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Cluster analysis of breast cancer genes in reproductive and menopausal age of women

Abstract

The results of immunohistochemical studies at reproductive age (up to 45 years–72 Breast Cancer) and postmenopausal age (after 52 years - 330 case histories) are presented. Just studied 402 history mammography Department for the period 2016-2017 Luminal type in 3.18 times more often in postmenopausal age (79.6±2.1%) than in reproductive age 25±0.9%). At the same time, three times negative breast cancer was 3.3 times more often in the reproductive age, including with defects of repair BRCA 1 (6.2% of the surveyed). An interesting fact was the predominant frequency of HER - 2 positive cancer in reproductive age. The difference is statistically significant (for different types p = 0.002 and 0.05).

The difference in the frequency of occurrence of luminal type B in the studied groups is not statistically significant.

Keywords: breast cancer, morpho-molecular types, reproductive age, postmenopausal

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Introduction

Every year more than 1 million new cases of breast cancer are registered in the world and 400,000 women die from this tumor.[1] Breast cancer (BC) is an extremely heterogeneous disease that requires a personalized approach to treatment based on the identification of genetic targets and their targeted blocking.[2] Proposed at the end of the last century by Perou C. M. et al., classification is based on the allocation by cluster analysis of the four major gene expression patterns. Each type is characterized by the peculiarities of the tumor response to the treatment and different outcome of the disease.[2,3] After the immunohistochemical study, it is possible to determine which subtype B C we are dealing with and to build an optimal scheme of anticancer therapy. Thanks to immunohistochemical research, we can personalize the treatment of breast cancer and make it as successful as possible, in particular: in the case of luminal type A and B (with receptors re and RP), at certain stages, it is advisable to prescribe endocrine therapy, and in the expression of NR2/neu without the appointment of Herceptin, the appointment of chemotherapy is of low effect. According to the national statistics, the average detection of molecular subtypes of cancer based on the main immunohistochemical genes (ER, PR, Her2neu) (Table 1) in relation to the frequency index (gene Ki-67.) the proliferative activity of the tumor is presented in Table 1.

Table 1 Average ratio of frequency of detection of molecular subtypes of cancer according to the national statistics

Molecular subtype of breast cancer	ER	PR	Her2neu	Frequency of detection (%)	Ki-67 %
Luminal A	+	+	-	45-60%	5-10%
Luminal B	+	+	+	12-17%	10-15%
Her2 positive	-	-	+	8-13%	15-40%
Three times negative	-	-	-	8-20%	50-90%

Currently, the immunohistochemical study of the expression of receptors to estrogen, progesterone, HER2/neu, Ki67 is the "gold standard" choice of adequate tactics of management of patients. The features of tissue components expression depending on the histological form of cancer, tumor localization and the prevalence of the process were studied.[3–5] However, the incidence of morpho-molecular subtypes and other tissue and serum components depending on the menstrual age period of the woman has not been studied.

Material and methods of research

Excluding perimenopausal women, a comparative study of morpho-molecular subtypes of breast cancer in the reproductive age (up to 45 years – 72 breast cancer) and postmenopausal (after 52 years - 330 case histories). In total, 402 medical histories of the mammological Department for the period 2016-2017 were studied. The frequency of morpho-molecular types of breast cancer from the standpoint of clinical practice in our material for all patients was:

Luminal type A – ER (+) and PgR (+) / HER2 neu (-) -48, 4±1,2%, has the longest survival;

Luminal type B (triplet-positive) - ER(+) and/or PgR(+)/ HER2 neu (+) – 27,0±0.9% and is a fairly aggressive form of cancer, despite the hormone-dependence, chemotherapy can play an important role;

The Herceptin type-ER(-) / PgR(-)/ HER2 neu (+) - is intermediate (up to 13.6±0.4%);

Basal-like (triplet-negative) –ER (-) / PgR (-)/ HER2 neu (-) - has the worst prognosis (up to 10.2±0.3% on average).

Family history of cancer breast and ovarian cancer in young women and women with history of blood relatives with this disorder is an indication for the determination of BRCA1, BRCA2 and other inherited genes that affect the further plan of treatment (typically neoadjuvant therapy cisplatin; mono, then radical mastectomy). The issue of the second breast is solved individually. In addition, prognostic factors of breast cancer are G1-4, Kj67 (degree of differentiation of tumor cells or proliferative actinicity). The last tissue markers for each type of tumor reflect the aggressiveness of the tumor (e.g., Kj67<20% and>20%). The latter can be determined by DNA cytometry.

Luminal type a (Table 2) 3.18 times more often in postmenopausal age (79.6±2.1%) than in the reproductive 25%(±0.9%). At the same time, three times the negative breast cancer was 3.3 times more often in the reproductive age, including with defects of repair of BRCA 1 (6.2% to the number of examined). An interesting fact was the predominant frequency of NON-2 positive cancer in reproductive age. The difference is statistically significant (for different types p=0.002 and 0.05). The difference in the frequency of occurrence of luminal type b in the studied groups is not statistically significant. Thus, the results indicate a significant difference in the frequency of BC subtypes in different menstrual-age periods of women.

Table 2 Comparative morpho-molecular types of breast cancer depending on the biological status of women

Molecular subtype of breast cancer	Reproductive age		Postmenopausal age	
	Abs. number	Frequency of detection %	Abs. number	Frequency of detection %
Luminal A	18	25%(±0,9%)	263	79,63(±2,1)%
Luminal B	4	5,5%	15	4,54 (±0,1)%
Herceptin type	8	11(±0,3)%	15	4,54(±0,1)%
Basal-like*	42	58,4(±1,2)%	48	17.5(±0,4)%
just	72*	100,0%	330	100,0%

Note:* 4 patients with a mutation of the gene BRCA 1 was in the group with triple negative breast cancer.

Conclusion

a. Breast cancer is more common in menopausal age, exceeding the reproductive 4.5 times, in which the luminal type a was 79.63±2.1%, significantly exceeding the total population of patients with breast cancer.

b. Three times negative breast cancer was more often in 3.3 times, more often in reproductive age, including with defects of repair of BRCA 1.

c. The obtained results allow to plan the regimens and regimen of therapy, which should be based on molecular biological types and their connection with menstrual - age periods of the sick women.

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Conflict of interest

The author declares there is no conflict of interest.

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