Original Article

Ultrasound findings in prediction of breast cancer histological grade and HER2 status

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Abstract:

Background: Breast cancer is the most frequent cancerous tumor and major cause of death from cancer between women all over the world.

Objectives: is to assess if ultrasound features of breast cancer can predict its histopathological grade and HER2 status of breast cancer for patients had their diagnosis in Oncology Teaching Hospital in Medical city complex from September 2014 to November 2015

Patients and Methods: This is retrospective study of 102 patients whom histopathologically proved breast cancer had reviewed their ultrasound findings and correlate them with histopathological grade and HER2 status.

Results: well circumscribed lesions, poorly defined and spiculated lesions are more likely to be of intermediate to high grade histopathology with negative HRE2 status while malignant LNs states are more likely to be from moderate to high grade with positive HER2.

Conclusion: Breast ultrasound is a good tool in prediction of histopathology and HER2 status by assessment breast lesion morphology, outline and margin

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Introduction:

Breast cancer is the most frequent cancerous tumor and the major cause of death from cancer in between women all over the world. Breast cancer is also a diverse and complex disease with separate morphologic, biologic and molecular characteristics. (1)Even though histopathological features of tumors have been used to demarcate prognosis and treatment of breast cancer, they do not offer precise informations due to tumor heterogeneity. For aforementioned reason, many definite molecular subtypes of breastcancer have been established based on gene expression patterns (2). St. Gallen International Expert Consensus determined a recent biological classification system based on the manifestation of three tumor markers: estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor 2-neu (HER2), and now Ki-67 which are measured routinely because of their helpfulness in guiding clinical care. This classification system classifies invasive breast carcinomas into five molecular subtypes: luminal A, luminal B (HER 2-), luminal B (HER 2 +), HER 2, and triple negative subtypes. (3, 4, 5)

Patients and Methods:

The sonographic appearances of 102 primary invasive breast cancer patients at our breast cancer center in oncology hospital –medical city complex that were diagnosed between the dates of September 2014- November 2015 were retrospectively weighted from the database. All patients were histologically proven from excisional specimens and sorted according to molecular subtypes. Patients with insitu breast cancer were excluded from our study.Ultrasound scans were carried out with a 13-5 MHz linear transducer using Siemens ACUSON X300. One radiologist assessed the ultrasound images of each tumor from the patient archives. All sonography exams were performed by radiologists and multiple images were recorded during this process.Ultrasound findings, including margins, border definition and lymph nodes status were retrospectively analyzed.Tumor margins were categorized as circumscribed and non-circumscribed. Non-circumscribed category is divided into indistinct and spiculated. These sonographic findings were then correlated with histological grade and HER2 status.

Histological Analysis

Histologic grading was justify on the modified Scarff-Bloom-Richardson System and grouped as: grade 1 (well differentiated), grade 2 (moderately differentiated) and grade3 (poor differentiated). For the design of the study, grade 1 and 2 were considered as low grade, whereas grade 3 was considered as high grade.Immunohistochemistry (IHC) The expression status of the, HER2 was evaluated by an immunohistochemical analysis with antibodies.

Results:

One hundred two patients diagnosed as breast cancer in

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oncology teaching hospital had their ultrasound findings of their diseases were assessed retrospectively from the databaseThe patients' age is ranged from 33 years to 67years with mean age of 50 years.

Breast lesions results:
The details about breast lesions by ultrasound and their correlation with histopathological grade and HER 2
are shown in table 1.

Table 1: ultrasound findings in correlation with grade & HER 2

Ultrasound findings	Number	Grade			HER2	
		Well differentiated	Moderate differentiated	Poor differentiated	-ve	+ve
Circumscribed	10(10%)	0 (0%)	6 (60%)	4 (40%)	8 (80%)	2 (20%)
Poor defined	72(71%)	4 (5%)	50 (69%)	18 (25%)	64%))46	26 (36%)
Spiculated	19(18%)	4(22%)	13 (66%)	2 (11%)	15 (78%)	4 (22%)
No mass	1(~1%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)
LNs	58(57%)	0 (0%)	40 (69%)	18 (31%)	14 (24%)	63 (76%)

Circumscribed lesions seen in ten patients (10 %) in whom axillary LNs show malignant criteria in 20% of them, while the poor defined lesions were seen in majority of patients (71%) the lymph nodes with malignant features present in 73% of them (table 2).

Table 2: breast lesions in correlation with lymph nodes status

Breast lesion	LNs status	
	-ve	+ve
Circumscribed	8 (80%)	1(20%)
Poor defined	20 (27%)	52(73%)
Spiculated	15 (78%)	4 (22%)
No mass	1 (100%)	0 (0%)

Spiculated lesions seen in 18 % of patient in whom pathological LNs are identified in 22%
Single patient shows focal heterogeneous area of breast tissue in upper outer quadrant with –ve LNs, her FNA reveals malignancy.
Breast lesions in correlation with histopathological grade:
Poorly differentiated lesions are seen in 40% of circumscribed lesions, 25% of poor demarcated lesions, 11% of spiculated lesions and 31% of them had LNs with malignant criteria.
Moderately differentiated lesions are seen in 60% of circumscribed lesions, 69% of poor demarcated lesions, 66% of spiculated lesions and 69% of them had LNs with malignant criteria.
Well differentiated lesions are seen in 5% of poor demarcated lesions and not seen in other lesions and did not have LNs with malignant features.
Breast lesions in correlation with HER 2 status:
Positive HER2 status seen in 20% of circumscribed lesion and 36% of poor demarcated lesions while seen in 22% of spiculated lesions and 76% of them had malignant LNs
Negative HER2 seen in 80% of circumscribed lesion and 64% of poor demarcated lesions while seen in 78% of spiculated lesions and 24% of them had malignant LNs

Discussion:
The use of breast ultrasound has become an effective method in helping to distinguish benign from malignant lesions (6), the use of new trend ultrasound system and high frequency linear probe aid in further characterization of breast lesions. (7) We find that poorly differentiated tumors were more likely than well differentiated ones to show poorly defined outline in addition to positive (+ve) pathological adenopathy and negative (-ve) HER2 status ,this in agree with Lambat al. who retrospectively investigated 120 invasive ductal carcinoma patients for the relationship between imaging features and histologic grade (8, 10). While the masses with circumscribed margins are associated with intermediate and high grade by histopathology, negative adenopathy and negative HER2 status and this also in agree with Shin et al. (9) Spiculated and irregular outline breast cancer are most likely to be low and intermediate grade, with negative lymph nodes involvement and negative HER2 status and this is in agree with Kojima et al. (11)\
Thus, breast ultrasound performed by experienced radiologist may help to predict HER2 status and molecular subtypes of tumors and this may consider as being sufficient in certain circumstances where there are no resources for lab testing to

depend ultrasonographic features to make decision for pre-treatment planning and understanding biological behavior of lesion. (12)

Conclusion:

Sonographic features were found to be significantly associated with molecular subtype, histological grade and hormone receptor status. Being able to predict the likelihood of molecular subtype by ultrasonography may also have an important role for earlier management and treatment. But still further work and prospective studies are necessary to determine the full potential of sonography in the evaluation of the molecular subtypes of malignant breast lesions.

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