CURRENT PERSPECTIVES OF NON-HODGKIN'S LYMPHOMA IN ELDERLY PATIENTS (LITERATURE REVIEW)

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Abstract. *Currently, Nohodzkin's lymphoma is one of the most common oncohematological diseases in the world. Non-Hodgkin's lymphoma accounts for almost half of all cases of malignant lymphoproliferative lesions. A recent study of the history of this neoplasm has reported a steady increase in the incidence of non-Hodgkin's lymphoma [1,4,42].*
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Among all registered malignant tumors, Nakhodzhkin's lymphoma accounts for 3.1 percent [Davidov M.I. 2009]. In the last 20 years, the incidence rate of Nakhodzhkin's lymphoma has increased significantly, in Russia it is 3-4% per year [4,34,7,40,35]. The increase in the rate of disease in relation to age is particularly noteworthy, in 1 year it is 0.7 per 100,000 population in children and 20 in elderly people[11].

US National Cancer Institute 's SEER program showed a nearly doubling of the incidence of lymphoma in the United States for all sexes and age groups during the last 28 years of the last century (from 10.2 per 100,000 per year in 1973 to 19 per 100,000 per year in 2000). .0) was found to have increased. A more severe increase in incidence was found in older age groups [38,22]. According to epidemiological data, the incidence in Western European countries is 12-15 cases per 100,000/year. In France, 1980-1989, the annual increase in the incidence of NXL was equal to 10.9% [13]. In Europe, the highest incidence of non-Hodgkin's lymphoma is reported in the Netherlands and Scandinavian countries [24]. In the countries of the European Community, the prevalence of Non-Hodgkin's lymphoma is approximately 230,000 with an annual incidence of approximately 70,000. Currently, the incidence in Europe is increasing by 4% per year [30,17]. For Russia, the incidence of Nokhodzhkin's lymphoma is 18,000 cases per year. The incidence of dangerous lymphomas in Uzbekistan is 3.1 per 100,000 population per year [10].

A differential assessment of the incidence rate of non-Hodgkin's lymphoma revealed a difference by gender and race, and the rate of increase also differed in groups with different morphological variants of lymphoma. Most types of non-Hodgkin's lymphoma are very rare in children. The average age of patients with non-Hodgkin's lymphoma is 53-57 years. Incidence among men is 1.2-2.2 times higher than among women. Primary extralymphatic damage is observed in 20% of cases [3,36,18]. The increase in the incidence of non-Hodgkin's lymphoma was caused by the increase in life expectancy, the improvement of the quality of diagnosis of lymphomas, and the AIDS epidemic [39,40].

Among Nakhodzhkin's lymphomas, Nakhodzhkin's lymphoma, which occurs in the elderly, occupies a special group. In 15-20-year-olds, compared to people over 75, the incidence rate of Nohodgkin's lymphoma is 10 times lower. This feature is typical for both sexes [16]. In accordance with the decision of the European regional bureau of the BDSSJ, the elderly are included in the age group of 60-70 years. We recruited people 60 and older in our study because

the term "elderly" in the English-language literature includes age 60 and older. More than half of all non-Hodgkin's lymphomas are diagnosed in people 60 and older. According to different authors, patients over 60 years of age have all variants of Nohodgkin's lymphoma. Due to the development of various methods of immunological diagnostics, it is possible to determine the lymphoproliferative variant by examining exudate or transudate from a small tumor tissue or by examining blood. The presence of these methods is especially important in the diagnosis of elderly patients, because the combination of somatic diseases in them limits the possibility of using invasive or some non-invasive diagnostic methods.

Non-Hodgkin's lymphoma is a malignant tumor of the immune system, which develops from immature precursors of T- and B-lines of lymphopoiesis. Approximately 90% of non-Hodgkin's lymphomas have a B-cell phenotype, that is, they develop from cells corresponding to different stages of B-lymphocyte development. B-cell Nohodgkin's lymphoma belongs to a heterogeneous group of diseases that differ in the morphological structure of tumor cells, clinical course and prognosis. They can be conditionally divided into two groups - high and low-risk Nohodgkin 's lymphoma [2,17,2 6].

With mature T- and NK -cell immunophenotypes are more common in Asia [27]. However, given that the incidence of Non-Hodgkin's lymphoma is higher in the "West" (number of new cases per 100,000 population per year) than in the "South", the incidence of T-cell lymphoma does not have strong differences in different geographic regions, at the expense of V-cell in North America and Europe. The incidence of V-cell tumors - Non-Hodgkin's lymphoma - is significantly different. The reasons for such differences remain unknown [41].

Non-Hodgkin's lymphoma is characterized by rapid generalization, with the increase in pathology of the bone marrow and central nervous system. Non-Hodgkin's lymphoma is a pathology of extranodal localization with a high proliferative potential, rapid growth and high sensitivity to polychemical therapy, as well as a high recurrence rate [18]. Five-year survival in non-Hodgkin lymphoma varies widely depending on the morphological variant of the tumor: in V-cell marginal zone lymphomas, MALT, follicular lymphomas, it exceeds 70%, which is interpreted as a very good prognosis, in T-lymphoblastic, peripheral T-cell Non-Hodgkin lymphomas, this indicator Below 30 percent [3,33].

Non-Hodgkin's lymphoma begins with the appearance of a single tumor node and spreads by means of lymphogenous and hematogenous metastasis. The primary tumor site can be located in the lymph nodes (nodal involvement) or in other organs and tissues (extranodal involvement) [19].

Clinical manifestations depend on the location of tumor foci. A clear difference in the rate of damage to different organs and tissues is noted: mediastinal lymph nodes - 15-25 percent (less than Hodgkin's lymphoma), lungs - 3-6 percent, spleen - 30-40 percent, liver - 15-50 percent, bones - 5 - 15 percent, gastrointestinal tract - 10-24 percent, bone marrow - 30-40 percent of cases are damaged [15]. Initially, the clinical variant with extranodal local damage of organs and tissues is defined as primary extranodal Non-Hodgkin's lymphoma. The rate of damage to different organs and tissues is not the same: separately, the most common is the gastro-intestinal tract (24.3 percent), the Pirogov-Waldeyer community (19.4 percent), the brain (10 percent), the relatively rare mammary gland (2 .0 percent), lungs, pleura (1.1 percent) are added [26,33].

Further pathogenetic changes that occur in the body due to lymphoma are related to the growth and metabolism of the tumor. In most cases, tumor cells suppress the development of

analogous normal cells and cause a state of immunodeficiency. In addition, immune reactions associated with the development of antibodies directed against self-tissue antigens may develop. Bone marrow damage (leukemia) in lymphoma leads to the development of bone marrow hematopoietic failure with the development of cytopenia in the peripheral blood. The growth of tumor nodes can disrupt the function of nearby organs and cause their dysfunction. Accumulation of tumor mass leads to the general failure of the organism - cachexia [1,24].

In patients older than 60 years, most of the non-Hodgkin's lymphomas in the first cases are very fast and quite aggressive with the appearance of large conglomerates of lymph nodes that compress or grow into vital organs and large blood vessels, metastasize to the liver and spleen , which causes serious suffering in such patients (expressed pains, constipation, mechanical jaundice, excruciating skin itching, difficulty urinating, swelling of the legs and external genitalia, etc.). In elderly patients with non-Hodgkin's lymphoma, the prognosis is less favorable than in younger patients, mainly in refractory or relapsed forms of the disease.

Another important aspect of Nohodzkin's lymphoma in the elderly is the difficulty in choosing a treatment strategy. The choice of treatment tactics in elderly patients with non-Hodgkin's lymphoma depends not only on the morphological variant of the disease, but also on the presence of additional somatic pathology, the effect of drugs received due to other somatic diseases. It should be said that the toxic effects of anticancer drugs are often observed in elderly patients. This is explained not only by the presence of somatic pathology, but also by a decrease in tolerance to chemotherapy, which is associated with a sharp decrease in the activity of polyorgans [34]. A comprehensive study of patients older than 60 years shows that patients in this group belong to a group that differs in terms of physical, psychological and intellectual status. Age-related changes are individual. All of the above is not clearly related to chronological age, accordingly, biological age is important in formulating treatment tactics, as it clearly reflects the characteristics of the patient's organism.

Despite systematic polychemotherapy, patients' quality of life remains low enough, primarily due to the strong toxic effect of the therapy. In this category of patients, it is difficult to carry out radiation therapy due to the extent of the tumor process and the severity of the general condition . In the majority of elderly patients, despite the effect of polychemotherapy performed at the beginning of treatment, Nohodgkin's lymphoma still relapses and worsens [6,8].

The complexity of the treatment of elderly patients with non-Hodgkin's lymphoma is thought to be explained by a decrease in the immunological mechanisms of resistance against the tumor, concomitant chronic diseases of the internal organs, a decrease in reactivity reserves, psychological and biological adaptation of the organism, as well as pharmacological resistance. But these factors require study [25].

Currently, there are no less than 8 classifications of Non-Hodgkin's lymphoma, which, in essence, reflect changes in the understanding of the nature of the cells that make up the tumor substrate in relation to progress in the fields of immunology, cytogenetics and molecular biology. Classification of non-Hodgkin's lymphoma by stages is carried out according to the Ann Arbor classification (1971) developed for Hodgkin's lymphoma. Several classifications - BJSST classification, Rappoport, Kilskaya classifications, Working formulation are used and they compete with each other, but their clinical significance is practically the same [30]. Due to the burden of conditions for widespread use of immunophenotyping, the classification of Working Formulation (1994) is the most appropriate in practice in MDX countries, this classification is

based on morphological principles and contains information related to the specific characteristics of the clinic and prognosis of the disease [21].

Differentiating different variants of Nohodzkin's lymphoma, which was originally based on the morphological characteristics of the tumor, is now complex based on the immunophenotypic characteristics of the tumor cells and taking into account the clinical picture and biological characteristics. Currently, the world uses a classification called REAL (European-American revision of lymphoid tissue tumors), which takes into account all these features of Non-Hodgkin's lymphoma. Based on the integrated assessment of all parameter values, all variants of Nohodzkin's lymphoma were divided into two groups depending on their origin - V- and T-cell variants, and high- and low-grade malignant tumors depending on prognosis [31,28].

Advances in immunology, cytogenetics, and molecular biology make it possible to distinguish specific subtypes of lymphomas that differ in clinical course, response to therapy, and prognosis. For example, depending on the subtype of lymphoma, the prognosis can vary from positive (survival 10-20 years) to very negative (survival less than 1 year). The prognosis of tumors is very diverse: positive variants (5-year survival greater than 60%) include the gastrointestinal tract, Pirogov-Waldeyer's people, eyeball, salivary glands, lungs, primary NXL, on the contrary, testis and ovaries, bone, primary lymphomas of the mammary gland are characterized by a high risk [22].

Based on a thorough study of all manifestations of non-Hodgkin's lymphoma, the most significant factors of a negative prognosis are age older than 60 years, an increase in the level of lactate dehydrogenase (LDG) (2 times or more), the general condition of the patient with a tendency to grade 2-4 (ECOG), stages Sh - IV of the disease, multiple extranodal lesions , bone marrow involvement, were confirmed. It was recognized as the basis of the International Prediction Index - XBI. According to XBI, different risk levels are determined in patients [2,21].

The presence of two or more factors has a negative effect on the prognosis of the disease, regardless of the morphological variant of the tumor.

To a certain extent, this explains the conditionality of the classification of Non-Hodgkin's lymphoma according to the level of risk, because depending on the risk factor, the prognosis varies significantly within a certain variant of the tumor (for example, in diffuse large B-cell Non-Hodgkin's lymphoma, the 5-year survival rate is 72 at the low risk level, equal to high level is equal to 22%, which is significantly different from the average indicator - 45% [14].

Treatment of Nohodzkin's lymphoma in the elderly is a very complicated process. In elderly patients with non-Hodgkin's lymphoma, the main concern is to reduce the relapse rate without increasing the toxicity of PXT. In a long-term study of non-Hodgkin's lymphoma patients, it became clear that the majority of deaths were not related to the lymphoma and its treatment, but to comorbidities (eg, secondary solid tumors) that were detected at the time of lymphoma diagnosis or occurred later [21,17 ,29].

The most common type of non-Hodgkin's lymphoma - diffuse V - large cell lymphoma (V - NXL) accounts for about 40% of newly diagnosed lymphomas. It is a disease of the elderly: 50 percent of patients are 60 years old, and the treatment of such patients poses serious challenges. CHOP has been treating this disease for about 25 years The course was considered the gold standard. However, in the elderly, complete remission is recorded in only 40-50 % of cases, 3-year recurrence survival and overall survival are 30 and 35 to 40 % , respectively [16,13]. It should be remembered that there are problems in the treatment of elderly people with a poor prognosis,

because of this, it is necessary to prescribe a chemotherapy regimen that includes anthracycline antibiotics, including full doses of doxorubicin. But such treatment can quickly lead to cardiac complications with the development of dilated myocardiopathy, and then decompensated chronic failure.

Thus, taking into account the aggressive course of Nohodzkin's lymphoma in elderly patients, reducing the rate of recurrence without increasing the toxicity of polychemotherapy is the main issue when choosing treatment tactics, taking into account their somatic diseases.

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