

MULTIMODAL RADIATION DIAGNOSIS OF BREAST CANCER

1. Мадумарова Зарнигор Шухрат кизи,

Katta Ukituvchi, PhD, ADTI, Tibbiy Radiology, Clinic Laboratory Diagnostics, Sanitary Hygiene And Epidemiology Department.

2. Хафизова Руфина Радиковна

assistant of ADTI Oncology and Radiology of the Department of Radiology.

Нишанова Ю.Х.

Ходжамова Г.А.

Хусанбаева Д.Д.

Ахмадова М.А

Tashkent Medical Academy, Bukhara Medical Institute

ABSTRACT

To date, one of the topical issues of modern oncology is the problem of breast cancer (BC), which ranks first in the structure of evilneoplasms in women. Every year, more than 1.5 million new cases of breast cancer are detected in the world, while more than 50% of women die from this pathology. According to the literature, the process of "rejuvenation" of breast cancer over the past decades has seen an increase in this disease among women at a younger age under 40 years [1]. In addition, breast cancer in young women may have a worse prognosis and more aggressive biological behavior than breast cancer in elderly patients approx. Previous studies have shown that in young women, breast cancer is diagnosed at a later stage, characterized by high proliferative activity, low differentiated Oh, with estrogen receptor negative tumors, with the presence of asular invasion lymphs [7; 10]. Previously, the definition of "young women" included patients under 35 years of age, since 2012, the World Health Organization has developed a new age classification [12], according to which: persons under the age of 44 are young; 45-59 years old - to mature; 60-74 years old to the elderly; 75-90 years old - to the elderly. The threshold of longevity is considered to be the achievement of 90 years or more.

Keywords: radiation diagnostics, ultrasound, RMH, MRI, breast cancer, IHC.

INTRODUCTION

Radiographic indicators of breast cancer in young women may vary, and the diagnosis of cancer may be more complex than in older people, since there are also different histopathological features [2; 7]. Most medical associations, including the American College of Radiology and the Society for Breast Imaging, recommend annual breast cancer screening starting at the age of 40, young women have lower mammography sensitivity due to denser breast tissue [8; 9]. The use of breast ultrasound is preferred for women under the age of 40 in the diagnosis of breast diseases, but mammography or magnetic resonance imaging (MRI) should be performed if malignancy is suspected [10].

Thus, the aim of this study was to evaluate the clinical, visual and histopathological features of breast cancer in women under the age of 44 years. A secondary objective was to investigate the relationship between radiological characteristics and histopathological signs.

MATERIALS AND METHODS

Between January 2017 and December 2019, a retrospective study was conducted in 100 women who underwent biopsy and diagnosis verification. Patients with benign pathological findings would have been excluded from the study, so 60 patients diagnosed with breast cancer were included in the study. The median age was 39.2 ± 3.6 years.

All patients underwent ultrasound, 40 patients had mammography, and only 27 patients had MRI. Patients aged >35 years with a family history of breast cancer underwent mammography as an initial method. For others, patients first an ultrasound was used, and then a mammogram was performed due to suspicious results. MRI was applied to 27 patients to assess the extent of breast cancer prior to breast-sparing surgery.

Ultrasound I- and images were obtained using a 15 MHz linear sensor on a Toshiba Aplio 500 device (Toshiba Medical Systems Corporation, Japan, 2016). For mammograms, standard mediolateral oblique and craniocaudal images were obtained using Onis essential mammography systems (Amulet S, Fujifilm, Japan, 2016). MRI scans were obtained in the prone position, on a 3.0 Tesla MRI scanner (PLIPS, in T1 VI, T2 VI, 3D modes) using a four-channel phased array chest coil. After preliminary contrasting of T1-weighted images at intervals, the following 5 axial T1-weighted post-contrast dynamic sequences were obtained in 1-5 minutes.

Pathologic studies were performed to determine histopathological type, tumor extent and immunohistochemical findings, including estrogen receptor (RE), progesterone receptor (RP) and human epidermal growth factor receptor 2 (Her2/neu). Her2/neu status was defined as positive for tumors with a score of +3 and negative for tumors with scores of 0 and +1. A negative result for all three hormone receptors was defined as triple-negative breast cancer. The results of the study on linear and histopathological features are presented in Table No.1.

Table 1. Clinical and histopathological features in examined patients with breast cancer

Characteristics	Number of patients, n=60	(%)
Clinical characteristics		
We palpatethe formation	37	61,7
Breast cancer on the maternal side	9	15,0
Bone metastasis	1	1,7
Histopathological type		
Invasive ductal cancer	48	80
Invasive - doljkovy cancer	8	13,4
Medullary cancer	2	3,3
Mucous carcinoma	2	3,3
Degree of differentiation		
G ₁	4	6,7
G ₂	14	23,3
G ₃	42	70,0
Immunohistochemical results		
RE positivity	19	31,7
RP positivity	23	38,3
Her 2/neu позитивность	34	56,7
Threetimes negative	13	21,7

Most breast cancer was detected by clinical symptoms, especially with palpable mass (37/60; 61,7%). The rest of the patients were asymptomatic and diagnosed with breast cancer when they underwent breast ultrasound due to a family history of breast cancer. The most common histological type of tumor was invasive - ductal carcinoma, 42 (70.0%) tumors were of a poorly differentiated degree, and 13 women (21,6%) the tumors were triple negative.

ULTRASOUND

Ultrasonography was performed in all patients. In 5 (8.3%) patients, no abnormalities were shown in ultrasound and these cases were diagnosed with microcalcium on mammograms. The predominant features on ultrasound were irregular shape (49/81.7%), contours uneven (47/78.3%) and hypoechoic structure (45/75.0%) (Table 2).

Table 2. Results of sonography in examined patients

Ultrasound - signs	Number of patients, n=60	%
Form		
oShaft-rounded	11	18,3
Wrong	49	81,7
Toontura		
Clear and clear	13	21,7
On the other hand,	47	78,3
Additional signs		
acoustic shadow from the back wall	36	60,0
Dorsal amplification	15	25,0
Echogenicity		
isoechoic	4	6,7
hypoechoic	45	75,0
hyperechoic	11	18,3

The majority of current patients (36/60.0%) showed an acoustic shadow from the posterior wall, and 15 (25%) patients had dorsal amplification.

X-ray mammography. Mammography was performed in 40 patients (66.7%), and an anomaly was detected on 37 (84.1%) of these images. The most common pathology in mammography was the presence of mass (34/40, 85.0%). In 5 (12.5%) patients, the diagnosis was established on the basis of the presence of pleomorphic microcalcium nates only on mammography (Tab. №3).

Table 3. Results of mammography in examined patients

X-ray signs	Number of patients, n=40	%
About education	34	85,0
in particles of asymmetric density	3	7,5
Скопление плеоморфных микрокальцинатов	5	12,5
Form		
o Shaft-rounded	7	17,5
Wrong	33	82,5
Contours		
Clear and clear	6	15,0
On the other hand,	25	62,5
with piculoids	9	22,5

The most common shape on mammograms was incorrect, and the most common shape of the contours was uneven, less spiculate about the spiculate.

MR mammography

In all patients, the results of ultrasound and mammography were used in the diagnosis. MRI was performed in 27 (45.0%) patients in the preoperative period to assess the degree of breast cancer. Of the 27 cases, 18 (66.7%) had a lesion, and 9 (33.3%) had the form of area of asymmetric density. Most patients showed a dynamic curve of type 2 or 3 (8/29.6% and 19/70.4%).

Table 4. Results of MR mammography in examined patients

MR – signs	Number of patients, n=27	%
Education	18	66,7
District	9	33,3
Graphical dependence of the change in signal intensity on formations		
Type II	8	29,6
Type III	19	70,4
Intensity at T2 VI		
isointensive;	16	59,3
Hypointense	2	7,4
Hyperintense	9	33,3

The intensity of the T2 VI signal was predominantly isointensive in 16 (59.3%) women, in 9 of 27 (33.3%) patients, breast cancer was predominantly hyperintense, and in 2 (7.4%) cases it was hypointense.

Association between histopathological signs and imaging findings

G3 tumors were associated with dorsal enhancement (G₁₋₂ - 10.9% and G₃ - 28.2% p = 0.03). O Tumors of poorly differentiated grade (G3) are more pronounced with spicule-like contours

than tumors of highly differentiated degree (G₁₋₂ - 11.8%, G₃ - 26.1%, p = 0.04). G₃ tumors showed greater intrinsic heterogeneity and hypoechogenicity. 2.) than tumors G₁₋₂ (G₁₋₂ - 8.7% and 10.9% / G₃ - 16.5% and 28.2%; p = 0.09 and p = 0.03).

Histopathological evaluation showed no association with radiographic findings, including shape, contours, and microcalcifications. All cases with the accumulation of microcalcifications occurred at G₃ degrees of breast cancer. There was no statistically significant association between immunohistochemical data and imaging data.

In MR mammography of T₁ VI images, isointensity was more often observed in grade G₃ tumors than in G₁₋₂ tumors (G₁₋₂-14.3%, G₃-40%, p = 0.3) (Figure 1). Thickening of the skin (G₁₋₂-13% and G₃-21.2%, p = 0.3) and the presence of axillary lymphadenopathy (G₁₋₂-50% and G₃-65.9%, p = 0.1) were more often observed in poorly differentiated tumors than in tumors with a high degree of differentiation, but these results were not statistically significant or significant.

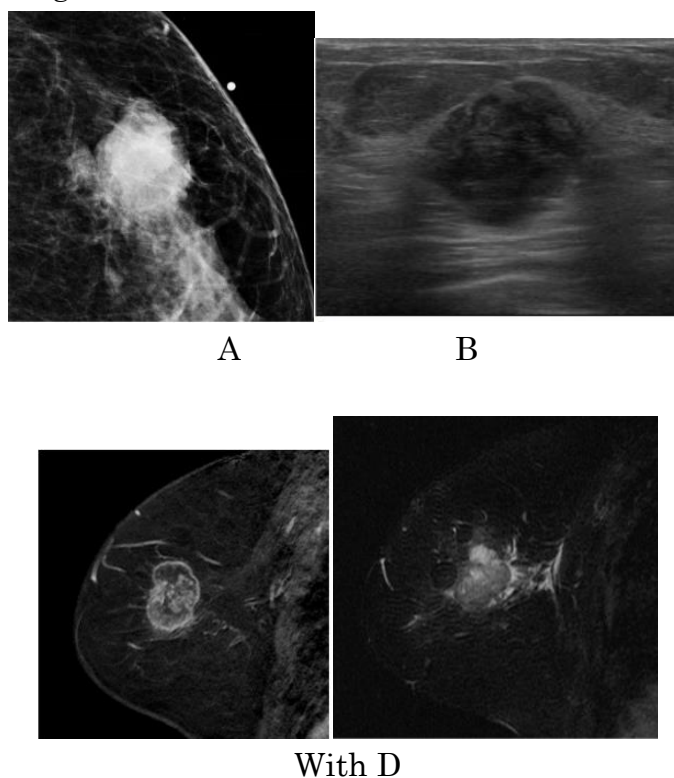
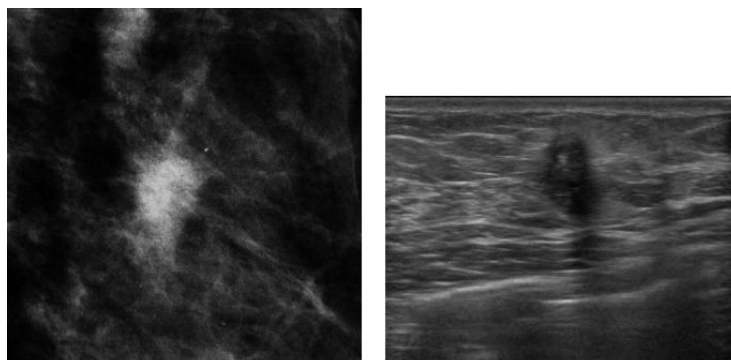


Figure 1. Patient K. 39 years old., **A.** X-rayammography - the formation of an irregular shape with fuzzy and uneven contours, without calciums determined. **B.** Ultrasound- the formation of an irregular shape with uneven contour and posterior acoustic amplification is determined. **C.** An MRI mammogram image enhanced with gadolinium T₁ shows an incorrect ring-enhanced mass. **D.** T₂-weighted MR image shows irregular mass with high internal signal intensity. Histopathology revealed invasive ductal carcinoma with a high histological degree. Immunohistochemical analysis showed that estrogen-negative receptor, progesterone-negative receptor, human epidermal growth factor 2-negative.



A B

Figure 2. Patient P. 35 years old., A. Mammography shows irregular formation with uneven contours. B. Sonogram shows an irregular mass with a spiny margin and posterior acoustic shading. Histopathology revealed invasive ductal carcinoma with low histological grade. Immunohistochemical analysis showed that the estrogen receptor is 85% positive, the progesterone receptor is 90% positive, and the human epidermal growth factor receptor is 2 negative.

DISCUSSION

In the study, the majority of cases of breast cancer in women under the age of 40 years were established symptomatically, especially with palpable mass, and more than half of the patients had axillary lymphadenopathy on ultrasound at the time of diagnosis. The reason for the poor prognosis may be late diagnosis and axillary or distant metastases in diagnosis. 9.14 According to An Y. Y., the results of the study showed that breast cancer in women under the age of 40 years was associated with a higher histological assessment [2].

Radiation diagnosis of breast cancer in young women is a more difficult task compared to the older age group of patients. Most medical associations recommend annual breast cancer screening for women in their 40s with an average risk. Mammography is currently the main method of screening breast cancer [6; 17]. However, breast cancer can hide breast cancer, and therefore the sensitivity of mammography in young women decreases due to the higher density of breast tissue [17]. Due to the higher density and overdiagnosis in young women, ultrasound can also be considered basic method of diagnosing breast cancer. In this study, ultrasonography was performed for all age groups of women. Of the patients who underwent mammography, breast cancer was found in 84.1%. In addition, 5 patients who could not be diagnosed by ultrasound were diagnosed by mammography. On mammography, the most common findings of tumors were pleomorphic-type microcalcifications and mass. The form of education was usually incorrect, which corresponded to the results of previous studies [2; 4]. The predominant marginal signs were ultrasound with irregular and darkening on mammography. In contrast to the current study, Bullier et al. found a predominance of spiculated-like contours in women with breast cancer at the age of <40 years [5]. The lower rate of spiculated-like contours in the current study can be explained by a higher percentage of tumors of a highly differentiated degree of malignancy.

Magnetic resonance imaging was performed on patients to assess the degree of breast cancer before breast preservation surgery. Most of the patient's mass had isointense T2 VI images and

dynamic curves were of 2 or 3 types, similar to the results of previous studies [2; 3; 19]. Dynamic curves of type 2 (plateau) and 3 (leaching), In particular, they can help the radiologist in diagnosing breast cancer in young women.

The relationship between imaging findings and the histological level was also investigated. Tumors of a highly differentiated degree were associated with posterior acoustic amplification, whereas tumors of a low-grade grade were associated with a spicule-shaped contour. In addition, in MR mammography T2VI images Isolation was more common in high-grade tumors than in low-grade tumors, but these data could not achieve statistical significance, probably due to the small number of patients with MRI data. The results of previous studies confirmed the results of the present study, and it was reported that high-grade and triple negative tumors can mimic benign lesions with a smooth contour and rear reinforcement [1, 3;18]. It is known that high-grade tumors exhibit higher cellularity and necrosis, which may be due to other internal heterogeneity and iso-intensity T2 VI images. However, tumors of a low grade usually show a higher stromal response and desmoplasia, which can cause spicule-like contours [5;11;16]. Thus, due to different imaging results, breast cancers under the age of 4-4 years may show excellent radiological results from their older counterparts.

There were some limitations of the current study. The main limitation was retrospective analysis. Secondly, the number of patients assessed by MRI was small, and this may be the reason for the lack of statistical significance. Finally, although immunohistochemical molecular subtypes have been studied, they could not be estimated due to the lack of Ki67 data in some patients.

In conclusion, it should be noted that breast cancer in women under 4 years of age is usually characterized by the presence of a palpable mass and may exhibit a variety of imaging results, including an acoustic shadow from the posterior wall on ultrasound, isointensity of T1 VI and hyperintensity of T2 VI images, and spicule-like contour due to lower differentiated histological degree. In the world, ultrasound is the main method for diagnosing breast cancer in young women, but mammography and MRI can help in both diagnosing and assessing the extent of the disease. Awareness of imaging and clinical and pathological data on breast cancer in young women helps doctors make an early and accurate diagnosis, and the mammologist to provide the right treatment.

REFERENCES

1. Semiglazov V.F., Krivorotko P.V., Paltuev R.M. Book. Immunology of breast cancer // M.: SIMK, 2019. p.179-195.
2. An YY, Kim SH, Kang BJ. Breast cancer in very young women (<30 years): Correlation of imaging features with clinicopathological features and immunohistochemical subtypes // Eur J Radiol. 2015; 84:1894–1902.
3. An YY, Kim SH, Kang BJ. Characteristic features and usefulness of MRI in breast cancer in patients under 40 years old: correlations with conventional imaging and prognostic factors // Breast Cancer. 2014; 21:302–315.
4. Bird RE, Wallace TW, Yankaskas BC. Analysis of cancers missed at screening mammography // Radiology. 1992; 184:613–617.

5. Bullier B, MacGrogan G, Bonnefoi H, Hurtevent-Labrot G. Imaging features of sporadic breast cancer in women under 40 years old: 97 cases // *Eur Radiol*. 2013; 23:3237–3245.
6. Destounis S, Santacroce A. Age to Begin and Intervals for Breast Cancer Screening: Balancing Benefits and Harms // *AJR Am J Roentgenol*. 2018; 210:279–284.
7. Han W, Kim SW, Park IA, Kang D. Young age: an independent risk factor for disease-free survival in women with operable breast cancer // *BMC Cancer*. 2004; 4:82.
8. Freer PE. Mammographic breast density: impact on breast cancer risk and implications for screening // *Radiographics*. 2015; 35:302–315.
9. Fredholm H, Magnusson K, Lindström LS. Breast cancer in young women and prognosis: How important are proliferation markers? // *Eur J Cancer*. 2017; 84:278–289.
10. Fredholm H, Magnusson K, Lindström LS. Long-term outcome in young women with breast cancer: a population-based study // *Breast Cancer Res Treat*. 2016; 160:131–143.
11. Chang JM, Won JK, Lee KB. Comparison of shear-wave and strain ultrasound elastography in the differentiation of benign and malignant breast lesions // *AJR Am J Roentgenol*. 2013; 201: -P. 347–356.
12. <https://www.who.int.ru> (2018)
13. Çelebi F, Pilancı KN, Ordu Ç. The role of ultrasonographic findings to predict molecular subtype, histologic grade, and hormone receptor status of breast cancer // *Diagn Interv Radiol*. 2015; 21:448–453.
14. Colleoni M, Rotmensz N, Robertson C, Orlando L. Very young women (<35 years) with operable breast cancer: features of disease at presentation // *Ann Oncol*. 2002; 13:273–279.
15. Gnerlich JL, Deshpande AD, Jeffe DB. Elevated breast cancer mortality in women younger than age 40 years compared with older women is attributed to poorer survival in early-stage disease // *J Am Coll Surg*. 2009;208:341–347.
16. Lamb PM, Perry NM, Vinnicombe SJ. Correlation between ultrasound characteristics, mammographic findings and histological grade in patients with invasive ductal carcinoma of the breast // *Clin Radiol*. 2000; 55:40–44.
17. Oeffinger KC, Fontham ET, Etzioni R. Breast Cancer Screening for Women at Average Risk: 2015 Guideline Update from the American Cancer Society // *JAMA*. 2015; 314:1599–1614.
18. Redmond CE, Healy GM, Murphy CF. The use of ultrasonography and digital mammography in women under 40 years with symptomatic breast cancer: a 7-year Irish experience // *Ir J Med Sci*. 2017; 186:63–67.
19. Yamada T, Mori N, Watanabe M. Radiologic-pathologic correlation of ductal carcinoma in situ // *Radiographics*. 2010; 30:1183–1198.