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THE ROLE OF HERPETIC INFECTIONS IN THE DEVELOPMENT AND COURSE OF NON-HODGKIN'S LYMPHOMAS

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SUMMARY

High infection with herpetic infections of patients with lymphomas was revealed. It is important to understand the relationship between the immunological criteria of the body and infection, which leads to viral contamination of the body, while increasing the risk of developing chronic virus carriage, which in turn leads to the development of the oncological process. Pathogenetically, it looks like this, the immune system protects the body by monitoring the appearance of tumor cells and oncogenic viruses, and chronic inflammation can increase tumor growth and metastasis. Despite everything, immunity remains a system that supports homeostasis in the body, but at the same time, immunodeficiency can contribute to the formation of lymphomas.

KEYWORDS: Herpetic infections, immune system, polychemotherapy, immunocompetent cells, non-Hodgkin's lymphoma.

The role of herpetic viruses in the induction of carcinogenesis is not yet fully understood, especially when the question is about carcinogenesis of immunocompetent cells. It can participate both in genetic rearrangements of lymphocytes, leading to a malignant transformation of these cells, and contribute to immunodeficiency states, against which increased proliferation of neoplasms occurs. There is no direct correlation between the already developed oncopathology in the conditions of virus association and the worst outcome of the disease, however, antiviral prophylaxis has a positive effect on the course of treatment of lymphomas.[2,8,10,11]

An analysis of modern literature shows that despite a sufficient amount of clinical material regarding virus-associated non-Hodgkin's lymphomas (NHL), many issues remain unresolved.[1,2,9,10] The discovery, made in 1964 by Anthony Epstein and Yvonne Barr, marked a new era in clinical and experimental oncology.[7,8] The subject of their discovery was the first human oncogenic virus, later named after the authors - Epstein-Barr virus (EBV).[2,4] Despite the over 45-year period of studying the biological properties of this virus, conducted in numerous laboratories around the world, EBV is still a mystery virus.[4,9,10] On the one hand, it is a ubiquitous virus that practically infects the world's population, on the other hand, it is a proven or suspected etiological agent for a number of benign and malignant neoplasms of lymphoid and epithelial origin.[3,7,9,11] The most convincing argument in favor of carcinogenicity of EBV is the detection of the genetic information of the virus in the form of clonal extrachromosomal episomes in malignant cells of tumors caused by it.[9,10] The carcinogenicity of EBV is far from unambiguous.[4,8] Despite the fact that the products encoded by the virus are capable of causing proliferation of infected cells, leading to the appearance of lymphomas in patients with immunodeficiency, these clinically aggressive tumors are quite often polyclonal and regress when the immune response to EBV is restored.[9,10,11] Tumors such as Burkitt's lymphoma (LB), Hodgkin's lymphoma (HL) are found not only in EBV-associated, but also in EBV-unassociated variants, which suggests that the pathogenesis of these neoplasms is associated not only with EBV.[2,6] These findings suggest that tumor cells can also occur under the influence of factors of non-viral origin, as well as depend on various stimulants that enhance cell growth.[2,5,11]

Despite all the above conflicting opinions, it has been proven that the Epstein-Barr virus (EBV) serves as the etiological agent for many malignant neoplasms of humans, including tumors of lymphoid, epithelial and mesenchymal origin.[2,5] Tumors of lymphoid origin are characterized by heterogeneity of morphological and molecular characteristics, as well as the clinical course.[6,7] Non-Hodgkin's lymphomas (NHL) make up about 70% of all malignant lymphomas, and Hodgkin's lymphoma (HL) - the remaining 30%. For HL, based on epidemiological observations and morphological data, an infectious nature and the presence of a small number of

clinical options have long been suggested.[11] The desire to understand the etiology of NHL was complicated by their heterogeneous composition, numerous clinical manifestations, and differing histopathological and immunological phenotypes.[5,8,10] Several attempts have been made to create an appropriate classification for neoplasms of a lymphoid nature.[5] The latest classification for hematopoietic and lymphoid tissue tumors was proposed by WHO in 2008.[6,9]

The aim of this study is to study the role of herpetic infections during lymphomas, taking into account modern literature data.

In our study, patients with non-Hodgkin's lymphomas (NHL) were divided into 2 groups: the I group - patients infected with herpetic infections; the II group - patients of the experimental group without infection. In the distribution of NHL patients by age, it was found that infection with herpetic infections leads to a rejuvenation of the disease: the peak incidence rate in group I is up to 30 years, while the same indicator for group II is over 50 years. The number of sick men with infection was 35.6 ± 4.56 years, among women - 27.2 ± 5.24 years, in the experimental group, the average age of men was 60.7 ± 3.80 years, women - 45.5 ± 6, 97 years old. The proportion of women in group I was 21.7 ± 6.44%, men - 78.3 ± 6.44%; in group II, women accounted for 44.4 ± 7.75%, men - 55.6 ± 7.75%. As the analysis shows, in the presence of infection with herpetic infections, the incidence of persons of a younger age is observed. It should be noted that the younger age of patients with lymphomas infected with herpetic infections is also indicated in the literature.[2,4,7,10] In all patients, the diagnosis was established on the basis of data and the results of a comprehensive study (clinical, biochemical, radiological, ultrasound, CT, myelogram, morphological).

Another important and specific criterion for infected patients was the affected lymph nodes. Thus, the lesion zones in non-Hodgkin lymphomas in patients with viral infection (group I) most often occurred in the cervical and axillary l / nodes (more than 50%), then in the mediastinal, supraclavicular, retroperitoneal and inguinal (25-45%), the least damage to the iliac l / nodes, spleen, Valdeyer (20% or less) was noted. In control group II, the picture of lymph node lesions differed from the experimental group — patients with affected cervical l / nodes were more than 70%, while the remaining lesion zones were less common: axillary, supraclavicular, inguinal l / nodes malignantly transformed in 30-40% of cases; mediastinal, retroperitoneal, iliac - in less than 20% of cases; Valdeyer ring damage was observed in more than 60% of patients. Consequently, viral infection changes the picture of lymph node damage in patients with NHL compared with patients without infection: in group I, axillary, mediastinal, supraclavicular, retroperitoneal, and inguinal l / nodes were transformed malignantly (25-45%). Group I patients were most often infected with HSV herpes simplex virus and Epstein-Barr virus (65-80%), cytomegalovirus infection (CMV) - in 68% of patients. The examination included patients undergoing examination in the chemotherapy department. All patients underwent clinical and laboratory blood tests, which included the study of a general analysis of blood and urine, biochemical and immunological parameters, as well as the blood coagulation system.

From the literary data it is known that EBV infects a person in childhood, then persisting in the host's body throughout his life. Infection is usually asymptomatic.[6] The constant presence of EBV in the human body becomes possible only due to latent infection of the fraction of circulating memory B-cells.[2,4] Currently, many researchers believe that the contribution of EBV to carcinogenesis is due to its ability to cause genetic and epigenetic changes that can stimulate cell growth directly or indirectly, inhibiting apoptosis, or protecting tumor cells from the influence exerted on them by the microenvironment and immune response of the host.[7,9]

In the WHO classification of "Tumors of the hemopoietic and lymphoid tissue", malignant lymphomas are assigned to a separate group, inside which they can be divided according to morphological, immunophenotypic and biological characteristics.[4,11] Groups of lymphomas have a clear epidemiology, clinical signs, and often a very special response to therapy.[7,9] Such differences are often explained by the biology of lymphomas, for example, the frequency of lymphoma cell division (as opposed to apoptosis), the activation of oncogenes, the loss of the influence of suppressor genes, the presence of chimeric genes, the development of multidrug resistance, the special microenvironment of cells and the connection with infectious agents of the NHL variant, the issues are not resolved treatment of relapses and resistant forms.[10]

Table: The distribution of patients with NHL depending on the infection with herpetic infections.

Groups	Virus infection,%			Immunological status,%	
	HSV	EBV	CMV	Norm	Depressed
Group I (infected with herpes viruses)	65.2±7.4	78.2±6.4	43.4±7.7	0	100
Group II (experimental)	-	-	-	44.4±7.7	55.6±7.7

Observations and clinical studies that show the increased risk of cancer with primary or acquired immunodeficiencies, autoimmune diseases, and the use of immunotherapy to treat chronic inflammation (for

example, an autoimmune nature) or therapeutic support for organ transplantation help the understanding of the mechanism of induction of malignant pathologies by viruses.[9,10]

Understanding the relationship between the immune status impaired by viral contamination of the body and the risk of developing cancer is usually based on a comparison of two paradigms: the immune system protects the body by observing the appearance of tumor cells and oncogenic viruses (an example of an immune model of carcinogenesis) and chronic inflammation can increase tumor growth and metastasis (inflammatory model).[7,9] While these models support the role of immune status in many types of cancer pathologies, they are insufficient to explain the disproportionate increase in the risk of B-cell lymphoma in a population of patients with chronic immunosuppression or inflammation. For example, the presence of the Epstein-Barr virus (EBV) in patients with lymphomas demonstrates the variable role of the virus in lymphogenesis.[11] Evaluation of DNA variations found in tumor cells and understanding of B-cell ontogenesis gives an idea of the extremely high sensitivity of lymphocytes, mainly B-cells, to tumor transformation.[3,9] Epstein-Barr virus (EBV) serves as the etiological agent for many human malignancies, including tumors of lymphoid, epithelial and mesenchymal origin. Tumors of lymphoid origin are characterized by heterogeneity of morphological and molecular characteristics, as well as the clinical course.[9] The desire to understand the etiology of NHL was complicated by their heterogeneous composition, numerous clinical manifestations, and differing histopathological and immunological phenotypes. Several attempts have been made to create an appropriate classification for neoplasms of a lymphoid nature.

Thus, it should be said that we revealed a high infection of patients with lymphomas with herpetic infections. It is important to understand the relationship between the immunological criteria of the body and infection, which leads to viral contamination of the body, while increasing the risk of developing chronic virus carriage, which in turn leads to the development of the oncological process. Pathogenetically, it looks like this, the immune system protects the body by monitoring the appearance of tumor cells and oncogenic viruses, and chronic inflammation can increase tumor growth and metastasis. Despite everything, immunity remains a system that supports homeostasis in the body, but at the same time, immunodeficiency can contribute to the formation of lymphomas.

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