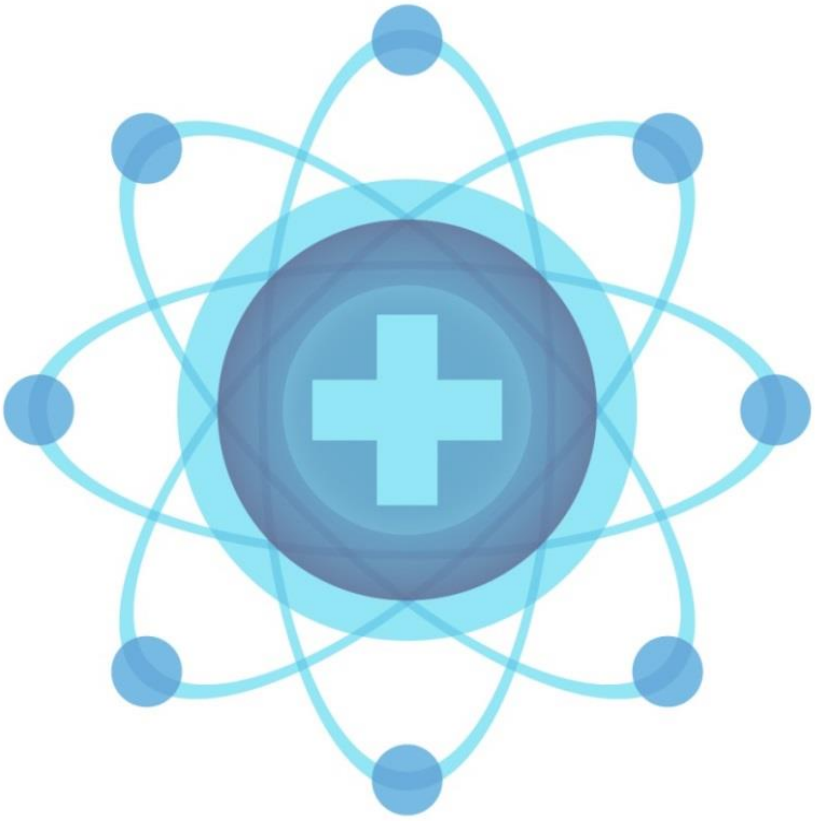

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FEATURES OF THE TREATMENT OF PATIENTS WITH HER-2/NEU+ TYPE OF BREAST CANCER

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Abstract: Research work was done in 106 patients with breast cancer stage I-II with 2/neu+ (positive) who were treated chemically in inpatient conditions, and a control group was selected from 26 patients diagnosed with 2/neu+ (negative) breast cancer during 2015-2020 at the Samarkand region branch of the Republican specialized oncology and radiology scientific-practical medical center. As a result, p53, VEGF and Ki-67 were found in 73.3, 80.0 and 76.7% of cases in the study of molecular-biological markers of tumors; The presence of Bcl-2 markers, the presence of EGFR in 36.7 and 30.0% of cases was determined. The greatest prognostic value in evaluating the effectiveness of the treatment was determined by the following markers: p53, VEGF, Ki-67, and correction of the therapy used in the treatment was recommended. The analysis of the main parameters of the immune system, clinical and biochemical parameters indicated the need for immunotherapy and the effectiveness of polyoxydonium in the complex treatment of Her-2 patients was proven.

Relevance

Breast cancer (BC) is one of the most important social problems in the world. It is now well known that breast cancer (BC) morbidity and mortality are increasing worldwide. This disease, according to world statistics, has a progressive increase in less developed countries.

The main way to reduce breast cancer mortality is through early diagnosis, and it has been confirmed that the disease is more common in women aged 35-40 years [11,12].

Breast cancer is the most common type of cancer, with more than 2.2 million cases in 2020. Breast cancer affects one of every 12 women. Breast cancer is the leading cause of death for women. An estimated 685,000 women died from the disease in 2020 [1].

There is a significant difference in the incidence of breast cancer between developed and underdeveloped countries: over 90% in developed countries in the last five years, but only 66% in India and 40% in South Africa [3-4].

According to the statistics of Russia and CIS countries, breast cancer takes the leading place in Russia 18-22%, in Belarus, Kazakhstan and Kyrgyzstan 25-33%, in Uzbekistan, Azerbaijan and Armenia up to 25% [7-9-10].

In Uzbekistan in 2008-2010 the intensive breast cancer incidence rate was 7.6% per 100,000 population, the standardized rate was 13.2%, which corresponds to the

world rates. In Uzbekistan, the incidence rate by regions ranges from 4.2% to 19.5%, the highest rate in Tashkent city, Bukhara, Navoi and Tashkent regions, and the lowest in Kashkadarya and Surkhandarya regions [8].

Dowsett M. and a group of scientists have stated that the increase in ER+PR+ receptor breast cancer is related to the age of patients, with a 17.6% increase in disease at ages 43-47, an increase in disease before age 50 [2].

The level of breast cancer carcinogenicity has changed significantly over the last decade. This is due to the study of molecular and biological features that influence the clinical course of the disease and the choice of optimal treatment tactics [5,6, 12].

Objectives

To evaluate methods of treatment and prevention of her-2/neu+ (positive) breast cancer patients.

Materials and methods

Between 2015 and 2020, 106 patients with her-2/neu+ (positive) expression were taken from 106 breast cancer patients of stage I-II who received chemotherapy at the Samarkand regional branch of the Republican Center for Specialized Oncology and Radiology. The control group consisted of 26 patients diagnosed with her-2/neu+ (negative) breast cancer.

Clinical, morphological, immunohistochemical, immunological, molecular-biological, instrumental, genetic and statistical methods were used in the work to analyze the results of complex treatment of her-2/neu+ (positive) breast cancer.

Results

We studied the characterization of a group of breast cancer patients, immunohistochemical detection and assessment of Her-2 receptor status in RBCs, as well as comparative evaluation of Her-2, Ki-67 expression levels with different ER+ and PR+ phenotypes in RBCs.

The 106 patients included in this study were divided by stage as follows: 28 patients (26.4%) T1N0M0 (stage I), 34 patients (32.1%) T2N0M0, T1N1M0 (stage IIa) 44 patients (41.5%) T2N1M0 (stage II b) (see Figure 1).

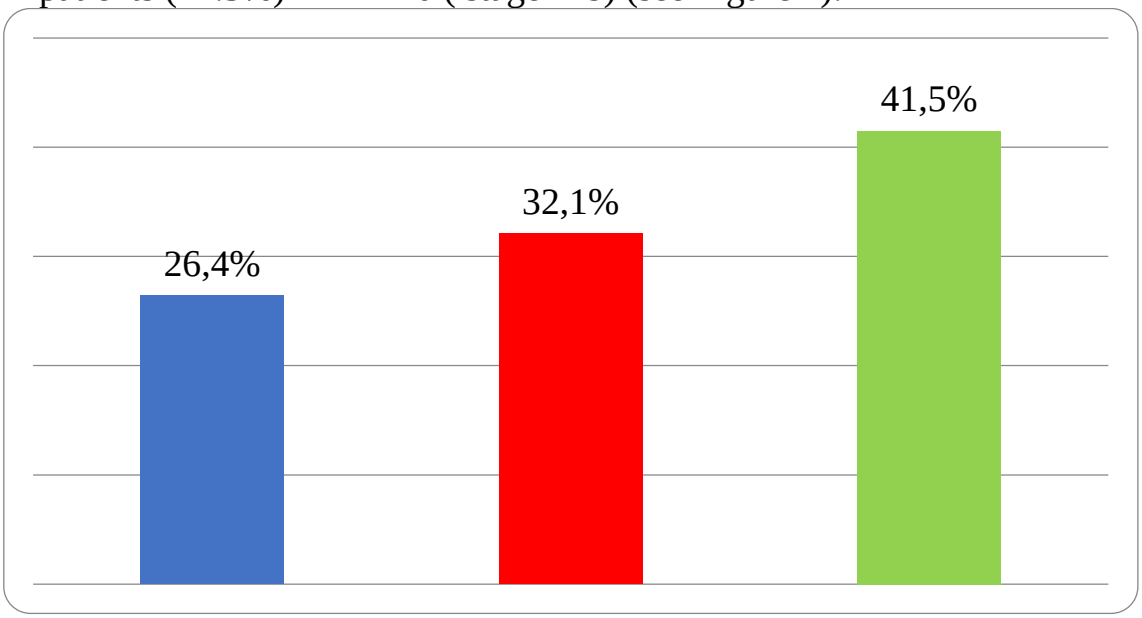

Figure 1. distribution of patients diagnosed with breast cancer depending on the stage of the process

The results of the study showed that in patients with PPS Her2(+), histological malignancies of high malignancy grade were more frequent in the analysis of malignancy grade. In a retrospective analysis of patients with low-grade malignancy G1-4 (3.8±0.3%), the majority of cases with an average grade of tumor malignancy were G2 - 63 (59.4 ± 4.1%), high grade G3 - 39 (36.8 ± 3.3%). %) was described. Correlation analysis showed an inverse correlation of malignancy process with the age of the patient.

According to the results of the study, significant expression of Her-2(++) was detected in 38.7% of patients, Her-2(+++) - in 25.5%, Her-2(+) - in 21.7% of patients. , justifying trastuzumab therapy, allows us to order. Her-2 phenotypes were detected with equal frequency, analysis of age groups revealed no significant difference. Among patients younger than 49 years of age, there was a tendency for Her-2 expression level to increase from 14% (Her-2(0)) to 38.7% (Her-2(++)), while in the elderly group (>60 years) tumors were frequently observed, Her-2 expression was undetectable and not statistically significant. No correlation between tumor size and Her-2 expression level was found in the studied groups.

The evaluation of Ki-67 expression level depending on ER and PR phenotypes revealed a negative correlation with the expression levels of ER-r=-0.36 and PR-r=-0.42 ($p<0.01$), which indicates the expression levels of estrogen and progesterone receptors, the higher, the lower proliferative activity (see Table 1).

Analysis of the obtained data shows that Ki-67 expression level has an inverse dependence on PR expression level; the table shows that Ki-67 level in PR (+) is 23.6%, in (weak+) - 30.2%, (negative) - 46.2%, that is high proliferative at SBS with weak positive expression It was found that index PR, and with negative ER/PR it significantly increased in comparison with positive state ER+/PR+ ($p<0.01$).

The higher the level, the higher the expression of Ki-67, which is determined by the severity of proliferative processes, aggressive nature, and unfavorable outcome of the disease. Increased expression of Ki-67 when assessing the expression of the progesterone receptor, dependent weakly positive expression of RP, allows us to characterize these ER-/PR- phenotypes as ER-/PR+ predictors of the disease and an unfavorable (negative) course of the disease.

Table 1.

Morphological characterization of patients according to Her-2 and Ki-67 expression levels

HER-2/neu gene expression:		
no expression	15 (14,2%)	
«1+»	23 (21,7%)	
«2+»	41 (38,7%)	$\chi^2=13,396;$ $p<0,01$
«3+»	27 (25,5%)	
Ki-67 expression:		
up to 20%	4 (3,2%)	
up to 40%	13 (10,3%)	$\chi^2=31,453;$
up to 60%	22 (17,5%)	$p<0,001$

up to 80% up to 95%	44 (34,9%) 43 (34,1%)	

Ki-67 level and ER (r=-0.48) and PR (r=-0.44) expression were also negatively correlated, that is, the higher ER and PR expression, the lower the proliferative activity.

Analyzing the above, we can conclude that the maximum reduction of the side effects of chemotherapy in the treatment of SCC patients, as well as improving their quality of life through the use of polyoxidone immunotherapy significantly improves immunological parameters in NAChT for SCC patients.

According to the study of molecular biological markers of tumors in this scientific study p53, VEGF and Ki-67 were detected in 73.3, 80.0 and 76.7% of cases, respectively; Bcl-2 markers, the presence of EGFR was detected in 36.7 and 30.0% of cases.

The level of the following markers had the greatest prognostic value in assessing treatment efficacy: p53, VEGF, Ki-67, PA. This allows us to recommend the therapy used in the treatment process as an opportunity for correction and control.

The study of the main parameters of the immune system, clinical and biochemical parameters made it possible to perform immunotherapy, create a preparation algorithm for SCC patients. The main factors in selecting the method of complex treatment of SCC patients in Her-2 state for further immunotherapy are: tumor size up to 10 cm; low level of comparison; Positive (positive) level of R-53, VEGF, Ki-67, considered high proliferative activity.

Conclusion

A retrospective analysis of breast cancer patients with Her-2 overexpression was performed, in which 36.8% of cases were diagnosed as malignant on the basis of high histological findings. An inverse correlation was found between the age of patients and the degree of tumor malignancy (r=-0.78).

Negative factors of neoadjuvant polychemotherapy included: high Ki-67 proliferative index (93%), grade II-III malignancy (96.2%). Correlation analysis showed that there was a correlation between the patient's age and tumor size (r=03), i.e. the older the patient, the larger the tumor size, a proportional relationship was detected.

Inclusion of the immunomodulator into the scheme of chemotherapy for breast cancer patients who underwent repeated immunotherapy with polyoxide preparation enabled to provide immune response similar to the humoral link of immunity and underdevelopment of cells, in which the decrease of CD3, CD4, CD16 lymphocytes was revealed. Inclusion of immunomodulator in the control scheme of immunotherapy requires determination of the activity indicators of the cellular and humoral parts of the immune system.

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