

**THE CURRENT STATUS OF THE PREVALENCE OF BREAST CANCER AND ITS
METASTATIC FORMS****Alimkhodzhaeva L.T.*, Yusupova N.B., Shodmonova D.S., Abdullaeva G.D., Narzieva D.F.**Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology of the Ministry of Health
of the Republic of Uzbekistan Farobi Street- 383, Tashkent City, Uzbekistan.***Corresponding Author: Dr. Alimkhodzhaeva L.T.**Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology of the Ministry of Health of the Republic of
Uzbekistan Farobi Street- 383, Tashkent City, Uzbekistan.

Article Received on 19/03/2020

Article Revised on 09/04/2020

Article Accepted on 29/04/2020

SUMMARY

One of the main ways to realize hormonal effects is through metabolism. On this basis, it is more correct to talk about endocrine-metabolic, and not purely hormonal disorders as carcinogenesis modifiers. Their role can be manifested both at the stage of the onset of neoplasm and in the process of tumor progression at various clinical stages of the disease.

KEYWORDS: metastatic breast cancer, incidence, osteoclasts, biophosphonates, lymph nodes, hormone-dependent tumors.

At the present stage, a steady increase in the incidence of malignant neoplasms is noted. This changes not only the structure, but also the dynamics of the incidence of cancer.

Breast cancer (BC) is one of the most common forms of malignant neoplasms. This, on the one hand, explains the great interest in studying various aspects of the diagnosis and treatment of this pathology, on the other hand, the possibility of obtaining high-quality scientific material in a relatively short time, which can be the basis of medical diagnostic standards.^[11,18]

In the Republic of Uzbekistan, breast cancer, as well as throughout the world, takes first place. If in 2010 19115 patients with oncology were first identified, then by 2017 it had grown to 22730, the difference between these years increased by 3615 in absolute numbers. Of these, with breast cancer in 2010, the number of newly diagnosed patients was 2273, by 2017 it was 3192, the difference between them was 919.^[18]

The general trend in the incidence of cancer of the organs of the reproductive system in women is an increase in the number of hormone-dependent tumors. The basis of this trend is a significant increase in the population of endocrine-metabolic disorders inherent in the diseases of civilization.^[9,16]

The pathology of the endocrine-metabolic system underlies many oncological diseases, including breast cancer. The basis of hormonal effects is a mechanism that has a direct effect on the proliferation and differentiation processes in the target tissue, as well as a

potentiating effect that increases the likelihood of genetic rearrangements.

Of course, the background that can have an undeniable effect on the biological and morphological properties of a developing tumor is the ontogenetic development of the endocrine system, along with ethnic, genetic, dietary, climatogeographic, and other factors that determine the functioning of the endocrine glands.^[7,12,13]

In general, malignant neoplasms are a disease of older age groups and this is due to both the effect of aging itself and the accumulation of external carcinogenic effects over time.

Endocrinological aspects of modern oncology are very diverse and at the same time, in the modern clinic there is the concept of "hormone dependence" of individual malignant tumors. It does not mean that hormonal factors in the pathogenesis and clinic of other tumors do not play any role, however, the selection of a group of such tumors is not accidental, and, of course, breast and endometrial cancer are primarily related to such tumors.^[3,5]

According to Peintinger F. (The Burnham Institute), breast cancer spreads to the bones in 70% of cases in the form of distant metastases. Patients with bone metastases often suffer from bone fractures, severe pain, hypercalcemia and paralysis. However, the mechanism of bone metastasis is still not clear. One possible reason is the penetration of a tumor into the bone marrow through the influence of cytokines and growth factors, which are responsible for the proliferation of breast

cancer cells. The mechanism of specific adhesion that occurs between bone endothelial cells (covering the walls of blood vessels) and breast cancer cells that enter the bloodstream more accurately explains this process.^[15] The authors proposed the hypothesis that this mechanism is realized through the interaction of specific receptors, and that modern and latest molecular studies are needed to confirm this mechanism. In their initial experiments, they used a massive set of various complexes in which protein particles were fixed on the surface of virus-sensitive substances called phages. Then they incubate these phage or peptide complexes with cultures of bone marrow endothelial cells. In particular, they revealed such complexes as glycosyl-phosphatidylinositol, a protein called CD59.^[10,14] The authors hope to prove this in an experiment in mice in order to further use certain markers to detect micrometastases or circulating complexes in the bloodstream. Those work, undoubtedly, has a scientific and preventive direction.

There are recent publications that vascular endothelial growth factor, factor-C, promotes lymph angiogenesis, which subsequently leads to further activation of lymphatic metastases (Nakamura Y., 2003). This was shown in 113 patients with invasive ductal breast cancer using the immunohistochemical method for determining the marker of lymphatic endothelial cells (subplanin). There was a significant correlation between the high density of lymphatic vessels, subplanin-positive invasion and metastases in the lymph nodes, which naturally adversely affects the prognosis of patients.^[4]

Approximately half of all pathological fractures occur in breast cancer. The main treatment methods at the same time, and this is the achievement of recent years, are bisphosphonates (Aredia, Fosamax, Didronel and others). These drugs block the progression of tumor cells in the bones, leading to a decrease in bone lesions and fractures. Bisphosphonates can also stop the spread of breast cancer to other organs, such as the lungs, but the cause of this protective mechanism is unknown. In bones, osteoclasts are stimulated by cancer cells and resorb calcium, leading to pain and fractures. These drugs block osteoclastic cells and prevent bone fragility. Some authors recommend that all breast cancer patients take bisphosphonates to prevent bone fractures.^[15]

Metastatic breast cancer is for the most part the last stage of breast cancer, or the final stage of tumor development. Metastatic cancer is characterized by the spread of tumor cells into various organs and tissues.

According to the latest data, tumors not only with distant metastases, but also with metastases to regional lymph nodes began to be attributed to metastatic breast cancer. Such breast cancer in domestic or Russian literature is referred to as locally advanced cancer. Nevertheless, on the recommendation of the memorandum of the 27th international symposium on breast cancer in San Antonio, USA since 2004, it was proposed to distinguish

two forms of the tumor - isolated or local and common or metastatic breast cancer.^[2]

Fleming F.J. et al. (2004) shows the role of axillary lymph node biopsy. A prospective analysis of 180 patients who underwent a biopsy of axillary lymph nodes from July 1999 to November 2002 was made, where 54 (30%) patients had one or more positive axillary lymph nodes. All of them were subject to total lymphatic dissection. Of this subgroup, 26 out of 54 patients had additional metastases in the form of extranodal lesions. (OR = 17.39, 95% confidence interval 1.69 - 178.96). The authors made an important conclusion that invasive breast cancer and positive lymph nodes, as well as extranodal lesions or macrometastases, are independent prognostic factors in assessing the prevalence of breast cancer.^[1]

Wernicke M. et al. (2001) showed that hyaluronin can play a leading role in the invasion and metastasis of breast cancer. Hyaluronin is an extracellular polysaccharide that is involved in tumor invasion and can cause stromal myxoid changes.^[2] The authors studied the relationship between these changes and the status of axillary lymph nodes, the degree of tumor differentiation and mortality. Patients had negative or positive lymph nodes and were followed up over a 10-year period. By the method of logistic regression, a strict relationship was shown between positive lymph nodes and stromal myxoid changes, tumor size, desmoplasia, lymphoid infiltration, the degree of tumor differentiation, tumor embolism and multifocal. Stromal myxoid changes were often combined with the young age of patients and lymphoid embolization ($P < 0.001$). When studying mortality and its relationship with stromal myxoid changes, a very weak correlation was found ($P < 0.01$). An obvious connection between them was in the case of low-differentiated myxoid changes and tumor sizes greater than 2 cm ($P < 0.008$).^[6,8]

Ohshiba T. and colleagues (2003) found that prostaglandin is involved in metastasis. So prostaglandin E2 (PE2) is produced mainly in bones by osteoblasts and stimulates bone resorption.^[4] In this study, they experimentally in mice by introducing breast tumor cells into the femur and tibia examined the role of PE2 in bone osteolysis in breast metastasis. It turned out that through the complex mechanisms of interaction of tumor cells, the expression of cyclooxygenase-2 (a key molecule in the differentiation of osteoclasts) PE2 can induce to produce and enhance bone resorption, i.e. has direct significance in the metastasis of breast cancer.

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