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IMMUNOGISTOCHEMICAL CHARACTERISTICS OF BREAST FIBROADENOMA DISEASE IN WOMEN LIVING IN ARAL SEA REGION

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Annotation: Breast cancer (BC),- the most common cancer in women is considered. 1.5 million new cases are detected every year and this is 25% of all malignant tumors. The incidence is growing rapidly in European countries. Especially often this process develops against the background of dyshormonal processes, based on this, a retrospective analysis was carried out in order to identify the role of dyshormonal pathology in the development of precancerous diseases.

Keywords: *breast cancer, dyshormonal diseases, immunohistochemical, mastopathy, dyshormonal hyperplasia, fibroadenoma, precancerous diseases.*

Introduction

The problem of breast diseases is one of the priorities of modern medicine, of which benign breast dysplasia (BDD) is the most common disease. Their frequency in the population is 30-43%. The development of BDD can be the result of many reasons. Among them, neuroendocrine diseases play a major role, a large amount of information has been collected about the dependence of this disease on absolute hormones [5].

Mastopathy is a mammary gland disease, which is a large group of morphologically diverse hyperplastic conditions based on dyshormonal processes. Most of them are characterized by the replacement of glandular tissue with fibrous tissue and the formation of cysts, and are mainly found in women aged 20-25 to 45-50 years. According to the terminology of the World Health Organization (WHO), mastopathy is a fibro-cystic disease of the mammary gland, as a result of which a number of changes occur in its tissue. Mastopathy (fibrocystic disease, dysplasia of the mammary glands), which occurs in every fourth woman under the age of 30, in 50-60% of women aged 30-50, and less frequently in menopause [7].

There are diffuse, nodular and fibro-cystic types of mastopathy. In addition, it is noted that fibroadenoma, cyst, adenosis, cystoepithelion and hakoza harmless tumors are found in mammary glands.

Nowadays, BC occurs 3-5 times more often among women, and it is considered that 30-40 times more often than the proliferation of the epithelium of the nodular form of mammary gland mastopathy against the background of good-quality tumors of the mammary gland. In this context, interest in the study of safe tumors has increased in recent years. We would not be mistaken if we say that reduction of mastopathy is the real way to reduce BC.

In recent years, there is a tendency to increase the number of BDD, they are diagnosed in every 4th woman under 30 years old and in 60% of patients over 40 years old. In addition, every second woman of late reproductive age has fibrocystic mastopathy (54%), nodular mastopathy (26%), fibroadenoma (18%), BC (2%) [5].About 10 years ago, carcinoma in situ was very rare, the frequency of its detection did not exceed 3% of all newly diagnosed cases of breast cancer. The overall survival rate for patients with noninvasive breast cancer approaches 100%. Unfortunately, in many areas, the problem of diagnosing non-palpable forms of breast cancer, including CIS, has not yet been practically solved. In

most patients, the noninvasive form of breast cancer is considered an incidental finding, therefore, if a patient is suspected of having a hidden carcinoma, it is very important to choose the right strategy. A clear algorithm of diagnostic measures is necessary to identify potentially curable forms of breast cancer[16].

In recent years, ideas about the etiology and prognosis of mammary adenosis (hyperplastic processes of mastopathy, which are observed with an increase in the glandular epithelium of the acinus and mammary ducts) have changed significantly [14-15].For a long time, adenosis found in a patient with breast cancer was considered an "invisible bystander" of harmless benign hyperplasia and oncological diagnosis [13]. However, later clinical and pathological methods proved that simple microglandular adenosis can directly transform into atypical and then invasive carcinoma, and immunohistochemical analysis methods proved that the histomorphological and immunophenotypic features of microglandular adenosis and invasive breast carcinoma are highly similar. [10-14]. In particular, in both cases, a lack of Her-2 protein expression with active expression of estrogen receptors, progesterone and S100 protein has been shown [8]. In the course of modern molecular genetic studies, a high similarity in the genetic profile of simple microglandular adenosis, atypical microglandular adenosis, and nonspecific invasive ductal carcinoma has been proven [9]. At the next stage of transformation, atypical cells appear in proliferates.

Materials and results Polyclinic department of Khorezm Branch of Republican Specialized Oncology and Radiology Scientific Applied Medicine Center, Operative materials from 120 patients of various age groups who received surgical treatment, average age from 18 to 82 years, were isolated and studied as objects of histological research.

In the general analysis, 18-49 years old 63 (52.5%) people, 50-59 years old 35 (29.2%) people, 60-74 years old 19 (15.8%) people, 74-90 years old 3 (2.5 %) made up people. (the average age of patients is 55 years).

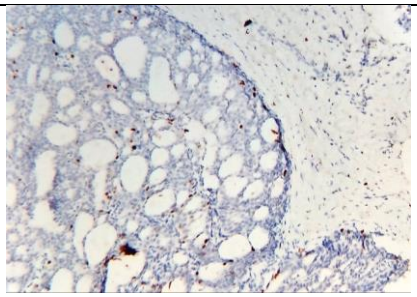
When the patients taken for the analysis were studied by districts: 16 (13.3%) people in Urganch city, 7 (5.8%) people in Urganch district, 12 (10%) people in Bogot district, 6 (5%) people in Yangibozor district, Koshkopir district 24(20%) people, 3(2.5%) in Khiva city, 8(6.6%) in Yangariq district, Khazorasp district 24 (20%) people, 5 (4.2%) people in Gurlan district, 2 (1.6%) people in Shavot district, 4 (3.3%) people in Khanka district, 9 (7.5%) people in Tortkol and Ellikala districts formed a person.

When analyzing the degree and duration of malignancy of precancerous diseases in women allocated to group 1, 47 patients (39% compared to the total number of patients) were observed for a certain period of time. 40 of the first group of women are 50 years old and older, and 20 are 18-49 years old. In 47 of them, tumors with mammary gland dysplasia, especially fibro-cystic disease and fibroadenoma, turned into a bad-quality tumor, i.e., cancer. Cancer in situ was found in 5 patients, and malignancy was not observed in 8 patients. These indicators show that hormonal background disturbances in patients can cause increased dysplastic proliferation of cells and their transformation into atypical cells. Most of the first group of patients had a precancerous process in both mammary glands, several pathological foci. When the duration of malignancy was analyzed, the longest duration of malignancy was 1 year, that is, benign tumors turned into malignant tumors in 1 year in 13 women. This requires oncologists to be alert and quick in treatment. In our second group, malignancy was not observed after surgery.

Immunohistochemical parameters were analyzed by groups, apoptosis and proliferation, Ki-67 expression in the lobes and excretory tracts, as well as the increase in the density of epithelial cell nuclei by this marker were analyzed. An increase in the proliferation process in mammary glands indicates the progression of precancerous processes of the mammary gland.

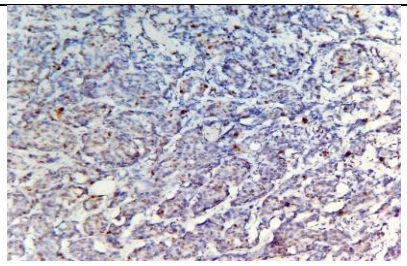
The intensity of staining of cells (or their nuclei - Ki - 67 protein to detect proliferative activity, Her 2 for estrogen receptor and progesterone receptor) was visually evaluated with a score from 0 to 3

(negative, weak, moderately stained) and the % of positively stained cells was each the value of the indicator intensity was calculated (500 in 10 fields of view at x400 microscope magnification minimum for epithelial and 500 stromal cells).

	Breast fibroadenoma. Low-level positive expression of Ki-67 marker. In the foci, different levels of positive expression of the Ki-67 marker in the epithelia of the gland, surrounding fibrous tissue is detected (1). Paint Dab chromogenic. Size 4x10.

In the immunohistochemical examination, mainly positively expressed cells, the size of which was measured in the process of morphometry, were used as a basis for expressing the trajectory of a certain limit by numbers. Determination of morphometric indicators, changes in the location of cells in this pathology provide a basis for determining the severity of the disease. According to the results of the examination, patients under 50 years of age have a low level of positive expression of the estrogenic ER marker, negative expression of the Her 2 marker, and foci of scarring in the stroma, while those over 50 years of age have a negative expression of the ER marker, as well as scarring and interstitial swelling in the stroma, and they have Her 2 Weak positive expression of the marker and the indicator of intense staining of the epithelial membrane of the glands are weak, and it is determined that the tumor index is low. Negative expression of the progesterone marker was detected in patients with malignant tumors in the first group.

The continuous proliferation of atypical cells depends on the decrease in the activity of suppressor and apoptosis genes. According to the general morphological law, aplasia, metaplasia, and dysplasia are the reasons for the transition of a tumor from safe to dangerous. Against the background of hormonal imbalance, a safe dysplastic process turns into a dangerous neoplastic process. Progesterone has an antiesterogenic property, and it was found that it decreased in the first group of patients with malignancy, and on the contrary, it increased in patients with fibroadenoma. Examination of hormones was carried out by means of enzyme immunoassay.

	Atypical hyperplasia of the breast. Moderate positive expression of Ki-67 marker. Different level of positive expression of Ki-67-marker in epithelia of the glands in the focus means that proliferation foci are improving(1). Paint Dab chromogenic. The size is 10x10.

Summary: The degree of malignancy of precancerous diseases in women was found in 39% of patients, and benign tumors, especially fibrocystic disease and fibroadenoma, turned into malignant tumors.In immunohistochemical analysis, a total of 500 cells were counted in the calculation of the cell proliferation index based on the Ki-67 marker, and the percentage of cells with a positive expression of this marker in the nucleus of some of them was as follows: 10% - low level, 2) 10-20% - medium level, 3) 20 The higher the %, the higher the expression.

ER and PR receptors marker confirmed the effectiveness of tamoxifen treatment, while the p53 marker indicated the presence of a mutation.

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