Study on the correlation between ultrasonic signs and molecular biological expression in breast cancer

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Abstract: Objective: To explore the correlation between ultrasonic signs and molecular biological expression in breast cancer, in order to improve the diagnostic level of ultrasound for breast cancer and provide reliable imaging information for the treatment and prognosis assessment of breast cancer. Methods: A total of 50 patients with breast cancer confirmed by surgical pathology were randomly selected and underwent high-frequency breast ultrasound examination, focusing on observing the shape, edge, posterior echo, microcalcification, internal blood flow, and axillary lymph nodes of the mass; immunohistochemistry was used to detect the expression of ER, PR, and CerbB-2 genes, and their relationship with ultrasound performance was analyzed. Results: ① The detection rate of microcalcification in breast cancer <2cm was the highest, followed by spiculated edge; the detection rate of irregular shape was higher in tumors >2cm. ② The positive rate of ER and PR in patients with a tumor aspect ratio >1 was 77.8% and 61.1%, respectively, which was higher than those with an aspect ratio ≤1 ($P<0.05$); ③ The positive rate of ER and PR in patients with spiculated edge signs was 65.5% and 55.2%, respectively, which was higher than those without spiculated edge ($P<0.05$); ④ The positive rate of ER and PR in patients with peripheral high echo dizzy was 73.3% and 60.0%, respectively, both higher than those without high echo dizzy ($P<0.05$); ⑤ The positive rate of PR in patients with anechoic area was 22.2%, lower than those without anechoic area ($P<0.05$); ⑥ The positive rate of CerbB-2 in patients with microcalcification was 83.3%, higher than those without microcalcification ($P<0.05$). Conclusion: There is a certain relationship between the ultrasound performance of breast cancer and the expression of molecular biological indicators, and the biological characteristics of the tumor affect the ultrasound performance of breast cancer. Ultrasound examination can provide imaging basis for the prognosis assessment and clinical treatment selection of breast cancer.

Keywords: Breast Cancer, Ultrasound, Molecular Markers

1. Introduction

At present, ultrasound is one of the important imaging methods for diagnosing breast cancer, but conventional ultrasound cannot effectively display small calcifications. Color Doppler Flow Imaging (CDFI) testing has certain limitations in distinguishing between benign and malignant tumors due to factors such as blood flow velocity, the angle between the ultrasound beam and blood flow, and the examination site. This study explores the correlation between the ultrasound manifestations of breast cancer and the status of molecular markers of breast cancer, providing reliable imaging information for the treatment and prognosis assessment of breast cancer, thereby further enhancing the value of ultrasound examination in the clinical diagnosis and treatment of breast cancer.

2. Materials and methods

2.1. General information

From January 2012 to June 2013, 50 female patients with pathologically confirmed breast cancer at Jinan Fourth People's Hospital were selected. The average age was (46.5±2.3) years old. None of them had a history of malignant tumors in other parts of the body, and upon admission, examinations confirmed no obvious metastatic lesions in other parts such as the liver and lungs. None of them had received surgical, chemotherapy, or radiotherapy treatments before blood sample collection.

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2.2. Equipment and methods

A Philips IU 22 color Doppler ultrasound detector was used, equipped with a high-frequency linear transducer with a frequency range of 7.5 to 10 MHz. Patients were placed in a supine position with both arms raised naturally to fully expose both breasts and axillae. Two-dimensional and color Doppler ultrasound scans were performed. After the lesions were detected, the largest cross-section displaying the lesion was recorded, noting the location, size, shape, edge spiculation, internal echo, presence of microcalcifications, and axillary lymph node enlargement. Color Doppler Flow Imaging (CDFI) was used to observe the blood flow around and within the lesion from multiple planes, and the Power Doppler Imaging (PDI) program was selected to freeze and store images from the area with the richest blood flow signals. Two experienced pathologists independently analyzed the expression of ER, PR, and CerbB-2, and the average values were taken.

2.3. Statistical analysis

Statistical analysis was conducted using the SPSS 13.0 software. Intergroup comparisons were made using the t-test. Categorical data were expressed as percentages, and intergroup comparisons were performed using the chi-square test with a 2x2 contingency table or the exact probability method. The significance level for hypothesis testing was set at $\alpha=0.05$. A difference was considered statistically significant if $P<0.05$.

Table 1: Ultrasound Malignant Signs in Breast Cancer Patients

Item	Number of Cases	L/T > 1	Irregular Shape	Spiculated Margin	Microcalcification	High Echogenic Halo	Anechoic Area	Posterior Acoustic Shadowing
Maximum Diameter < 2cm	9	4 (44.4%)	2 (22.2%)	5 (55.5%)	6 (66.7%)	2 (22.2%)	1 (11.1%)	2 (22.2%)
Maximum Diameter ⩾ 2cm	41	14 (34.1%)	30 (73.2%)	24 (58.5%)	24 (58.5%)	13 (31.7%)	8 (19.5%)	13 (31.7%)

3. Results

3.1. Ultrasound malignant signs (Table 1)

In this study, the detection rate of microcalcification was the highest in breast cancer with a maximum diameter <2cm, followed by spiculated margins; in those with a maximum diameter ≥2cm, irregular lesion morphology had the highest detection rate, followed by spiculated margins and microcalcification.

3.2. Correlation between breast cancer ultrasound signs and molecular markers (table 2)

In this group, the positive rates of ER and PR were higher in patients with a tumor aspect ratio >1 compared to those with an aspect ratio ≤1 (both $P<0.05$); the positive rates of ER and PR were higher in patients with spiculated margins compared to those without (both $P<0.05$); patients with a peripheral high echogenic halo had higher positive rates of ER and PR compared to those without a halo ($P<0.05$); the positive rate of PR was lower in patients with anechoic areas compared to those without ($P<0.05$); patients with microcalcification had a higher CerbB-2 positivity rate compared to those without microcalcification ($P<0.05$).

Table 2: Association between Breast Cancer Ultrasound Signs and Molecular Markers

Ultrasound Signs		Number of Cases	ER		PR		CerbB-2	
			Cases (%)	χ^2 value	Cases (%)	χ^2 value	Cases (%)	χ^2 value
Aspect Ratio	>1	18	14(77.8)	12.052*	11(61.1)	6.201*	13(72.2)	0.611

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	⩽1	32	15(46.9)		12(37.5)		25(78.1)	
Spiculated Margin	Yes	29	19(65.5)	8.031*	16(55.2)	5.835*	20(69.0)	2.893
	No	21	9(42.9)		7(33.3)		17(81.0)	
High Echogenic Halo	Yes	15	11(73.3)	8.331*	9(60.0)	5.201	11(73.3)	0.902
	No	35	17(48.6)		14(40.0)		27(77.1)	
Anechoic Area	Yes	9	5(55.6)	0.053	2(22.2)	4.935*	6(66.7)	1.255
	No	41	23(56.1)		20(48.8)		21(51.2)	
Microcalcification	Yes	30	19(63.3)	3.011	15(20.0)	3.201	25(83.3)	5.221*
	No	20	10(50.0)		7(35.0)		13(65.0)	

4. Discussion

Breast cancer is one of the most common malignant tumors among women. According to statistics, more than 1.2 million women are diagnosed with breast cancer globally each year, and about 500,000 die from the disease [1]. To date, the etiology of breast cancer remains unclear. Although environmental factors and lifestyle are known to have some impact on the development of breast cancer, more than 60% of breast cancers do not have obvious risk factors [2]. Early detection, diagnosis, and treatment are key to reducing the mortality rate of breast cancer and improving prognosis. Currently, the early diagnosis of breast cancer mainly relies on imaging examinations such as mammography and ultrasound, but the differences in equipment and the level of diagnosticians limit the overall level of early diagnosis. Investigating the mechanisms of breast cancer development and searching for highly sensitive and specific biomarkers and serum markers for diagnosis and prognosis assessment have become one of the hot topics in recent breast cancer research.

4.1. Tumor morphology

Thomas et al. [3] pointed out that during clinical examination, the tumor aspect ratio can be used as a criterion for diagnosing the nature of the tumor. When the ratio is greater than 1, it indicates that the tumor growth has exceeded the range of the normal plane, and the possibility of malignancy is high. In this study, the positive rates of ER and PR in patients with an aspect ratio greater than 1 were 77.8% and 61.1%, respectively, which were higher than those with an aspect ratio of 1 or less. This suggests that the positive expression of ER and PR is related to the tumor morphology.

4.2. Tumor edge

In clinical practice, the edge of the tumor is often observed to assist in clinical diagnosis and treatment and is considered one of the important bases for diagnosis [4]. In most patients with breast cancer, the ultrasound manifestations show spiculated edges (Figure 1), and the ER and PR test results are positive, indicating better tumor differentiation and better prognosis and treatment outcomes. This study found that the positive rates of ER and PR in patients with spiculated edge signs were 65.5% and 55.2%, respectively, which were higher than those without spiculated edges.

4.3. High echogenic halo sign

The high echogenic halo sign is also an important indicator in clinical examination. This sign is similar to the spiculated sign, as both indicate that cancerous tissue is distributed in a strip or band and spreads to surrounding tissues, leading to the continuous expansion of the lesion [5]. Ultrasound shows a naked eye easily distinguishable band-like high echo surrounding the surface of the hypoechoic tumor, with a halo thickness of more than 1.5mm [6] (Figure 2). This study found that the positive rates of ER and PR in patients with a peripheral high echogenic halo sign were 73.3% and 60.0%, respectively, both of which were higher than those without a high echogenic halo sign.

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4.4. Internal echo

Internal echo is a common indicator in ultrasound examination and is of great significance in understanding the nature of tumors. This study indicates that there is a correlation between internal echo and the characteristics of ER and PR, meaning that when ER and PR are negative, there is a higher probability of having a lower internal echo. Patients with anechoic areas had a PR positivity rate of 22.2%, which is lower than those without anechoic areas.

4.5. Microcalcification

Microcalcification in breast tumors mainly manifests as punctate strong echoes, which can be located within the tumor or around it, or scattered throughout the glandular tissue. Microcalcification in the breast presents as clustered punctate strong echoes within or around the tumor or distributed along the ducts. Analyzing the imaging data of breast cancer patients, it was found that the area of calcification is relatively small, which may be related to cellular dissolution [7]. This study shows that microcalcification is related to CerbB-2 (Figure 3). In this group, the CerbB-2 positivity rate in patients with microcalcification was 83.3%, higher than those without microcalcification.

In summary, there is a certain correlation between the ultrasound manifestations of breast cancer and molecular biological markers. It is possible to preliminarily infer the expression status of ER, PR, and CerbB-2 in patients based on the imaging manifestations of breast cancer ultrasound, reducing the issues of missed diagnoses or overtreatment, enhancing the evidence-based nature of treatment, and providing a reliable basis for the early diagnosis of breast cancer.

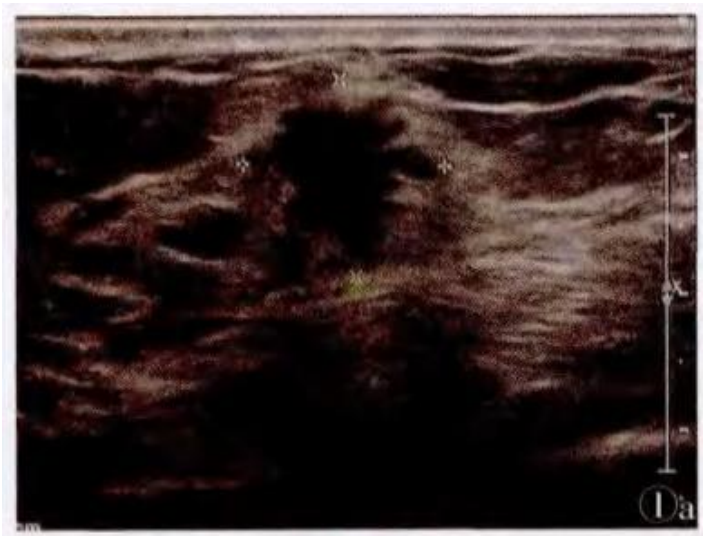

Figure 1: Female, 48 years old, infiltrating edge of the tissue.
Figure 1a: Ultrasound image showing obvious spiculated margins of invasive ductal carcinoma.

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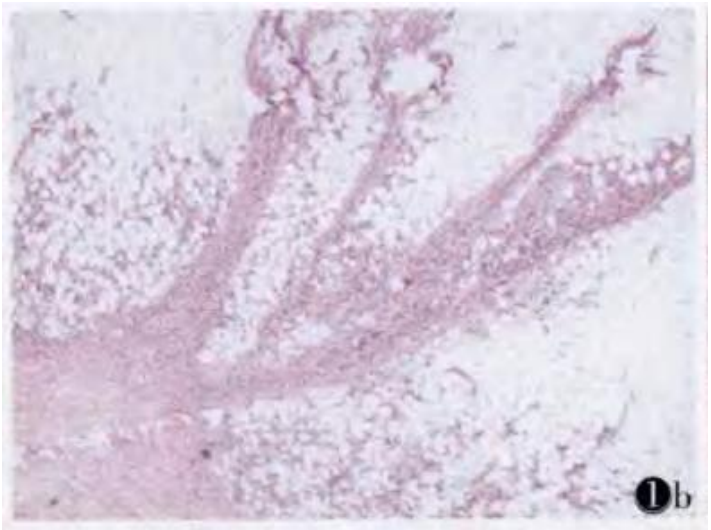

Figure 1b: The pathological section shows "flame-like" protrusions at the edge of the tumor, similar in morphology to the spiculated sign observed in ultrasound (H&E x100).

Figure 2: Female, 54 years old, with a high echogenic halo sign.
Figure 2a: The sonogram shows a obvious high echogenic halo around the invasive ductal carcinoma.

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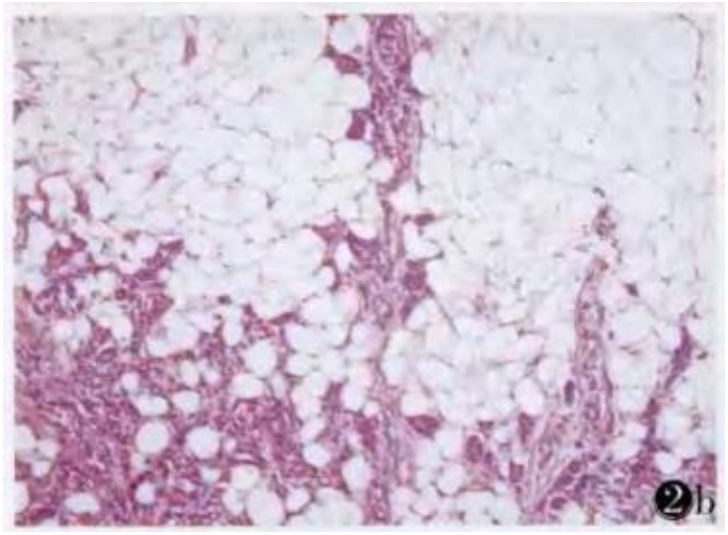

Figure 2b: The pathological section shows the edge tissue components corresponding to the high echogenic halo, with the majority being cancerous tissue, a small amount of fibrous components and lymphocytes, and the cancerous tissue interwoven with adipose tissue (H&E ×200).

Figure 2c: The sonogram demonstrates low internal echoes within the invasive ductal carcinoma, with spiculations and a high echogenic halo around the periphery.

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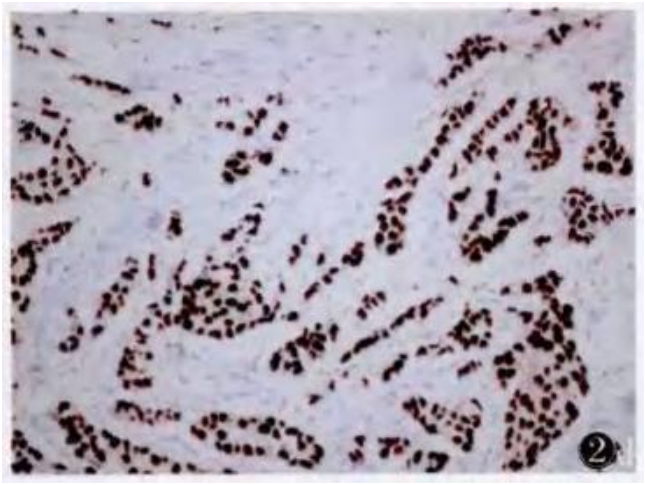

Figure 2d: The tumor shows positive expression for ER (IHC ×200).

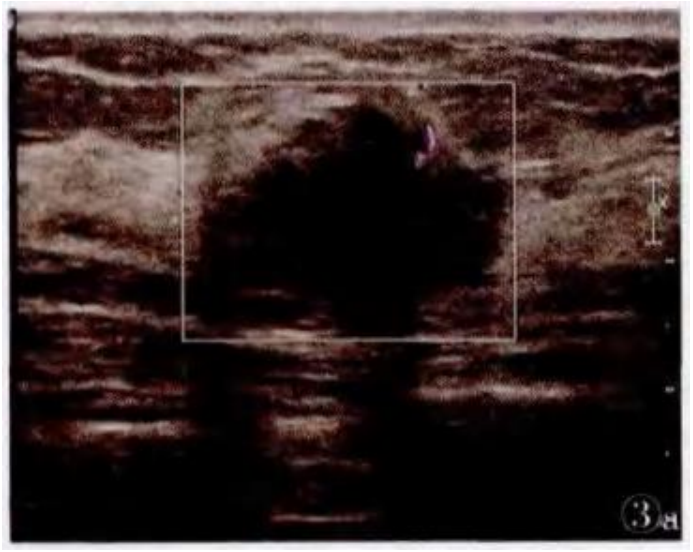

Figure 3: Female, 43 years old.
Figure 3a: Ultrasound shows anechoic areas and punctate strong echoes within the ultrasound mass of invasive ductal carcinoma.

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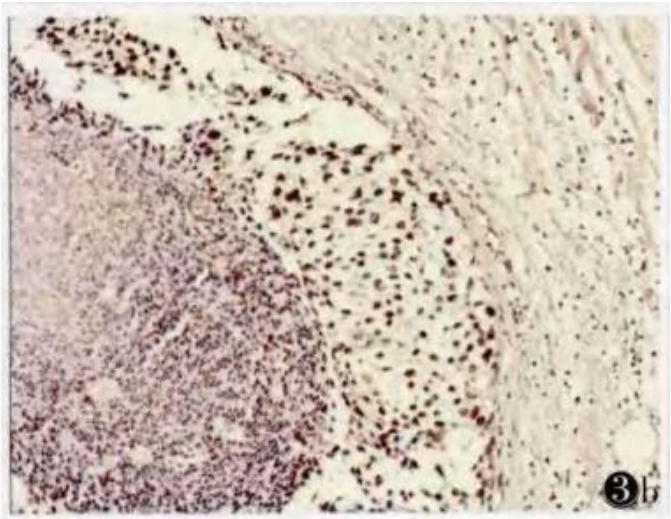

Figure 3b: The pathological section shows extensive necrosis within the invasive ductal carcinoma (H&E ×200).

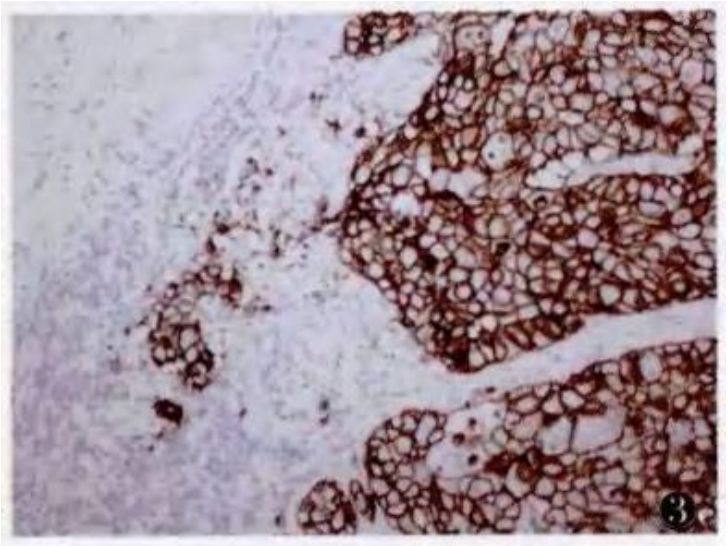

Figure 3c: The tumor exhibits positive CerbB-2 expression (IHC ×200).

5. Conclusion

By analyzing the relationship between ultrasound characteristics such as tumor morphology, edge, and internal echo, and the expression of molecular markers like ER, PR, and CerbB-2, we can more accurately predict the biological behavior of tumors, thereby providing patients with more precise treatment strategies. Additionally, this study emphasizes the importance of ultrasound examination in the management of breast cancer, especially in resource-limited areas. As an economical, non-invasive, and readily available imaging tool, ultrasound examination is irreplaceable for the screening, diagnosis, and treatment monitoring of breast cancer.

6. References

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