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Original Research Paper

Radio-Diagnosis

MOLECULAR PREDICTION OF BREAST CANCER ON THE BASIS OF MORPHOLOGICAL FEATURES IN ULTRASONOGRAPHY

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ABSTRACT

Breast cancer is one of the most common types of cancer affecting women worldwide. Early detection and accurate prediction of breast cancer can improve treatment outcomes and survival rates. Ultrasonography is a non-invasive imaging modality that can detect breast lesions and help guide biopsy procedures. Recently, there has been increasing interest in using ultrasonographic features, such as lesion morphology, to predict the molecular subtype of breast cancer. This approach has the potential to improve personalized treatment plans and reduce unnecessary procedures. Several studies have investigated the correlation between ultrasonographic features and molecular subtypes of breast cancer. Morphological features such as shape, margin, echo pattern, and calcifications have been shown to be associated with specific molecular subtypes. This study aimed to investigate the feasibility and potential of predicting breast cancer molecular subtypes based on morphological features observed in ultrasonography images. Further studies are needed to validate these findings and develop more accurate prediction models for breast cancer subtypes.

KEYWORDS : Breast cancer; molecular subtyping; ultrasonographic findings of breast cancer.

INTRODUCTION

Breast cancer is one of the most common tumors in the world and it remains a worldwide public health dilemma. Breast cancer accounts for one in every four cancer cases and one in every six deaths due to cancer. At present various imaging modalities are available for evaluation of breast lesions like mammography, ultrasonography, colour doppler, breast galactography and MRI.

Ultrasonography (US) is the most widely used adjunctive tool in breast diagnostics. Molecular subtyping and hormone receptor status are strongly associated with certain radiological features and thus ultrasound features of breast cancer remain a potential tool in the diagnosis and subtyping of breast cancer. The correlation of ultrasound features with certain types of biological behaviour of breast cancer has been studied in few papers. Thus, this can help differentiate the molecular subtypes which in turn can supplement the diagnosis provided by a pathologist especially when the findings are discordant.

AIMS AND OBJECTIVES

To assess the various morphological features of breast cancer with ultrasonography and correlate them with molecular subtypes

METHODS AND MATERIALS

- Present study is a prospective study of patient using Ultrasonography and correlates it clinically and pathologically. 100 cases having or suspected to have breast carcinoma were chosen at random among the indoor and outdoor patients referred to the department of Radiodiagnosis for imaging. The study was carried among period of 1 year. Results were checked by two radiologists (PI and CO-PI) and final comparative data had been prepared from Ultrasonography. All the patients included in study were first subjected to surgery department of our hospital, then they were referred to our department for ultrasonography where they were subjected to real time ultrasound scanning with 3-16 MHz linear array transducer on USG machine. A gray scale image of the mass was acquired. Then patients were subjected to core biopsy or operative procedure.
- Histopathology (biopsy)
- Immunohistochemistry

Inclusion Criteria

- All women with breast cancer coming to our centre who had undergone ultrasonography
- Female breast cancer patients with histopathological reports and with results of immunohistochemistry panel
- Nonspecific axillary lymphadenopathy.
- Family history of breast carcinoma.

Exclusion Criteria

- Women who were unwilling or unable to undergo biopsy/surgery.
- Non-co-operative patient.

OBSERVATION AND RESULTS

Table 1: Correlation Of Morphological Features With Molecular Subtypes In Usg

Morphological Features		Molecular Subtype								Total	
		Her 2		Luminal A		Luminal B		Triple Negative			
		Count	%	Count	%	Count	%	Count	%	Count	%
Mass Shape	Oval	2	8.60%	2	6%	1	2.30%	2	40%	7	7%
	Round	0	0.00%	1	3.33%	4	9.50%	0	0.00%	5	5%
	Ill defined	17	91.30%	27	90%	37	88%	3	60%	88	88%
	Total	23	100.00%	30	100.00%	42	100.00%	5	100.00%	100	100.00%
Margin	Indistinct	-	0%	-	0%	4	9.50%	2	40%	6	6%
	Angular	7	30.40%	10	33.30%	13	30.90%	0	0.00%	30	30%
	Micro lobulated	8	34%	11	36.60%	13	30.90%	2	40%	34	34%
	Spiculated	5	21.70%	6	20%	9	21.40%	1	20%	21	21%
	Circumscribed	3	13%	3	10%	3	7.10%	0	0%	9	9%
	Total	23	100.00%	30	100.00%	42	100.00%	5	100.00%	100	100.00%

Posterior acoustic features	No change	4	17.40%	4	13.30%	10	23%	0	0%	18	18%
	Enhancement	12	52.17%	11	36.60%	16	38%	5	100%	44	44%
	Shadowing	5	27.70%	15	50.00%	13	31%	0	0%	33	33%
	Combined	2	8.60%	0	0.00%	3	7.14%	0	0%	5	5%
	Total	23	100.00%	30	100.00%	42	100.00%	5	100.00%	100	100.00%
Mass with Calcification	No	8	34.70%	14	46.60%	20	47.60%	3	60%	49	49%
	Yes	15	65.30%	16	53.30%	22	52.38%	2	40%	51	51%
	Total	23	100.00%	30	100.00%	42	100.00%	5	100.00%	100	100.00%

We took 100 patients with mass in breast and their USG features were correlated with molecular subtypes. Our analyses showed association of shape of the lesion in USG with molecular subtyping with p value of 0.05. However, it is not statistically significant but we found some associations. Irregular shape was common in all subtypes whereas oval shaped tumors were common in TNBCs. About 37 out of 42 patients with luminal B tumors, about 17 out of 23 patients with HER2 enriched type and about 3 out of 5 TNBC patients showed irregular shaped mass. 2 out of 5 TNBC patients showed oval-shaped mass.

No significant association was found between the margin of the lesion in USG with molecular subtyping (p value was 0.16). There was association of posterior acoustic features of breast cancer in USG with the molecular subtyping, however it was not statistically significant (p value of 0.10). 5 out of 5 patients with TNBC and 12 out of 23 patients with HER 2 enriched subtype showed posterior enhancement. 15 out of 30 patients with luminal A tumor showed posterior shadowing.

The result also showed no statistically significant correlation between breast cancer presenting as mass with calcification in USG and molecular subtyping (p value was 0.67). Out of 23 patients with HER 2 enriched subtype, 15 had mass with calcification. Out of 5 patients with Triple negative breast cancer only 2 were found to have mass with calcifications whereas out of 42 patients with Luminal B cancers, 22 patients had mass with calcification.

DISCUSSION

Breast cancer is a heterogeneous disease and in the current era, the management and treatment of breast cancers greatly rely on the receptor status of the tumor by immunohistochemistry and also on histological grading of the tumor. The development of breast cancer molecular biology allowed for targeted treatment based on the molecular subtype. According to the St. Gallen Consensus 2011, molecular subtypes of breast cancer can be classified into Luminal A (ER+/PR+/HER2-/low Ki- 67); Luminal B (ER+/PR+/HER2-/+/high Ki-67); HER2-overexpression (ER-/PR- /HER2+), and triple-negative breast cancers/TNBCs (ER-/PR-/HER2-) (1). Tumors of certain molecular subtypes behave in certain ways like Triple-negative lesions have a high and Luminal A tumors have a low recurrence risk; like there is much higher incidence of recurrence in opposite breast in Triple Negative Breast Cancers (TNBCs) when compared to other subtypes (2). Thus, it is important to know the molecular subtypes for predicting how the tumor will behave and to plan the treatment accordingly. Ultrasonography is one of the most commonly used imaging techniques for breast cancer detection due to its non-invasive and cost-effective nature. Previously various studies have shown the association of molecular subtyping with imaging features of breast cancer. In our study we analysed the association of various ultrasonographic features of breast cancer with molecular subtyping.

The main objective of this study was to investigate the feasibility of predicting breast cancer molecular subtypes based on morphological features observed in ultrasonography images. The results of this study showed that certain morphological features, were associated with specific molecular subtypes of breast cancer.

In our study, we could see some association of shape of mass in USG with molecular subtyping. The most common shape of mass in USG was found to be irregular (88%) which was similar to study shown by Kim SH et al (3) and by Au FW-F et al who found 69% and 83% incidence of the same (4). Most of the tumors of luminal A (about 90 %) and luminal B (88%) and HER 2(91.3%) enriched subtype had irregular shape. In luminal (ER positive) subtypes 80 to 90 % of tumors showed irregular shape whereas only <10% showed oval or round shaped lesions which is similar to study shown by Au FW-F et al (4). But in case of TNBCs 60% showed irregular shape and 40% showed oval shaped.

Though irregular shape is the most common shape in all molecular subtypes and even in TNBCs, the distribution of oval tumors was common in TNBCs. Also, hormone positive tumors were mostly irregular in shape and only very less percentage showed oval or round shaped lesions which was similar to study shown by Au FW-F et al (4). The results were similar to study by Au FW-F et al, who found no statistically significant correlation (P value of 1.0) between shape of mass and molecular subtyping (4). But our result is very close to statistically significant p value (p=0.05).

We found some correlation between the posterior acoustic features of tumor with molecular subtyping of breast cancer (p=0.13). The most common posterior acoustic feature of breast cancer in our study was posterior enhancement and the next common pattern was posterior shadowing. Posterior acoustic enhancement was the most common posterior feature in TNBCs and HER 2 enriched subtypes which was seen in 100% and 52.17% respectively. 50% of Luminal A types of breast cancers were associated with posterior acoustic shadowing. Luminal B subtype showed an almost equal distribution of shadowing and enhancement in our study 31 and 38 % respectively.

Posterior enhancement was seen in 38 % of Luminal B tumors and 36.6 % of Luminal A tumors. About 52.17 % of Her 2 enriched tumors showed enhancement. All TNBCs showed enhancement. Our results are similar to studies done by Lamb et al and Rashmi S et al who showed significant association of posterior acoustic enhancement with triple negative breast cancer (5). They also showed that posterior enhancement is common in TNBC and Her2 neu enriched subtype of breast cancer (5). Posterior shadowing is common in luminal A tumors whereas enhancement is more common in TNBCs and HER2 positive tumours. Posterior shadowing was seen in 50 % of Luminal A tumors and about 31% of luminal B tumours. Our result was similar to study done by S Rashmi and S Kamla who showed that posterior shadowing is common in luminal A or B subtype of breast cancer (5). None of the TNBC showed posterior shadowing.

Calcification more commonly appeared in HER2 subtype (65.3%). This finding is similar to study done by Khalaf, L.M.R., Herdan. (6) However, there was no statistically significant difference among the four molecular subtypes regarding the calcification.

We could not find a significant association between the margin of the mass in USG with molecular subtyping. Our results were not similar to studies done by Aho M et al and Celebi F et al (7) (8) who showed correlation of margin of mass with molecular subtyping. The most common margin found in our study was microlobulated margin followed by angular margin.

It was expected previously that posterior acoustic shadowing and spiculated margins were suggestive of malignancy. But now it has been widely accepted that breast cancers can have varying posterior acoustic features. Many studies showed that oval or round shape, circumscribed and microlobulated margins and posterior acoustic enhancement were seen in receptor negative tumors. Hence mass showing round or oval shape with well-defined margin and posterior enhancement can be TNBCs.

The ability to predict breast cancer subtypes based on ultrasonography images has several potential clinical applications. First, this approach may help clinicians make more informed treatment decisions. Different molecular subtypes of breast cancer respond differently to various treatments, and accurate molecular subtype prediction can help ensure that patients receive the most effective treatment for their particular subtype. Second, this approach may facilitate the development of personalized treatment plans tailored to each patient's specific molecular subtype without of much interventions or invasive procedures. Third, this approach may aid in identifying patients who are at higher risk of developing specific molecular subtypes of breast cancer, allowing for earlier detection and more effective treatment.

However, it is important to note that this study has some limitations. The sample size was relatively small, and the study was conducted on a specific population. Further studies with larger sample sizes and diverse populations are needed to validate the findings of this study.

CONCLUSION

The association between shapes of mass in USG with molecular subtyping was close to statistically significant values. Irregular shape was the most common shape in all subtypes. But oval or round tumours were more common in TNBCs and were less common in luminal tumours. Most of the Luminal A tumors were showing posterior acoustic shadowing whereas most of the TNBCs and HER 2 enriched variety showed posterior acoustic enhancement. No significant correlation was found between calcification in mass in ultrasonography with the molecular subtyping. Calcification is more commonly seen in her2 enriched subtype. Thus, there was a strong association of certain sonographic features of breast tumors with molecular subtyping. Since breast lesion is very heterogeneous, biopsy of small samples may not always accurately predict the molecular subtyping especially when the patient undergoes neoadjuvant chemotherapy. Hence knowledge of the imaging findings which can potentially predict the molecular subtyping may be useful in treating and prognosticating the patients. In conclusion, ultrasonography can provide valuable information for predicting the molecular subtype of breast cancer based on morphological features. This approach has the potential to improve personalized treatment plans and reduce unnecessary procedures, but further studies are needed to validate and standardize these findings

A 68-year-old woman diagnosed with an invasive ductal carcinoma NOS in the left breast.

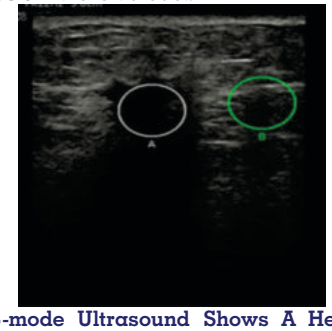

Figure 1: B-mode Ultrasound Shows A Heterogenously Hypoechoic Taller Than Wider With Spiculated Margins And With Posterior Acoustic Shadowing.

Biopsy proven case of invasive ductal carcinoma NOS with Luminal A Immuno-histochemical profile, Ki-67 of < 10 %

A 40-year-old woman diagnosed with an invasive ductal carcinoma NOS in the right breast.

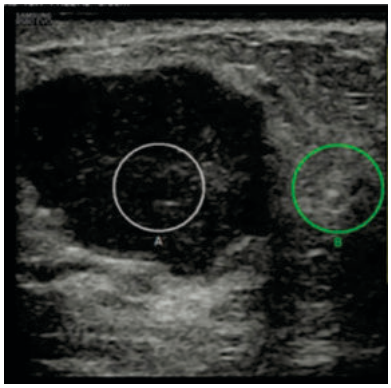

Figure 2: B-mode Ultrasound Shows An Oval Shaped Heterogenously Hypoechoic Wider Than Taller With Spiculated Margins And With Posterior Acoustic Enhancement.

Biopsy proven case of invasive ductal carcinoma NOS with TNBC Immunohistochemical profile

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