Epigenetic regulation of the proliferation in breast tumours

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Abstract

The study was aimed was to compare the activity of gene methylation GSHR in patients with breast cancer and patients with fibro- cystic mastopathy. There was demonstrated that mean activity GSHR gene methylation in patients with breast cancer is significantly higher than in patients with FKM (respectively $51,6 \pm 2,5\%$ and $4,9 \pm 1,2\%$. Determined confidence intervals for the parameter methylation activity suggest that when it values above 24.9% can not exclude the development of malignant tumors of the breast.

Key words: breast tumours, epigenetics, diagnosis.

The problem of improving early diagnosis and prediction of breast cancer (BC) remains one of the most pressing contemporary oncology practice [1-3]. At present the only real way to successfully reduce mortality from breast cancer is to improve the quality of early diagnosis. According to the National Cancer Registry over the world for the past 30 years, mortality from breast cancer increased by 30 % , with those suffering from this disease mostly women active working age. Unfortunately in transition economies running shape breast cancer is about 50 % of all diagnosed cases, patients with Stage I form no more than 15-20 % in the total incidence of breast cancer. It should also be noted that the five-year survival rate for early detection of breast cancer is 95-97 %, whereas in the 3rd stage - only 45-50 % [1 , 2].

Current clinical protocols involving the use of an algorithm for the detection of early breast cancer with the release of three main phases [4]. On the stage of screening there were conducted bilateral ultrasound (women under 35) and mammography (for women older than 35 years). For diagnostic methods there is necessary performed general clinical examination and cytology. Finally, at the stage of in-depth diagnostic studies used the entire arsenal available in modern oncology research methods including radioisotope , morphological, clinical laboratory , medical genetics etc. .

In recent years more and more popular in the world acquire methods for studying epigenetic factors of predisposition to cancer [5]. Thus, the study of national and Western experts convincingly proved that despite the relative rarity of mutations in CTNNB1 FIS or breast cancer , activation of signal transduction in the Wnt- cell path plays an important role in oncogenesis . Thus one possible mechanism controlling the proliferative activity of tumor cells can act epigenetic gene activation antahonystiv Wnt, including members of the family Dickkopf (DKK). So DKK4 gene methylation plays an important role in the development of breast cancer. On the other hand, given the pathogenic role of processes of detoxification of xenobiotics and peroxide stress in breast tumorogenesis is considerable interest in epigenetic regulation of gene activity of glutathione reductase (GSHR). However, until recently, such studies either in Ukraine or abroad was conducted.

The aim of the study was to compare the activity of gene methylation GSHR in patients with breast cancer and patients with fibro- cystic mastopathy .

Material and methods. Research carried out at the Regional Oncology Center and the Regional Hospital (Odessa) during 2010-2011 were examined according to clinical protocols approved by the Ministry of Health orders number 676 100 women , including 50 - with verified breast cancer , and 50 - with FCM . In addition to routine methods The study gene methylation activity GSHR using a test set EpiTect QIAGEN (USA). Purified DNA samples were obtained from whole blood of patients , taken on an empty stomach by the standard method .

Statistical analysis was conducted using the nonparametric Wilcoxon criteria and the Mann- Whitney test in complex software Statistica 8.0 (StatSoft Inc., USA) ..

The results of their research .

Averaged age of the patients was 51,5 ± 1,8 in patients with breast cancer and 35,3 ± 1,5 years in the group of patients with FCM . In determining the frequency of various forms of FCM in patients found that they often recorded fibradenoma (19 cases or 63.3 %), much less met local fibroadenomatoz (6.6 %), adenomatosis (6.6 %), solitary cyst of breast and other forms.

Burdened gynecologic history and hereditary identified in 50.0 % of patients with FCM and 70.0 % of breast cancer. The majority (62.0) patients with FCM were related gynecological diseases , including PCOS, endometriosis and uterine fibroids. However , in the group of patients with breast cancer concomitant gynecological pathology identified in 46% of cases.

In patients with breast cancer frequently encountered tumor stage T2 (23 cases, ie 76.0 %), less T1 (18.0 %), in rare cases - more advanced stage. In three cases identified metastasis to regional lymph nodes (N1- 2). Distant metastases were not in any patient.

When comparing the activity of gene methylation GSHR (Table 1) revealed that in the group of patients with breast cancer average ratios were an order of magnitude higher than the values set out in patients with FCM .

Due to the presence of statistically significant differences in age of patients with breast cancer and FCM to exclude the influence of the age factor were calculated weighted methylation activity coefficients.

Table 1

GSHR gene methylation in clinical groups

Groups	number	M	σ	m
Breast cancer	50	51,6	13,6	2,5
Benignant tumour	50	4,9	6,6	1,2

In their comparison we determined that the difference between groups is statistically significant (Z = 4,7 p = 3,0 x10- 6). Thus, the values of GSHR gene methylation in patients with tumors of the breast less 17.5% (M +1,96 σ) is the probability of malignant neoplasms For breast cancer the activity of gene methylation GSHR above 24.9 %. When gene methylation activity values in the range 17,8-24,9 % solution of the nature of cancer should be taken with additional diagnostic criteria.

It should also be noted that women with FCM in 20 (40.0 %) cases GSHR gene methylation was absent . This explains the high variance in the index group.

Conclusions:

1. Mean activity GSHR gene methylation in patients with breast cancer is significantly higher than in patients with FKM (respectively 51,6 ± 2,5% and 4,9 ± 1,2%

2. Determined confidence intervals for the parameter methylation activity suggest that when it values above 24.9% can not exclude the development of malignant tumors of the breast

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