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LOCALIZATION OF NON-HODGKIN LYMPHOMAS IN CHILDREN

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ABSTRACT

Non-Hodgkin's lymphomas are a heterogeneous group of diseases that develop due to malignant monoclonal proliferation of lymphoid cells in the lymphoreticular tissue in the lymph nodes, bone marrow, spleen, liver and gastrointestinal tract. The most common symptom is peripheral lymphadenopathy. However, there are cases without lymphadenopathy, with the presence of circulating atypical lymphocytes. At the time of detection, the disease is likely to be disseminated, and the diagnosis is usually based on a biopsy of the lymph node or bone marrow, or both.

Key words: Non-Hodgkin's, lymphomas, spread, causes, occurrence.

INTRODUCTION

In young children, almost all types of NXL are identified according to data from different authors, but their frequency is not always appropriate in different age groups. In different age groups, nexodzhkinsky focused on the study of lymphomas, an epidemiological study of 2,531 patients shows [1].

Relying on the results obtained from this study, it is possible to conclude that in most cases the frequency of occurrence of different variants of NXL in sick children under 5 years of age and older than 5 years is almost the same. The

exception to anaplastic T/0-cell lymphoma and Berkitt's lymphoma is much more pronounced.

E. Maartense, J. Hermans, .S. Kluin-Nelemans et al. In their research in the Netherlands, a group of patient children between the ages of 7 and over 7 were studied. The study showed that most cases (32% and 36%, respectively) were diagnosed with diffuse V-large cell lymphoma. The second largest frequency of occurrence in both age groups was follicular lymphoma (34% and 15%, respectively), in which its mainly cytological Type I-II was identified (18% and 10%, respectively). The identification of other variants of NXL did not depend on age. But Thieblemont S, Grossoeuvre A, Houot R. et al. In studies of sick children under the age of 10, it was shown that the patient was most often diagnosed in this group of children as well as diffuse V-cardiac cell lymphoma (in 40% of cases), while in second place by definition was marginal area lymphoma (26%), at which time follicular lymphoma was detected only in 7% of sick children [2].

Clinical manifestations of nexodzhkinsky lymphomas in sick children have varied. In most cases, NXL begins with the appearance of a solitary tumor node and spreads through lymphogenic and hematogenous metastasis. Primary tumor foci can be located in both lymphatic nodes (nodal injury) and other organs and tissues (extranodal injury) [5].

In the most cases, the primary manifestation of the disease is damage to the lymphatic nodes (50%). Often peripheral lymphatic nodes are involved in the process (40%). Basically, they are initially dense, painless and do not associate with the surrounding tissues. Conglamerates can then be formed by attaching to and or crushing the adjacent limb and tissues. Clinical presentation often depends on the location of the tumor foci. Expressive differences in the frequency of damage to various organs and tissues are noted: lungs - 3-6%, esophagus - 15-40%, liver - 10-50%, bone - 5-15%, gastrointestinal tract - 10-24%, marrow-30-40%. The clinical variant of the disease, which is initially accompanied by location and injury in the extranodal organ and tissues, is identified as primary extranodal NXL. In this, the frequency of damage to different organs and tissues is not the same: most often the gastrointestinal tract (24.3%), the Pirogov-Valdeer ring (19.4%), the cranium (10%), less often-the mammary gland (2.0%), lungs, pleura (1.1%) are involved [1,2,5].

Research data focused on the study of clinical specificities of NXL in the elderly contradict each other. Some of them, including multicenter types, have shown that there is no significant difference between clinical signs of NXL in patients of different ages. Thus, the diagnosis of I-II Bashkirs was made in 20% of sick children and 17-25% of sick children under 7 years of age. Other predictors

such as the number of extranodal areas and LDG levels have also been Age-Related. Depending on the location of the lesion, the frequency of nxl ni tuli extranodal symptoms varied from 4% to 30%. However, conflicting but interesting information can be found when the focus is on particular types of NXL [10].

It has been shown by some authors that a patient under the age of 12 with an aggressive type of NXL has a small overall ESOG status at the time of diagnosis in children, a large frequency of disease-spreading stages with extranodal injury and diffuse tumor growth [11].

While various researchers discuss the specifics of clinical and laboratory signs of NXL in sick children, there are few age-related studies as an independent negative predictor factor that increases the frequency of development of relapses that reduce the likelihood of achieving complete remission. So Shipp M. and hammual. in their studies, it was shown that being older than 10 years of age is an independent predictive factor in children with aggressive lymphomas and gives less chance (relative risk 1.8) in achieving complete remission and has a higher frequency of relapse development (relative risk 1.6). A large number of relapses were shown by other authors, as well as in patients with nehodzhkinsky lymphomas. Fisher R. and hammual. their observations showed that complete remission was achieved in 65% of cases when a patient under the age of 15 used the chop regimen in children, while in individuals over the age of 15 - 37% of cases. In another study, it was noted that relapses occur at a decreasing frequency for the first 7 years, and the effectiveness is directly related to age: the PR frequency and the median of survival are much lower compared to sick children under 15 years of age (65% and 101 months) [20].

It is known that the various clinical and laboratory symptoms of NXL are a negative predictive factor. The most significant factors of the negative prognosis are: the general condition of the patient corresponding to 2 - 4 degrees (ECOG), stage III-IV of the disease, the presence of more than one foci of extranodal injury, the involvement of the marrow. These indicators were put on the basis of the international forecast index - XPI. Each of the factors is equal to one point, and by their sum, the patient falls into one of the four groups of children of the early outbreak of the disease:

low (0-1 point,
intermediate-low (2 points),
Intermediate-High (3 points)
high (4-5 points).

International forecast index (XPI) M. It was developed by Shipp on the basis of a retrospective analysis of 2,031 cases of high-risk lymphoma, and it has been studied and applied in practice in detail for more than 15 years [21].

Long-term use of XPI in various clinical cases nxl has led to different effects of particular negative predictive factors in the fate of existing patient children. Xpi indications are aggressive and indolent lymphomas are not always equally relevant for patient children. This is especially clearly observed in follicular lymphomas of the 1 - 2 cytological type. Based on the same data, a number of researchers have developed a specific international prognostic index for follicular lymphomas, the FLIPI (Follicular Lymphoma Intemational Prognostic Index). It was based on 5 indicators of independent predictive significance. In accordance with the Ann Arbor classification, the III-IV stages of the disease are significant. Follicular nxl present in the mummy state of the patient children and the presence of more than one occtranodal furnace in them did not have a separate predictive value. At the same time, it was found by various researchers that the area of special nodal and extranodal injuries is more than four, as well as the level of hemoglobin in the blood is less than 120 g/l, is considered an independent negative factor for this nosology. Risk groups of early outbreaks are formed by the number of initial negative factors of the forecast: low risk (0-1 factors), Intermediate (2 factors), high (more than 2 factors) [25]. In the case of lymphoma in the cells of the mantle area, the actual prognostic factors were not only the age, somatic state and LDG level of the patient child, but also the level of leukocytosis in the peripheral blood [21,28].

All models for predicting the results of the above treatment and the duration of life are created for all categories of sick children, regardless of age. Considering that the importance of predictive factors is not the same for Sick Children of different ages, being 5 years old and older, as stated earlier, is considered an independent negative predictive factor, an age-adjusted (Age-Adjusted) predictive index for Sick Children has been developed. Based on the available data on the role of each indicator of XPI, it was concluded that the following indicators are most significant for Sick Children: general stages (III-IV); increased LDG levels; a general condition corresponding to 2-4 degrees according to the ECOG measure. The formation of risk groups for Sick Children has also undergone changes: low - level risk - the absence of predictive factors, Low/Intermediate - 1 negative factor, high/Intermediate - 2 negative factors, high-3 negative factors. It is also advisable to divide existing sick children under 5 years of age and older into a separate group when discussing therapeutic problems [22].

Considering the age of Monand treatment and the issues of the possibility of palliative therapy are widely discussed. Some authors attribute the low overall survival rate to the frequent development of complications on the side of the cardiovascular system in sick children. Most patients will have one or another Cardiology problem at the beginning of pediatric chemotherapy, namely damage to myocardial cells. Atrophic and dystrophic processes leading to myocardial cardiosclerosis and fibrosis negatively affect the functional and compensatory capabilities of the myocardium. Under these conditions, there is a possibility of increased cardiotoxicity of anthracyclines. However, in the absence of severe cardiovascular diseases, the risk of developing cardiotoxicity increases on a legal basis after reaching a certain cumulative dose of drugs [25].

It is worth noting that the polyethiological decrease in the function of the parenchymatous organs will have different symptoms. The metabolic function of the liver depends on blood flow in the liver, the rate of excretion of drug drugs with hepatocytes, intracellular concentration and activity of liver enzymes. The study of the activity of anti-tumor agents made it possible to note that the metabolism of drug drugs in the liver occurs with sequential implementation of oxidation reactions (I-phase) and conjugation reactions (II-phase) in the presence of two main , water-soluble substances with bile and urine excretion: the P-450 cytochrome system.

The activity of these reactions has been shown to be influenced by both age and various drug preparations. After the disease, a decrease in blood flow in the liver, protein-synthetic function and a decrease in the activity of the enzyme systems R-450 cytochrome occur in sick children. Changes in I-phase reactions can affect the activity and toxicity of metabolizing drugs through this mechanism (cyclophosphane, ifosfamide, idarubicin). Child-specific polypragmasia (the appointment of a large amount of drug drugs) can be the cause of the increase in the activity of R-450 cytochrome. Impaired liver function when kidney function is in moderation does not require correction to the dosage of most alkylating agents. A number of authors believe that doses of vinblastine, doxorubin, and mitoxantron should be reduced by 50% when bilirubin levels increase by 1.5 mg/dl and by 75% if bilirubin levels exceed 3.0 mg/dl (Beretta modified table, 1991). It is worth saying that the pharmacological control of any of the liver functions, in particular the appointment of hepatoprotectors, did not lead to a significant improvement in the effectiveness of the disease and a decrease in the symptoms of hepatotoxicity after their cancellation [16].

One of the most persistent functional changes characteristic of sick children is a decrease in the rate of ball filtration. The determination of serum creatinine levels

does not make it possible to correctly assess kidney functions: one of the cases is a decrease in the formation of creatinine in young children due to loss of muscle mass (including due to a decrease in physical activity), as well as its level leads to deceptive normalization. The creatinine clearance of kidney function is more pronounced. The main way to release a decrease in glomerular filtration is through the kidneys calculated chemical preparations (bleomycin, methotrexate, cisplatin, alkeran), as well as the increased toxicity of anti-tumor agents, the metabolites of which are excreted with the forehead. For this reason, the determination of creatinine clearance before starting any type of chemical therapy in sick children, as well as the implementation of monand adaptation of the cytostatics to be administered, is a universally recognized method [18].

Age-related changes in the central and peripheral nervous system increase the risk of developing both peripheral and Central neurotoxicity of anti-tumor drugs (vincaalcaloids, glucocorticoids) [6]. Thus, in studies of tax 326, it was noted that chemical therapy carried out with cisplatin in harmony with dosetaxel or vinorelbin is observed with an increase in the frequency of peripheral neuropathy of Level III-IV in individuals over 15 years of age. According to other authors, against the background of chemotherapy with cisplatin in harmony with Ethoposide or paclitaxel, the symptoms of Central neurotoxicity were found to be more common in children over 15 years of age when compared with children under 15 years of age. Thus, Level III-IV toxicity was found in 88% of patients under the age of 15 and in 94% of patients over the age of 70 (R=0.06); due to toxicity, treatment was stopped in almost half of patients over the age of 70 (46%) and only 26% of younger patients (r=0.003) [10].

Also elderly patients may develop decreased marrow reserves, which in turn can lead to unexpected myelotoxicity. This is manifested both in standard chemotherapy and when relatively low hematological toxin regimes are used. In older humans, the depth of myelodepression increases from course to course, indicating cumulative myelotoxicity. The risk of developing dangerous infections forces doctors to reduce the dose of drugs or increase the interval between cycles, which significantly reduces the intensity and effectiveness of treatment. According to various data, nexodzhkinsky lymphomas have up to 73% of patients have delayed the next administration of cytostatics for 7 or more days due to neutropenia [10], which in turn negatively affects the recurrence of the disease and the survival of patients [4]. This can be clearly observed when the disease is present in elderly patients. In a retrospective analysis of 577 patients with aggressive nexodzhkinsky lymphomas, it was shown that the age of 65 + is associated with a statistically significant decrease in the chances of obtaining all 6

planned courses of chemical therapy (35% against 22%, R>0.05) and a greater risk of decreased treatment intensity [15].

Thus, the risk of developing life – threatening neutropenia in patients over 70 years of age when undergoing chemical therapy according to the chop scheme increases from 40%, the risk of infectious diseases – by 21-47%, and lethal cases – by 5-30%, according to various research data. The use of Colony – triggering factors reduces the risk of developing neutropenia and infectious complications by 32-83% [4] and increases the possibility of carrying out treatment in an optimal mode [9]. For this reason, NCCN and ASCO, as well as the International Society for geriatric oncology (SIOG) recommend primary prevention of G-KSF in all patients over the age of 70 who are undergoing chemotherapy in similar regimens to it in print and intensity [5]. ASCO's revised end recommendations in 2006 noted that the reduction in the risk of febrile neutropenia after the appointment of cytostatics is considered an important clinical goal, and if the risk of this complication is greater than 20% and the effectiveness is equal, and the use of KSF is not alternative regimens of low – toxicity chemical therapy. KSF can be assigned to individual patients receiving low-intensity chemotherapy but with high risk of neutropenia and infection (age greater than 65 years, presence of burn diseases, previously observed episodes of Febral neutropenia, tumor damage to the marrow, exhaustion, open wound or presence of current infection, spread tumor) [13].

Side diseases are an independent negative predictor factor that negatively affects the general condition and duration of life of the patient. In addition, side diseases and their complications can lose their effectiveness in chemical therapy. The most significant are: coronary heart disease, heart failure, chronic obstructive pulmonary disease, kidney failure, cerebrovascular diseases, diabetes mellitus and their complications in the vein, neurological diseases, including common sclerosis, anemia [13].

Also elderly patients often have reduced physiological tolerance to aggressive and toxic effects. Due to age-related changes and/or diseases experienced, these patients often experience changes in drug absorption, distribution, activation, detoxification, and metabolism [30].

The volume of distribution of chemical preparations depends on the amount of adipose tissue and fluid in the body, the level of serum albumin and the number of erythrocytes. With an increase in age, an increase in the percentage of adipose tissue (from 15% to 30% of body weight), a decrease in the volume of total and intracellular fluid occurs. There is also a decrease in albumin and hemoglobin levels. Under such conditions, there is a possibility of increased toxicity of

cytostatics that bind to protein or erythrocytes (anthracyclines, taxanes, epipodophilotoxins, camptotesin, antpasenidions). Anemia transport may be the cause of decreased efficacy of erythrocyte-mediated drugs (anthracyclines, camptotesin). In addition, anemia can cause decompensation of cardiovascular diseases, which are very common in elderly people, as well as a decrease in tolerance to chemical therapy [21]. Coltman S.A., Dahlberg S., Jones S.E., Miller T.R. the severity of the patient's condition, the duration of the inpatient treatment, considers anemia to be the cause of the decrease in the duration of the patient's life [54]. All of the above explains the attempts to reduce doses and use low-aggressiveness chemical therapy to avoid the risk of developing serious toxicity. This in turn reduces the chance of recovery [11, 15]. SWOG was shown by an American Research Group to have a total frequency of remission of only 37% in patients with NXL over 65 years of age who received initial chemical therapy at reduced doses of cyclophosphane and doxorubicin, at which time the frequency of remission was 52% in patients who received full doses of cytostatics [76]. In some studies, deterrent regimens of chemotherapy allow high remission frequency to be achieved and are not observed with high toxic lethality [155, 131]. A 2-week modification of chop has been developed for elderly (over 70) individuals in which doxorubicin is replaced with epirubicin [7]: cyclophosphane 500 mg + farmorubicin (epirubicin) 30 mg + vincristine 1 mg + decortin 120 mg — v 1.8.15 days.

These works spurred control studies on the use of low-toxicity regimens in elderly patients. In most of them, approaches have been developed to reduce complications of cardiovascular disease, notably cardiotoxic doxorubicin with low cardiotoxicity mitoxantrone [13], idarubcin [3] replaced, or with less-than-life therapy with 1/3 administration of drugs 1 time per week [11, 13]. Zinzani in elderly patients R. Found equal indicators of efficiency and overall survival in reliable improvement of the toxicity profile when comparing the Chop and SIOP modes [11, 16]. The total number of remissions was 63% in the chop group and 59% in the SIOP group.

For the purpose of prophylaxis of cardiotoxicity of doxorubicin, cardioxan can be used. However, it should be borne in mind that this drug is not studied in elderly patients. In the literature on the possibility of increased hematological toxicity when it is applied, majwood data should be taken into account, which is especially important in patients over 60 years of age [11].

Particular attention is paid to the effectiveness of the treatment of NXL in elderly patients – in several promising randomized studies, the effectiveness of treatment was studied. In a study conducted in Canada, the effectiveness of weekly

administration of drugs at a dose of one-third of the standard was compared with the standard chop-21 regimen in patients with aggressive nxl over 65 years of age. There was no difference in total remission and survival rates before the outbreak, but overall 2 – year survival was statistically low in patients receiving weekly therapy-51% against 74%, respectively (R=0.05). A study in the Netherlands compared chop and Snop efficacy in diffuse V-large cell lymphoma in patients over the age of 65 [142]. The frequency of complete remissions was 49% and 31%, respectively, and the 3-year total survival was 42% and 26% respectively. An EORTC led brogan randomized study used chop therapy or etoposide, mitoxantron, prednimustin-containing regimen in patients over 70 years of age with aggressive lymphomas [12].

The frequency of complete remissions without outbreaks and 2 years of viability were higher in the chop group, at 77% and 65% respectively, at which time in the comparison group these indicators were 50% and 30%, respectively. One of the randomized studies of the GELA group was conducted in patients with follicular lymphomas. Patients over 59 years of age received doxorubicin, teniposide, and fludarabine or cyclophosphamide in combination with prednisolone and interferon [1]. The use of tcyclophosphamide was observed with a high frequency of achieving complete remissions, while 2-year survival without treatment without success was 63%, with 49% (R<0.05) in patients taking fludarabine. Overall survival was also low in the group of patients who used fludarabine in their treatment – 62% and 77% respectively (r<0.05).

Although elderly patients admitted to control studies have had a certain choice [7], the results of most studies have shown that they are in a state of tolerance to regimes that include anthracyclines, in particular – doxorubicin [9, 12].

In this case, in the relatively good condition of patients, the results of their treatment did not differ from the results of therapy in younger patients, which was confirmed by the results of studies of the German group of aggressive NXL (DSHNHL). The intensity of the CHOP-21 regime by reducing intervals between courses – the chop-14 scheme and the condition for the use of G-KSF, increased the effectiveness of therapy in elderly patients: the frequency of complete remissions increased from 63% to 77%, 5-year survival from 50% to 64%, the median of observations was 40 months [3, 19].

Thus, the tendency to reduce the dose of drugs does not justify itself in the group of elderly patients who are in a good somatic state. Patients should receive similar regimens that can be reduced in the case of standard therapy or poor tolerance [19]. Patients whose somatic condition does not allow conducting

monand therapy according to the morphological variant of nxl should receive chemistry (hormone) therapy, which is maximally effective at least toxicity, and when it is impossible to conduct it – palliative treatment [9, 19].

There is follicular lymphoma with both local and general stages of the tumor somatic in weakened elderly patients, monotherapy with alkylating drugs (chlorambusil, cyclophosphane) is used [16]. In most cases (75% of patients), tumor regression is achieved, but there are very few cases when complete remission is achieved [4]. Elderly patients with a satisfactory somatic condition, indolent NXL, may undergo therapy similar to that in young patients [2].

Follow-up therapy, in particular the use of Colony-triggering factors, makes it possible to significantly reduce the period of neutropenia and, accordingly, reduce the risk of infectious complications, which significantly reduces the number of toxic lethal cases [5, 17]. This makes it possible to prescribe aggressive regimens of chemical therapy (for example – chop-14) in elderly patients.

In 1997, the introduction of the first monoclonal antitanes, rituximab (Mabtera), into practice, showed efficacy in pre – clinical research as well as safety in CD-20 positive lymphoproliferative processes.

Rituximab has found widespread use in V-cell indolent and aggressive lymphomas due to its high anti-tumor efficacy as well as its low number of opposite effects[15].

Started in 1988, the results of the first large multicenter randomized study of the Gela group are impressive, in which the diagnosis of diffuse V-large cell lymphomas was confirmed, with patients over 60 years of age involved. The inclusion of Mabters in the Chop-21 scheme has been shown to reliably increase its effectiveness in elderly patients with NXL with high levels of risk. A comparison of the R-chop - 21 and chop-21 schemes in 328 patients confirmed that the introduction of Mabters into the chop scheme increased the frequency of total remissions by 82% compared to 66%, the frequency of complete remissions by 63% to 76% (r=0.005), and the 2-year survival by 70% compared to 57% (r=0.007). Initial data on these long results were also confirmed in subsequent observations: a clear improvement in the overall survival rate was 5 years (R-chop-5 years in the 21 group accounted for 58% of total survival, and 45% in patients treated under the chop scheme) and was observed in the 7 – year period-overall survival was 53% and 36%, respectively [50].

The difference between patients receiving therapy on R-chop and chop schemes is surprising when a detailed review of 7 – year overall survival in age subgroups: at 60-69 years of age, overall survival was 58% and 40% respectively, at 70-74 years of age – 41% versus 55%, and at 75-80 years of age, the difference

was most significant-at 21% versus 41% [9]. The use of the R-chop-21 scheme significantly reduced the risk of therapy failure and death (risk levels of 0.58 and 0.64, respectively). These results were obtained without major changes in clinically significant toxic symptoms [5], however, in a group of patients who received R-chop-21, a tendency to frequent development of infections was noted (in 12 cases out of 202 compared to 6 out of 197).Increased efficacy of follicular lymphoma therapy when the Sor scheme is enhanced with mabtera is demonstrated by m39021 (Marcus R. and hammual)study. In 2003, her findings on the comparative study of CVP and CVP circuits in harmony with mabtera (R-CVP) were published in 322 patients in Phase III-IV of follicular lymphoma in I-line therapy. When they were compared, it was revealed that 8 cycles of R-CVP increased the frequency of total responses to 81% compared to 57% in the CVP group ($r<0.0001$). The frequency of complete remission and unconfirmed complete remissions when mabtera was used was 41% and 10% in the CVP group ($r<0.0001$). Observations showed that the period without relapses in the R-SVP Group extended to 7 months when it lasted 18 months, and the risk of treatment without success fell by 67%. These results were obtained without significant change in the tokcyclic profile [108]. The use of the R-COP scheme made it possible to increase the time median by almost 4 times until treatment without success (up to 27 months) [109].

Studies in Russia also showed an increase in efficiency when using the R-COP scheme compared to the COP scheme (patients receiving COP had an eventless survival median of 7 months, while the R-COP scheme did not achieve). In the treatment of patients with follicular lymphoma, supportive therapy is a special aspect, aimed at increasing the period without recurrence and overall survival. Alpha-interferon (a-IFN) was used to improve long-term outcomes before the mabteras were put into practice. The effectiveness of using a-IFN as a supportive therapy in follicular NXL, whose prognosis is negative (symptoms of intoxication, large tumor masses, presence of foci of extranodal injury), has been shown: prolonged use of a-IFN 3 times a week at a dose of 3 = 5 ME (for 18-24 months) reliably prolongs the median of irreversible survival by 17 months [2, 15].

Supportive therapy provides for the cessation of disease progression using the onset of a-IFN effects after full remission has been achieved or from the moment of partial remission onset (the duration of the period without relapses as well as the frequency of relapses did not depend on the use of a-IFN) [8,17].

In Europe (1998), a conducted meta-analysis of a-IFN application results in 136 centers showed reliably that its use in low-risk nxl should be the standard method of supportive therapy, the results of its use should be reliably good when used against a PR background, the dose of a-IFN in supportive mode should not be

less than 9 mln. The duration of treatment should be at least 1 month, when administered three times a week (the results deteriorate 2 times when the total weekly dose decreases).

Compliance with these rules improves 5-year survival by 20% (50% vs. 70% without a-IFN supportive therapy). But the use of a-IFN was limited by its relative complexity and toxicity to the patient. Mabtera's efficacy as well as satisfactory efficacy have been confirmed in several different randomized studies. According to the results of the EORTC 20981 study, the effectiveness of supportive therapy with mabtera does not depend on the completeness of the effect achieved-it is effective when both complete and partial remission are achieved. The effectiveness of supportive therapy improves long-term outcomes by more than 3 times when using print circuit induction (the median of the period without relapses is 42.2 and 11.6, respectively). When using rituximab during the induction period, the difference in results can also be clearly seen (52 and 23 months, respectively).

Judging from the data in the literature, rituximab is a drug with high efficiency, patients have satisfactory efficacy against it, and it can be used with expressive clinical effect in monorrhea in the elderly with indolent lymphomas. Mabtera is also used as supportive therapy once complete or partial remission is achieved. Supportive therapy with Mabtera reliably increases overall survival in primary patients with follicular lymphoma. Thanks to such therapy, the survival from treatment free from failures increases to years, not very – months.

Thus, analyzing the data on the problem of clinical and immunological specificities of NXL in elderly people given in the literature, it can be said that these issues are coming without full development. Of particular interest is the determination of the likelihood of chemotherapy in elderly patients, as well as the ratio of the likelihood of obtaining the expected result with possible complications, which greatly affects the quality of life of patients. Most studies have focused on determining the possibility of monand therapy in somatically maintained patients and – if necessary-intensification.

A special direction is the attempt to develop a comprehensive assessment of the functional state of elderly oncological patients, which allows you to combine geriatric and oncological predictive measurements, more accurately assess the individual functional reserves of the body, the approximate duration of life and, accordingly, tolerance to chemical therapy.

The analysis of any clinical aspects in elderly individuals is not carried out in full size, without considering the problem of polyinoplasia.

Primary-multiple malignant tumors or polyneplasia – concomitant or one-on-one occurrence of neoplasms.

The initial published observation of primary-multiple tumors is a condition described by Abu Ali ibn-Sina (Avisenna) as bilateral lesions of the mammary glands. In the first half of the XIX century, separate reports of primary-multiple tumors also appeared in European literature. Interest in the study of polineoplasias has grown with an increase in clinical observations and experimental studies that allow identification of specificities in the development and incidence of malignant tumors. In the structure of oncological diseases, the frequency of polineoplasias, on average, is 13 – 15% [13]. With the accumulation of clinical and sectional data, the criteria for primary multiplicity were formed:

1) each tumor must have a specific rate of malignant tumor;

2) tumors should be located separately;

3) it is necessary to exclude as much as possible the possibility of metastasis from one tumor as compared to another [18].

Polineoplasias develop independently and separately from each other within one or more anatomical areas of the human body. Depending on the duration of development and/or diagnosis, polineoplasias are classified into synchronous (diagnosed at the same time or in series within 6 months) and metachronous (diagnosed in the longer term of 6 months). It is also considered significant that when several tumors begin to develop at the same time, one of them, with a more intensive growth tempo, can present clinically aggressively as well as be diagnosed earlier [15]. The use of modern endoscopic and ultrasonic methods, as well as computed and magnetic resonance tomographs, serological, immunological and immunoformological studies, makes it possible to identify tumors during the pre-clinical period of their development.

Currently, the detection of many tumors when targeted examination of patients using the best diagnostic methods is higher than the probability of detecting them when routine clinical observation of oncological patients, or of random "findings" in autosopia [78, 159, 163]. The results of a large selection of estimates of the expected and original frequency of primary multiple malignant tumors showed that the risk of developing second and subsequent malignant tumors was approximately 1.3 times higher in patients who had been diagnosed with tumors compared to individuals who had not been previously observed [15]. The risk of the occurrence of malignant tumors, including polineoplasias, is determined by the intensity of exposure of negative factors in the external environment, their degree of hereditary predisposition to development and other factors. There is an opinion that in the formation of tumors, carcinogens, genetic identities of patients, as well as the age of the patient (over 60 years old) perform the main role [6, 8, 13]. In patients with lymphoproliferative diseases observed

with expressive immunodeficiency, a state of development of second and subsequent tumors is most common. The problem of polineoplasias is considered relevant for elderly patients, since the risk of developing both lymphoproliferative diseases and large tumors increases with a greater age.

N.E.Kosich, S.3.Savani, D.V.According to Smirnov primary-with a large number of tumors, the incidence increases more and more by the age of 65, followed by a sharp increase in the incidence of the disease in patients aged 80 years and older [2, 8]. D.M.Abdurasulova I K.E.Nikishina brings interesting data: in individuals who died at the age of 70-73 years – primary multiple tumors were observed in 13.5% of cases, and at 80-90 – in 14.8%, and over 90 – in 22.7% of cases [8, 9, 12]. In addition to the age factor, the increase in metachronous polineoplasias is influenced by improving the survival rate of patients with both large tumors and lymphoproliferative diseases. The main part of the work currently published is devoted to the study of various harmonies of large O'osmas with a large number of Primary [8, 9, 12].

In conclusion, it can be said that there are a small number of large-scale, epidemiological significant cases covering all age categories of elderly patients. The most studied group is 60-79-year-old patients with diffuse V-large cell and follicular lymphomas. The clinical and morphoimmunological specifics of nxl in elderly patients are practically defined in the general structure of nxl. The main problem of elderly patients is somatic pathology without a side tumor as well as age changes that determine the general condition and the possibility of using chemotherapy as a consequence. It is worth mentioning that in geriatric practice, ADL and IDAL measurements have been developed and are being used to determine the general condition of patients.

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