ANDROGEN RECEPTOR VALUES FOR PREDICTION OF SURVIVAL OF PATIENTS WITH THREE TIMES NEGATIVE BREAST CANCER

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ABSTRACT

Breast cancer retains its leading position in terms of the incidence of malignant neoplasms in women. Triple negative breast cancer (TNBC) accounts for 12–20% of the entire group of breast cancers (BC). TNBC is characterized by the absence of estrogen receptors (ER), progesterone receptors (PR) and HER-2/ neu expression. This study shows that the presence and detection of androgen receptors (AR) by IHC-expression of TN breast cancer cells opens up prospects for the development of targeted therapy for this type, taking into account the presence or absence of androgen receptors. To rationalize the therapy of TN in breast cancer, it is certainly necessary to summarize a large number of materials with a thorough analysis of all clinical and morphological parameters, taking into account survival rates and the options for chemotherapy regimens used. Thus, breast cancer TN is currently an unresolved scientific and practical problem in the field of oncology, requiring additional research both in terms of finding optimal approaches to the use of already available diagnostic and treatment options, and in searching for new treatment options, as well as fundamental research. in the field of studying the biological characteristics of the disease. The definition of AR is an important factor that plays a role in the prognosis of breast cancer in all molecular subtypes, especially in TN breast cancer, which can become a targeted target for planning targeted therapy. In the course of the study, informative and significant clinical, morphological and parameters were studied and determined on the basis of the prognosis model, allowing with a sufficient degree of probability to predict the outcome of the disease in patients with TN, including when determining a positive AR status, which determines a more favorable prognosis. The presence and detection of androgen receptors (AR) by TN breast cancer cells during IHC-expression opens up prospects for the development of targeted therapy for this type, taking into account the presence or absence of androgen receptors.

Thus, androgens, like estrogens, can act as stimulators of breast cancer cell proliferation, which requires study, which was carried out in this study.

KEYWORDS: *triple negative breast cancer, androgen receptor (AR), prognosis.*

INTRODUCTION

Currently, breast cancer is one of the five most common cancers in the world and is the leading cause of death for women under the age of 50. Detection of breast cancer during preventive examinations throughout the country remains low, and the rate of neglect IIIB - IV stage , which is the leading criterion for the quality of diagnosis, on the contrary, is high. The real way to improve the results of treatment of breast tumors is early, and in some cases, preclinical diagnosis [1,6] .

These features of the tumor and the clinical course, as well as the limited therapeutic arsenal, cause an unfavorable prognosis of the disease, and, accordingly, a low survival rate of patients, even when treated in patients with early stages of the disease, especially in advanced processes. This requires the search for new approaches to treatment, as well as diagnostics, which was the main motive for this scientific study [3].

Determining the level of androgen receptors in the tumor in patients with breast cancer is a very relevant and promising direction in studying the prognosis of the disease and finding new additional approaches to the endocrine therapy of breast cancer, especially with a basal-like molecular subtype [2,4] . In domestic and foreign literature, there has recently been an increased interest in the study of androgen receptors (AR) in various molecular subtypes of breast cancer [5,7] .

Thus, androgens, like estrogens, can act as stimulators of breast cancer cell proliferation, which requires study, which was carried out in this study.

PURPOSE OF THE STUDY

The purpose of the study is to determine the presence of androgen receptors (AR) in triple-negative breast cancer cells by

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immunohistochemistry and evaluate its role in the diagnosis and prognosis of the disease.

MATERIALS AND METHODS .

To solve the set tasks and achieve the goal of the study, pathomorphological, immunohistochemical and statistical methods were used. There were 126 patients with TNBC (T1-4N0-3M$_0$), who received in 2015-2018. complex treatment in the department of oncomammology and chemotherapy of the Tashkent city branch of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology. To determine the significance of RA and their role in the treatment of patients with TN breast cancer, an IHC study was conducted to determine the level of its expression. Immunohistochemical examination was carried out according to this technique on the basis of the diagnostic clinic Mediofarm Ltd. "PREMIUM DIAGNOSTICS". Androgen expression was assessed according to DAKOHercep criteria. Test ™. Only the membrane reaction was taken into account. To control the quality of the immunohistochemical reaction, before assessing the degree of androgen expression according to the HercepTest criteria , normal mammary ducts were analyzed on the same section. In the absence of a reaction in them, the results of an immunohistochemical study were recognized as reliable.

RESULTS AND THEIR DISCUSSION

The evaluation of treatment results began with a statistical analysis of the prognostic value of the signs that affect the outcome of the disease. In patients in the study groups, the distribution of patients was as follows: among the group of patients with breast cancer with AR (-) status, patients aged 35-44 years prevailed - 41.5%, and with AR (+) status aged 45-64 years - 39, 3%, average age with AR (+) status among patients was higher than that of AR (-) (60.0±13 years and 57.1±12 years, respectively). No correlations were found between the levels of AR and the age of patients (r = 0.01; p> 0.05), (Table 1).

An analysis of the level of presence or absence of AR depending on menstrual status showed that the majority of patients with AR (-) menstruated - 35.4% or were in perimenopause - 32.3%, which cannot be said with AR (+) status, in which a large some patients were in menopause - 47.5% (r = 0.03; p > 0.05). The distribution of patients according to the stages of the tumor process depending on AR showed that with AR (+) status, the bulk of patients were in stages IIb - IIIa , which amounted to 29.2% and 20.0%, respectively. With AR (-) status, the largest number of patients had stage IIIb - 34.4% (r = 0.13; p > 0.05).

Table 1.
Characteristics of patients depending on AR status

	Characteristics of the tumor process	AR status		
		AR (-) (n=65)	AR (+) (n=61)	Total patients (n=126)
Age group (n=126)	<35 years old	13 (20.0%)	11 (18.0%)	15 (11.9%)
	35-44 years old	27 (41.5%)	18 (29.5%)	45 (35.7%)
	45-64 years old	16 (24.6%)	24 (39.3%)	40 (31.7%)
	>65 years old	9 (13.8%)	8 (13.1%)	17 (13.5%)
Menst - royal status	Menstruating	23 (35.4%)	5 (8.2%)	28 (22.2%)
	perimenopause	21 (32.3%)	9 (14.8%)	30 (23.8%)
	menopause	12 (18.4%)	29 (47.5%)	41 (32.5%)
	postmenopause	9 (13.8%)	18 (29.5%)	27 (21.4%)
Stage	I (n =12)	9 (13.8%)	3 (4.9 %)	12 (9.5%)
	IIa (n =19)	13 (20.0 %)	6 (9.8 %)	19 (15.1%)
	IIb (n =28)	19 (29.2 %)	9 (14.8 %)	28 (22.2%)
	IIIa (n =27)	13 (20.0 %)	14 (2 3 , 0 %)	27 (21.4%)
	IIIb (n =31)	10 (15.4 %)	2 1 (3 4.4 %)	31 (24.6%)
	IV (n =9)	1 (1.5%)	8 (13.1 %)	9 (7.1%)
Histology	Invasive ductal carcinoma, (n =84)	43 (66.2%)	41 (67.2%)	84 (66.7)
	Lobular cancer , (n=14)	11 (16.9%)	3 (4.9%)	14 (11.2%)
	Medullary cancer , (n=19)	8 (12.3%)	11 (18.0%)	19 (15.1%)
	Apocrine cancer (n= 7)	1 (1.5%)	6 (9.8%)	7(5.6%)
	Metaplastic . cancer , 0 (n=2)	2 (3.1%)	-	2 (1.6%)
G	III degree (n= 0)	-	-	-
	II degree (n=57)	14 (21.5%)	43 (70.5%)	57(45.2%)
	I degree (n=69)	51 (78.5%)	18 (29.5%)	69(54.8%)

Evaluation of the degree of breast cancer depending on AR status showed that with AR (-) the largest number of patients had G -3 – 78.5%, and with AR (+) – G -2 – 70.5% (r = 0.13; p > 0.05) of the disease stage. According to the histological forms of breast cancer in AR (-), as well as in AR (+), the largest number of patients had invasive ductal cancer, which amounted to 66.2% and 67.2%, respectively. With AR (-), lobular cancer had a significant advantage, which occurred in 16.9% of cases, and with AR (+) medullary cancer was relatively common – 18.0% (r = -0.09; p >0.05).

Table 2
AR expression level on a 3-point scale

AR, points	Total patients (n=126)
0	59 (46.8%)
1	6 (4.8%)
2	13 (10.3%)
3	48 (38.1%)

As can be seen from Table 2, in most cases, the severity of AR corresponded to 3 points (38.1%). In the absence of the severity of AR in all patients, a non-specific form of breast cancer with II or III degree was verified. In patients in the study groups, the distribution of patients was as follows: in 61 (48.4%) - positive expression of AR (+) was found, in 65 (51.6%) - AR (-) negative. The histological grade of malignancy in AR(-) was higher than in patients with AR(+) tumors.

CONCLUSIONS

This study shows that the presence and detection of androgen receptors (AR) by IHC-expression of TN breast cancer cells opens up prospects for the development of targeted therapy for this type, taking into account the presence or absence of androgen receptors. In conclusion, it can be concluded that the lack of AR expression in breast cancer patients determines the worst prognosis, despite the more favorable molecular subtype of the tumor.

LIST OF USED LITERATURE

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