp. Physiol. - 2010. - Vol. 298, №3. - P. 713-719.
10. Bhausaheb b. Jankar, devesh d. Gosavi (2017) adverse drug reaction of lithium carbonate-a review. Journal of Critical Reviews, 4 (1), 1-6. doi:10.22159/jcr.2017v4i1.14555
11. Vasilescu A., Heath S.C., Ivanova R. Genes Immun. 2003. Vol. 4. Iss. 6. P. 441.
12. Vale M.L., Marques J.B., Moreira C.A. et al. Antinociceptive effects of interleukin-4, -10, and -13 on the writhing response inmice and zymosan-induced knee joint incapacitation in rats / J. Pharmacol. Exp. Ther. - 2003. - Vol. 304, №1. - P. 102-108.
13. Waehre T., Halvorsen B., Damas J.K., et al. Inflammatory imbalance between IL-10 and TNFalpha: potential plaque stabilizing eff ects of IL-10 / Eur. J. Clin. Invest. - 2002. - Vol. 32, №11. - P. 803-810.
14. Mahmoudi,&Laylipour,C. (2015). A discrete binary version of the Forest Optimization Algorithm. *International Academic Journal of Innovative Research*, 2(12), 10-23.
15. Yuvarajan, A.,&Priyadharshini,V.M. (2014). Fixed Width Booth Multiplier Using Adaptive Conditional Probability Estimator. *International Journal of Communication and Computer Technologies*, 2(1), 56-63.
16. Guo, W. On the functional recovery mechanism of the cerebral nervous system in diabetic state under the combination effect of exercise and medication (2018) NeuroQuantology, 16 (1), pp. 63-70.
17. Song, D. Visualization of information (2018) NeuroQuantology, 16 (1), pp. 32-36.

DOI: 10.37200/IJPR/V24SP1/PR201222
Received: 18 Jan 2020 | Revised: 07 Feb 2020 | Accepted: 27 Feb 2020