



CYTOKINE STATUS IN HIV INFECTED WOMEN WITH INFLAMMATORY DISEASES OF THE GENITALS

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ABSTRACT

The aim of the study was to study the cytokine profile in HIV-infected women with acute vaginitis during treatment. Materials and methods- the study examined 35 women for 2019-2020 with HIV infection and 20 women who were conditionally healthy, a control group. The level of cytokines (IFN γ , IL-17) in the serum of peripheral blood was studied by enzyme-linked immunosorbent assay using test systems "Vector-Best". Results and discussion: the ratio of IFN γ / IL-17 (pro-inflammatory / anti-inflammatory cytokines or Tx1 / Tx2) in healthy women was 2.2. In the presence of a pronounced inflammatory process, that is, in women of the main group, this indicator was 0.96. After immunocorrecting treatment with the use of Imunorix in women with nonspecific vaginitis, IFN γ approached the control values, the content of IL-17, and after treatment did not normalize, remaining 5.5 times higher than in women of the control group, the ratio of IFN γ / IL-17. in women of the main group, after treatment, this indicator decreased to 0.42. Conclusion: A violation of the ratio of pro- and anti-inflammatory cytokines to talk about the presence of a previous immunodeficiency state and was manifested by the presence of complications in the presence of acute vaginitis.

Key words: inflammatory process HIV infection, immune system, cytokines.

RELEVANCE

The problem of infection in women caused by the human immunodeficiency virus (HIV) has been studied in obstetrics and gynecology in Uzbekistan since the early 90s. Acute and chronic inflammatory diseases of the genitalia in HIV-positive women, which are an indicator of acquired immunodeficiency syndrome (AIDS), have been identified and described, the symptoms of genital lesions in HIV-infected women with AIDS have been studied. [1,3,5]

In connection with a significant increase in the number of cases of HIV infection, the likelihood of contact between a gynecologist and HIV-infected patients is increasing. In HIV infection, there are often various manifestations of the disease with damage to the genital organs. Gynecologists, as well as other specialists, already have to take an active part in the diagnosis, treatment of HIV-infected persons, preventive work, which, of course, will require knowledge of the peculiarities of the pathology of the genital organs in HIV infection [2,8,9,11]

The variety of clinical manifestations of HIV infection is due to the addition of opportunistic infections, among which fungal, bacterial and viral infections are of the greatest importance. The classic manifestation of HIV infection that a gynecologist may face is the development of acute vaginitis. Vaginitis is one of the most common bacterial infections in women with a normal immune system, but the peculiarities of the course of these diseases in immunodeficiency are not well understood [4,12].

In women infected with the human immunodeficiency virus, fungal infections in the genital area caused by *Candida* spp. and *Cryptococcus* spp. met significantly more often than uninfected. Due to the fact that HIV-infected women usually had a cellular-functional "imbalance" of the immune system, they had diseases caused by *aspergillus*, *penicilli*, *mucor* and other fungi [1,3,14]

HIV infection increases the risk of damage to the external genital organs by the human papillomavirus, contributes to an earlier and more frequent development of severe dysplasia and cervical cancer. Moreover, the higher the degree of immunosuppression and the lower the level of T-helper cells (CD4-lymphocytes), the more often highly oncogenic strains of HPV (human papillomaviruses) and intraepithelial diseases of the cervix uteri, up to cancer, are detected. At the same time, there are opposite opinions, asserting that the likelihood of more frequent occurrence of intraepithelial neoplasia and cervical cancer in patients with HIV infection has not been proven. Thus, the world literature has highlighted the negative role of HIV infection in the development of severe HPV-induced diseases of the cervix, such as CIN (cervical intraepithelial neoplasia) and cancer. However, despite a significant number of works presented in foreign literature, today there is no consensus about the features of the pathogenesis, therapy and prevention of intraepithelial lesions in HIV-infected women, as well as the clearly developed tactics of managing HIV-infected women with cervical disease. uterus [3,4,6].

Meanwhile, our own experience and the few data from clinical trials that are available to date suggest that inflammatory diseases of the genitalia, in acute, chronic and recurrent forms, are common in HIV-infected women, although in most cases, the etiology, symptoms and the course of inflammatory diseases of the genitalia in HIV-infected women and in women with a normal immune system is the same, however, a protracted, severe or unusual course of these infections, with frequent relapses, or the isolation of atypical bacterial pathogens (including pathogens of opportunistic infections) should alert doctor regarding possible HIV infection [13,14]. When women turned to a gynecologist, they paid attention to the presence of diseases of the genital area. But also the presence of opportunistic infections, such as: condilematosis of the anal and perianal region, Kaposi's sarcoma, cervical cancer, etc.), as well as drew attention to a history of syphilis, gonorrhea and other diseases that are associated with the risk behavior of women. This alarms the gynecologist in order to send the patient for further examination for HIV infection and its complications.

This disease has long attracted the attention of gynecologists, especially since the time when observations and studies appeared, indicating a link between acute vaginitis and HIV infection. [6,7,10]

The aim of the study is to study the cytokine profile in HIV-infected women with acute vaginitis against the background of complex conservative treatment

MATERIALS AND RESEARCH METHODS

For the period from January 2018 to March 2020 under our supervision there were 55 women aged 25 to 55 years with acute vaginitis, of which 35 women with HIV infection, which is the main group and 20 women without HIV infection, which made up the control group. The research was conducted on the basis of the AIDS Center, on an outpatient basis. The diagnosis of HIV infection was established on the basis of order No. 480 of the Ministry of Health. The level of CD4-lymphocytes in peripheral blood in the examined women of the main group averaged 420, VL (viral load) -1500 copies, received ARV therapy according to the ABC + 3TC + EFV

regimen. Complaints of patients with headaches, pain and discomfort in the lower abdomen, discharge from the vagina and burning sensation in the genital area.

All women were examined regardless of the presence of complaints, except for standard methods of examination (complete blood count, urine analysis, bacteriological and biochemical studies), we conducted a thorough gynecological examination for all HIV-infected women. All examined women were routinely examined and, as a result of the study, according to indications, were hospitalized for adequate treatment.

Sick women received traditional antibacterial, anti-inflammatory and local therapy in a hospital setting, then immunocorrection was prescribed, for which the domestic drug Immun-5 was used (The drug is a balanced mixture of natural biologically active substances, the action of which is aimed at activating the body's immune system. the body's resistance to inflammatory diseases. Effective remedy for HIV / AIDS, hepatitis and tuberculosis. Application of 1 capsule 2 times a day for 60 days. The drug manifests its effects, primarily through the effect on the system of endogenous interferons and on the expression of functionally associated interferons of cytokines - IL-2, IL-4, IL-6, IL-10 and IL-17). The level of cytokines (IFN γ , IL-17) in the serum of peripheral blood was studied by enzyme-linked immunosorbent assay using test systems "Vector-Best" (Russia).

RESULTS AND ITS DISCUSSION

The results of a study of pro-inflammatory and anti-inflammatory cytokines in the serum of peripheral blood in women with exacerbation of inflammation of the genitalia (vaginitis) are presented in Table 1.

Table # 1.

The content of pro-inflammatory and anti-inflammatory cytokines in the examined women before and after treatment

Show	Control group without HIV infection (n = 20)	Basic group with HIV infection (n = 35)
ИФН γ , пг/мл	23,70 $\pm$ 5,38	<u>82,80$\pm$25,07</u> 21,93 $\pm$ 5,28
ИЛ-17, пг/мл	10,95 $\pm$ 3,65	<u>86,08$\pm$25,72</u> 52,04 $\pm$ 15,06

*Note. In the numerator there are data before treatment, in the denominator - after compared with the control group; * - $P < 0.05$.*

The analysis of the obtained results revealed the presence of significant differences between the values of the control group and women of the main group. Thus, in healthy women, the level of IFN γ was 23.70 ± 5.38 pg / ml, while in women of the main group, this indicator was 82.80 ± 25.07 pg / ml. Thus, the level of IFN γ in women with acute inflammation of the genitalia was increased by 3.5 times, which indicated the severity of the inflammatory process and the presence of purulent discharge from the genital tract.

According to the literature, activated T-lymphocytes and natural killer cells are the source of IFN γ . Among T-lymphocytes, both cytotoxic CD8 + and CD4 + helper cells are producers of interferon gamma, however, when the latter differentiate into Th1 and Th2, the ability to produce interferon gamma is retained only

by Th1 cells. The most important function of $\text{IFN}\gamma$ is its participation in mediating the relationship between lymphocytes and macrophages and in the regulation of the ratio of the cellular and humoral components of the immune response. Being the main product of Th1 cells, $\text{IFN}\gamma$ reduces the secretory activity of Th2 cells. Thus, $\text{IFN}\gamma$ enhances the development of cellular immunity and suppresses the manifestations of humoral immunity. Therefore, $\text{IFN}\gamma$ plays an important role in immunoregulation, being a key cytokine of the cellular immune response and an inhibitor of the humoral immune response.

The level of IL-17 in the group of women in the control group was 7.9 times lower than in the patients of the main group. It is known that interleukin-10 has been described as a stimulating factor for B-lymphocytes because it causes B-cell proliferation. It is known from the literature that the main producers of IL-17 are T-helpers of the 2nd class. IL-17 is also synthesized by mast cells and B cell lines. IL-17 suppresses the function of macrophages and their secretion of IL-1, TNF and IL-8, while providing an anti-inflammatory effect. Thus, IL-17 is the main product of Th2 cells and stimulates their differentiation. It causes the proliferation and differentiation of B and T lymphocytes, affects the development of hematopoietic cells, macrophages, natural killer cells, basophils, being a functional antagonist of cytokines produced by Th1 cells. IL-17 promotes the development of allergic reactions, has a pronounced anti-inflammatory effect [11,13].

Comparative analysis showed that the ratio of $\text{IFN}\gamma$ / IL-17 (pro-inflammatory / anti-inflammatory cytokines or Th1 / Th2) in healthy women was 2.2. In the presence of a pronounced inflammatory process, that is, in women of the main group, this indicator was 0.96. There was a pronounced imbalance in the state of the main regulatory cytokines, which was expressed by a sharp rise in the level of anti-inflammatory cytokines and suppression of pro-inflammatory cytokines, which are the main regulators of acute inflammatory conditions. Thus, in acute inflammation of the genitalia (vaginitis), a pronounced stimulation of the production of both pro-inflammatory and anti-inflammatory cytokines occurs, which can be regarded as a necessary condition for protection against an infectious agent and the systemic damaging effect of high concentrations of pro-inflammatory cytokines.

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After carrying out immunocorrective treatment with the use of Immun-5 in women with nonspecific vaginitis, $\text{IFN}\gamma$ approached the control values. As for the content of IL-17, after treatment it did not normalize, remaining 5.5 times higher than in women in the control group.

As noted above, the ratio of $\text{IFN}\gamma$ / IL-17, in women of the main group, after treatment, this indicator decreased to 0.42.

CONCLUSION

Thus, the improvement in the clinical condition of HIV-infected women, along with the suppression of the level of the pro-inflammatory cytokine $\text{IFN}\gamma$, was accompanied by the disappearance of signs of inflammation of the genitalia, an improvement in the general condition of women (on days 9-10 after standard treatment, the condition of sick women improved, headaches, pain and discomfort in the lower abdomen, vaginal discharge and burning sensation in the genital area have decreased).

However, it should be noted that the revealed change in the level of IL-17 and the violation of the ratio of pro- and anti-inflammatory cytokines indicated the presence of an immunodeficiency state, which apparently manifested itself in the presence of complications against the background of acute vaginitis.

REFERENCES

1. Bugubaeva MM, Kadyrova RM Clinical and epidemiological characteristics of children with perinatal contact for HIV infection // Reference book of a general practitioner. - 2015. - No. 3. - S. 54-58.
2. Burkhanov RA, Mamanov MM Phenotypic risk factors for HIV infection and the development of Acquired Immunodeficiency Syndrome // News of Dermatology and Venereology .- (Central Asian Scientific and Practical Journal). - 2019. - No. 3. - S. 39-41.
3. Varpakhovskaya IM Acquired Immunodeficiency Syndrome: immunomodulators, vaccines, new methods of treatment // Remedium. - Moscow, 2015. - No. 1. - S. 64-68.
4. Kubanova AA, Akovbyan VA, Toskin IA Modern concepts of the epidemiological process of sexually transmitted infections and HIV infection // Bulletin of Dermatology and Venereology. - 2016. - No. 6. - S. 1-4.
5. Kulakov V.I., Baranov I.I. HIV: prevention of mother-to-child transmission. - M., 2017. -S. twenty.
6. Merkusheva TA, Mirakhmedova NN, The concentration of cytokines IFN-gamma and IL-4 in HIV / AIDS disease in children and adults // Journal of Theoretical and Clinical Medicine. - Tashkent, 2017.- C.163.
7. Moskalova EV Dynamics of immune status indicators against the background of antiretroviral therapy correction in children with perinatal HIV infection // Days of immunology in Siberia: mater. vseros. scientific-practical conf., dedicated. 30th anniversary of the GUNII honey. problems of the North of the SB RAMS and the 25th anniversary of the GU Research Institute of Clinical Immunology of the SB RAMS. - Krasnoyarsk, 2016. -- S. 140-141.
8. Moskalova EV Changes in interleukin status indicators in children with perinatal HIV infection against the background of immunocorrection // Questions of modern pediatrics. - 2016. - No. 1. - P. 392-393.
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. Narzullaev N.U. The Incidence of exudative otitis media in HIV-infected children // International Journal BIOMEDICINE (IJB) 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. - 2020. - Vol. 2, No.3. - pp. 83-88.
12. N. A. Nuraliev, G. A. Ikhtiyarova, N. I. Olimova, F. Sh. Oripova. Diagnostic Value Determination of Antibodies to Antigensof Micro-Organisms in Women with Inflammatory Diseases of the Pelvic Organs. American Journal of Medicine and Medical Sciences 2020, 10 (2): 124-126