ROLE OF MORPHOLOGICAL CHANGES BY ULTRASONOGRAPHY IN PREDICTION OF BREAST CANCER MOLECULAR SUBTYPES

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Introduction

Breast cancer is the most common cancer in women. It is a complex disease. The molecular subtyping of breast cancer has emerged as a vital component of breast cancer management recently, and it is now essential for prognosis and therapeutic planning.According to the St Gallen conference (2011) four molecular subtypes can be defined by using the following biomarkers: ER, PR, HER2 and Ki-67. The 4 subtypes are: Luminal A, luminal B, HER2-enriched, and triple negative breast cancer. Breast imaging may have a role in predicting the molecular subtypes of breast cancer. Mammography and ultrasonography are the primary imaging modalities. Ultrasound is known for its high sensitivity and specificity with being non invasive. Consequently, we are attempting to correlate between the molecular subtypes and morphological changes detected on ultrasound such as shape, margins, orientation, surrounding desmoplastic reaction, related parenchymal architecture distortion, calcifications and vascularity.

Aim of the work

The aim of this study is to evaluate the role of morphological changes detected on ultrasonography in prediction of breast cancer molecular subtypes.

Patients and Methods

PATIENTS: The study was conducted on 50 patients presenting to radiology department for ultrasound and mammography assessment then tissue sampling with histopathology and immunohistochemistry.

METHODS: Patients underwent history taking and clinical examination, then referred for Mammography (MLO and CC view) using an X-ray mammography unit (Siemens, MAMMOMAT Nova machine) then ultrasonography (GE LOGIC P5 machine) with superficial transducer 12 MHz linear probe if above 30 years old and only ultrasonography if under 30 years old.

The results were interpreted using the ACR BIRADS. Image guided /excisional biopsies were scheduled for patients with suspicious lesions, then fixed in 10% solution of formalin and stained with Hematoxylin-eosin for histopathology. Immunohistochemical staining results of ER, PR were assessed by Allred score and those of HER2 were assessed according to ASCO / CAP criteria. Ki-67 index was assessed using a cutoff value of 20%: less than 20% were considered as low expression, more than or equal to 20% were considered as high expression.

Results

A statistically high significant correlation was found between Her-2 enriched subtype and both presence of calcifications in the mass lesion with p value <0.001 and multiplicity with P value 0.003. A statistically high significant association was found between triple negative subtype and regular shape (round /oval shapes) with p value <0.001and with rather non spiculated margins with P value 0.006. Hormone receptor positive status of breast cancer (ER and PR) showed a statistically significant relation with lesion's posterior shadowing on ultrasound basis with P value = 0.007 and 0.002 respectively. Moreover, triple negative subtype showed a statistically significant correlation with absence of surrounding desmoplastic reaction with P value =0.048, while LA subtype showed a statistically significant correlation with presence of surrounding desmoplastic reaction with P value = 0.02.

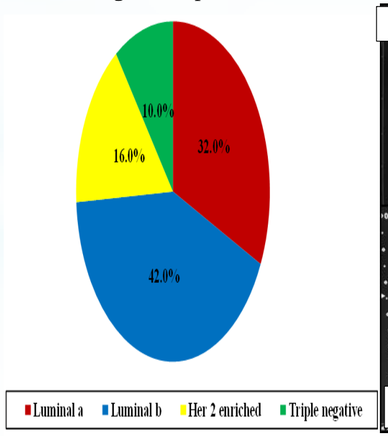

Figure (1):Distribution of the studied cases according to molecular subtype (n = 50)

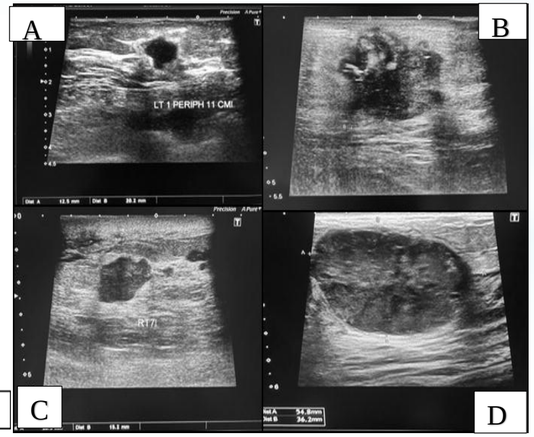

Figure (2): Ultrasound of 4 molecular subtypes. (A)Luminal A subtype shows spiculated strongly shadowing mass lesion with surrounding desmoplastic reaction. (B) Luminal B subtype shows spiculated mass lesion with surrounding desmoplastic reaction. (C) HER-2 enriched subtype shows irregular mass lesion with intralesional calcifications. (D) Triple negative subtype shows oval shaped mass lesion with no desmoplastic reaction.

Table (1): shows the statistically significant ultrasound morphological features for prediction of molecular subtypes.

	Molecular Subtype							
	Luminal A (n = 16)		Luminal B (n = 21)		Her 2 enriched (n = 8)		Triple negative (n = 5)	
	No.	%	No.	%	No.	%	No.	%
Shape								
Oval / Round	0	0.0	0	0.0	0	0.0	4	80.0
Irregular	16	100.0	21	100.0	8	100.0	1	20.0
p_1	$^{FE}p=0.292$		$^{FE}p=0.129$		$^{FE}p=1.000$		$0.001^{*}<^{FE}p$	
Margin								
Indistinct	1	6.3	2	9.5	0	0.0	2	40.0
Angulated	0	0.0	1	4.8	0	0.0	0	0.0
Microlobulated	0	0.0	2	9.5	1	12.5	2	40.0
Spiculated	15	93.8	16	76.2	7	87.5	1	20.0
p_1	$^{FE}p=0.316$		$^{FE}p=0.924$		$^{FE}p=0.848$		$^{FE}p=0.006^{*}$	
Posterior features								
Enhancing	3	18.8	0	0.0	0	0.0	0	0.0
Shadowing	13	81.3	15	71.4	8	100.0	5	100.0
Indifferent	0	0.0	6	28.6	0	0.0	0	0.0
p_1	$^{FE}p=0.007^{*}$		$^{FE}p=0.002^{*}$		$^{FE}p=0.749$		$^{FE}p=1.000$	
Calcifications								
No	13	81.3	14	66.7	1	12.5	5	100.0
Yes	3	18.8	7	33.3	7	87.5	0	0.0
p_1	0.118		0.933		$^{FE}p=0.001^{*}$		$^{FE}p=0.152$	
Architecture diastortion								
No	1	6.3	2	9.5	4	50.0	3	60.0
Yes	15	93.8	19	90.5	4	50.0	2	40.0
p_1	$^{FE}p=0.138$		$^{FE}p=0.160$		$^{FE}p=0.041^{*}$		$^{FE}p=0.048^{*}$	
Desmoplastic reaction								
No	0	0.0	7	33.3	0	0.0	3	60.0
Yes	16	100.0	14	66.7	8	100.0	2	40.0
p_1	$^{FE}p=0.020^{*}$		$^{FE}p=0.073$		$^{FE}p=0.184$		$^{FE}p=0.048^{*}$	
Multiplicity								
No	15	93.8	19	90.5	3	37.5	4	80.0
Multiplicity	1	6.3	2	9.5	5	62.5	1	20.0
p_1	$^{FE}p=0.240$		$^{FE}p=0.271$		$^{FE}p=0.003^{*}$		$^{FE}p=1.000$	

Conclusion

•Hormone receptor positive breast cancers are more likely to have lesions showing posterior acoustic shadowing on ultrasound. •HER-2 enriched subtype is more correlated to intralesional calcifications, absence of surrounding parenchymal architecture distortion and to multiplicity. •Triple negative molecular subtype can be easily mistaken for benign looking features on ultrasound showing oval/round shape, non-spiculated margins with no surrounding parenchymal architecture distortion or surrounding desmoplastic reaction.