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Neutrophilic granulocytes reactive response in candida vulvovaginitis patients with intracellular microorganism persistence complications

Abstract: Polymorphic neutrophilic granulocytes reactive response and body immune reactivity in general considerably decrease in patients suffering from candida vaginitis on the basis of intracellular microorganisms persistence.

Keywords: candida vaginitis, neutrophilic granulocytes reactive response.

Among frequently occurring infections candida vulvovaginal takes a considerable place affecting 70–75% of women of child-bearing age at least once a lifetime. Primary episodes of VVC with subsequently recurrent infection (RVVC) are experienced by 5%-10% of women while RVVC is defined as at least three-four episodes of the disease within one year. There is a primary RVVC identified with unknown predisposing factors and secondary RVVC that has an acute form due to the certain predisposing factors [1, 1–2].

Despite the existence of acquired cell-mediated candida-specific immunity, the studies of vaginal candidiasis in women show the lack of the local and systemic adaptive immunity protection. These data provide few clues to the protective mechanisms against the infection and the high rate of asymptomatic vaginal fungal persistence in adolescents has considerably limited the insights into the immunopathogenesis of vaginal candidiasis [2, 2939].

Objective of the research is to establish reactive response of polymorph nuclear neutrophilic granulocytes of periphery blood in women suffering from candida vaginitis at the presence of chronic persistent intracellular infection.

Resources and methods. Clinic laboratory and special examination was conducted in 107 women suffering from candida vaginitis. Clinic diagnosis was confirmed by yeast-fungi secretion of Candida genus and content from vaginas of all women in population level 5.69±0.37 lg CFU/ml in monoculture and in association with non-pathogenic bacteria or trichomonas.

Calculation and analysis of periphery blood elements were conducted according to the recommendations listed in "User's manual" of analyzing device [3, 58].

Investigation results and their discussion.

Viruses and other intracellular microorganisms add their contribution to the weakening resistance of a human body. The presence of persistent viral infection was identified by the increase of IgM and IgG concentration in the periphery blood. The investigation of the IgM and IgG concentration was held in 57 patients suffering from candida vaginitis. The persistent viruses and other intracellular infections investigation results according to the ELISA data are given in the table1.

For uncovering the persistence mechanisms of intracellular non-pathogenic microorganisms in women suffering from candida vaginitis, the ecological method was used. It allowed to investigate the co-existence characteristics of ecosystem representatives "microorganism-microbiota" and trace the ecosystem changing direction. Dominant typology was completed on the basis of the constant index iden-

tification, Simson's domination indexes and Berger-Parker's indexes of generic abundance. Cytomegalovirus and viruses of Herpes Simplex type 1, 2 are considered to be dominant species.

Table 1. – The generic content of persistent intracellular microorganisms in women suffering from candida vaginitis

Intracellular microorganisms with identified IgG	The amount of examined patients	The amount of identified IgG to microorganisms	Index of constancy	Frequency	Marhaleph's generic abundance index	Simson's generic domination index	Berger-Parker's generic abundance index
Cytomegalo virus	57	17	31,48	0,31	0,30	0,10	0,321
Herpes Simplex virus type 1, 2	57	15	27,78	0,28	0,26	0,08	0,283
Rubella virus	57	5	9,26	0,09	0,08	0,01	0,094
C. trachomatis	57	5	9,26	0,09	0,08	0,01	0,094
M. hominis	57	3	5,56	0,06	0,04	<0,01	0,057
T. gondii	57	8	14,81	0,15	0,13	0,02	0,151
Hepatitis C virus	57	1	1,75	0,02	0,01	<0,01	0,019

Rubella virus, Chlamydia, Mycoplasma and Toxoplasma are additional intracellular microorganisms that persist in a human body.

Margaleph's generic abundance index was calculated for persistent microbiota abundance characteristics. This index is believed to be rating to characterize spatial cellular resources and environmental conditions for providing the existence of intracellular microorganisms. The highest indexes of the persistent intracellular biota were identified in Herpes viruses (Herpes Simplex viruses type1, 2 and Cytomegalovirus). Viral and other intracellular microorganisms persistence always leads to the development of the secondary immunodeficiency state established during the study of the neutrophilic granulocytes reactive response level. An approximate level of the intracellular viral and other microorganism concentration was identified according to the IgG concentration level in the serum of the patients. IgG concentration study results in the serum of the women suffering from candida vaginitis are given in table 2.

Table 2. – Ig G concentration in the serum of women suffering from candida vaginitis

Intracellular microorganisms	Units of measure	IgG concentration in the patients' serum	IgM concentration in the patients' serum
Cytomegalovirus	m.o/ml	6,42±0,37	negative
Herpes viruses type1,2	Optical units	9,88±0,49	negative
Rubella virus	m.o/ml	92,40±0,87	negative
Chlamydia	Optical units	3,73±0,31	negative
Mycoplasma	Optical units	1,56±0,14	negative
Toxoplasma	m.o/ml	130,31±1,19	negative
Hepatitis C virus	Optical units	0,497	negative

Given IgG concentration depends on the antigen (virus or other microorganisms). The absence of IgM increase suggests that there is no acute inflammatory state, stipulated by persistent intracellular microorganisms, and the Ig 5G titre increase justifies the chronic inflammatory process, at which the secondary immunodeficiency state is formed. Candida vaginitis persists on the basis of this state.

It is known that candida of any localization refers to the opportunistic mycosis. The fungi of Candida genus are widespread. A carrier has got 46–52% of

these fungi on his mouth mucous membrane, 80% in faeces, 12% on vagina mucous membrane and this amount may considerably increase to 30–35% in the last trimester of pregnancy. However, this result must not exceed Ig 3–4 CFU/ml. Vaginitis development persists on the immunodeficiency state background, and particularly on the basis of granulopenia. Neutrophilic granulocytes possess the functions of hemotoxis, phagocytosis and secretion. They are the first to penetrate the inflammation foci that is connected with hyper susceptibility to hemoattractant substances that provide the direct cell penetration into inflammation foci. The importance of neutrophilic granulocytes in anti-infective unspecific protection became the basis for the establishment of neutrophilic granulocytes reactive response in the periphery blood in patients suffering from candida vaginitis (table 3).

Table 3. – Polymorphic neutrophilic granulocytes reactive response in the periphery blood of patients suffering from candida vaginitis

Immuno-hematologic indexes	Measure units	Patients suffering from candida vaginitis (n=30) M±m	Healthy people (n=30) M±m	Level of immune disturbance	P
Neutrophilic granulocytes reactive response index	equivalent units	2,67±0,26	2,97±0,29	–I	>0,05
Neutrophilic lymphocytic coefficient	equivalent units	1,71±0,17	2,50±0,22	–I	<0,05
Neutrophils shift index	equivalent units	0,110±0,011	0,033±0,009	+III	<0,01
Leucocytes shift index	equivalent units	1,52±0,16	2,15±0,19	–I	<0,05
Lymphocyte-granulocyte index	equivalent units	0,57±0,05	0,40±0,04	+II	<0,05
Neutrophils and monocytes ratio index	equivalent units	9,43±0,17	16,50±0,19	–II	<0,001
Leucocytes and ESR ratio index	equivalent units	0,63±0,05	0,43±0,4	+I	<0,05
Leukocytic index	equivalent units	1,57±0,13	0,85±0,10	+III	<0,05
Unspecific body reactivity index	equivalent units	0,40±0,03	0,64±0,06	–II	<0,05
Immunologic reactivity index	equivalent units	5,80±0,45	6,90±0,55	–I	>0,05
Body resistance index	equivalent units	310,15±3,11	802,12±5,40	–II	<0,001

For identification of informational index changes in neutrophilic granulocytes reactive response of the periphery blood, as probable prognostic meaning of candida vaginitis development, complicated by intracellular infection, the immunologic disturbance level of each immunohematologic index was established. At the presence of reactive response insufficiency there was a negative number and the index with "+" indicated the hyper function of the immune system. Neutrophilic granulocytes reactive response index in the periphery blood of patients suffering from candida vaginitis has a decreasing tendency by 11,24%. Neutrophilic-lymphocytic coefficient falls by 46,20%, leucocytes shift — by 41,45%, but at the same point it increases in 3,33 times that serves as an evidence of appearance of new forms (rod-nuclear) of neutrophilic granulocytes in large amount that cannot substitute the function of mature forms. Decrease of neutrophils and monocytes ratio index certifies the weakened function of neutrophilic granulocytes in

comparison with monocytes/macrophages function which activity prevails over neutrophilic function. Increase of leucocytes and ESR ratio index by 46,51% proves the development of autoimmune process, leading to cell destruction infected by intracellular microorganisms, and the leucocytes index increase to 85,88% justifies the immune response humoral component prevalence over the cell chain.

Conclusions:

1. The development and persistence of candida vaginitis is accompanied by a considerable (by 35,38%) decrease of factor activity and mechanisms of unspecific protection against the infection, and also the specific immune reactivity by 62,41% that causes body resistance decline in patients by 29,78%.

2. Body resistance decline in patients suffering from candida vaginitis is conditioned by Herpes viruses persistence in the body (Cytomegalovirus and Herpes simplex virus), Rubella virus and other intracellular viruses — Chlamydia, Toxoplasma, Mycoplasma.

3. Candida vulvovaginitis persistence, associated with intracellular infection (Herpes viruses, Rubella virus, Chlamydia, Toxoplasma etc.), is accompanied by the decline of polymorph nuclear neutrophilic granulocytes reactive response that leads to unspecific reactivity decrease (inherent immunity) by 60,0%, immunologic body reactivity by 18,97% that is conditioned by general body resistance decline in 2,59 times.

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