Clinico- Pathological Features And Out Come Of Triple Negative Breast Cancer

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Abstract

Background: Triple-negative breast cancer is a distinct entity of breast cancer, which is associated with aggressive behavior and poor prognosis, and typically do not express hormone receptors (estrogen receptor-negative, progesterone receptor-negative) and negative HER-2 and characterized by high proliferation rate and BRCA1 gene dysfunction. Currently patients with this type of tumor cannot be managed with existing targeted treatments (trastuzumab and hormonal therapy).

Aim of study: To evaluate the clinico-pathological features, and outcomes of women with triple-negative breast cancer and compared with other types of breast cancer.

Method: A retrospective study was done in 2009 for all women with breast cancer treated at the Al-Sadder teaching hospital in AL-Najaf from January 2006 to December 2008, the pathological reports were reviewed, details about the age at diagnosis, tumor grade, lymph node status, pathologic tumor size in centimeters, the paraffin-embedded blocks was requested for antibody staining in the laboratory of Al-Sadder teaching hospital .The clinico-pathological features of tumor were compared with other groups using a *t* test for means and x^2 statistic for frequencies.

Results: From 232 women with breast cancer (12.5%) had triple-negative breast cancers and mostly are in the younger age groups, a high proportion of triple negative (86%) were found in Body mass index more than 30, and (62%) of them had positive lymph node, and according to the size of tumor (13.8%) of the triple-negative tumors were more than 5 cm, and (62%) of them had grade III tumors. A higher proportion of patients with triple negative had BRCA1 (20.68%), and (65.5%) of them had history of contraceptive pills, with higher proportion of distant recurrence (17.2%) and mainly to brain metastasis (10.2%), and there is no statistical significant in the local recurrence between triple negative breast cancer and others (6.8%) and (6.4%) respectively.

Conclusions: Triple-negative breast cancers have a more aggressive clinical course than other forms of breast cancer.

Introduction

In 2008, it is estimated that over 1 million women worldwide will be diagnosed with breast cancer, of which 172,695 will be classified as triple-negative[1] and this phenotype encompasses a breast tumor subtype that is negative for expression of the estrogen and progesterone receptors (ER and PR) and lacks overexpression of the HER2 protein, with unique prognostic and therapeutic implications. Several epidemiological studies have provided insight into risk factors associated with triple-negative breast cancers were more likely to arise among women with a younger age at menarche, higher parity, younger age at full-term pregnancy, shorter duration of breast-feeding, and higher body mass index (BMI) especially among premenopausal patients and regardless of the stage at diagnosis, and had poorer survival than those with other breast cancers. The relative survival for all women with triple-negative tumors was 77% at 5 years, compared with

93% for other breast cancers, this poorer survival was consistent for each stage of cancer and each race group. Recent studies suggest that patients with triple-negative breast cancer have a high incidence of visceral metastasis, including brain metastasis[2,3]. Although triple-negative breast cancer is associated with a generally poor breast cancer specific outcome, and it is not resistant to chemotherapy . In the adjuvant setting, retrospective review of a subset of patients treated on Cancer and Leukemia Group B suggested that the benefit of a taxane added to an anthracycline was primarily among patients whose disease overexpressed HER2 or were double-negative (ER/HER2), most of which are likely to be basal-like[4] chemotherapy had been the mainstay of systemic treatment for triple-negative breast cancer, since currently available targeted agents, including endocrine therapy and HER2-directed therapies, are ineffective. Triple-negative breast cancer is highly responsive to primary anthracycline and anthracycline/taxane chemotherapy.[5]

Method

This study was done in 2009 for all women with breast cancer treated at the Al-Sadder teaching hospital in Al-Najaf from January 2006 to December 2008 and followedup regularly during this period, the medical records and pathological reports were reviewed. Patient information was recorded with details about the patient's age at diagnosis (in years),history of contraception,body mass index(weight)/(height)^2,tumor grade, lymph node status, pathologic tumor size in centimeters,.Diagnosis of metastasis was done by using chest X-ray,abdominal ultrasound,abdominal and brain CT scan, a set of representative paraffin-embedded blocks was requested for antibody staining in the laboratory of Al-Sadder teaching hospital and some others in private laboratories , ER and PR status and HER2 detected by using the LSAB(Labelled Streptavidin–Biotin System)[6] method, the HER2 positivity was defined as strong complete membrane staining with score 3+ only, the clinico-pathological features of tumor were compared between the triple-negative and other groups using a *t* test for means and x^2 statistic for frequencies. We evaluated the differences in method of detection between the triple-negative and other group using the x^2 statistic, and p-value less than 0.05 is significant

Results

From 232 women with breast cancer 29(12.5%) had triple-negative breast cancers and mostly are in the younger age groups with mean age at presentation 40 years versus 59.8 years in the other groups women breast cancer with $P < 0.04$, a high percentage of triple negative 25(86%)were found with body mass index more than 30 $P < 0.002$. 18(62%) of triple-negative had positive lymph node was higher than other group 91(44.9),and according to the size of tumor 4(13.8%) of the triple-negative tumors were >5 cm at presentation while 19(9.4%) in the other groups women breast cancer *(*$P <$ 0.001).18(62%) of triple negative have grade III tumors while 49(24%) in the other groups of breast cancer $P < 0.00015$, a higher proportion of patients with triple negative had BRCA1 6(20.68%) while 8(3.9%) in other groups $P < 0.006$, 19(65.5%)of triple negative had history of contraceptive pills while 65(32%) in the other type of breast cancer $P < 0.02$, table -1

Table 1. Clinico-pathological features of the triple-negative compared with other breast cancers

Categories		Other types of breast cancer	Triple negative	P – value
Mean age at diagnosis (y)		59.8	40	0.04
Body mass index	<30	89(44%)	4(14%)	0.002
	≥30	114(56%)	25(86%)	
Lymph node status	Positive	91(44.9%)	18(62%)	0.8
	Negative	112(55.1%)	11(38%)	
Tumor size (cm)	<2	105(51.7%)	10(34.5%)	
	2 to 5	79(39%)	15(51.7%)	
	>5	19(9.4%)	4(13.8%)	0.001
Tumor grade	I	56(27.6%)	4(14%)	
	II	98(48.3%)	7(24%)	
	III	49(24%)	18(62%)	0.00015
BRCA1 mutation	Present	8(3.94%)	6(20.68%)	0.006
	Absent	175(86.2%)	23(79.32%)	
	Not available	20(9.85%)	0	
History of Contraceptive pills		65/203(32%)	19/29(65.5%)	0.02

Patients with triple-negative breast cancer had higher proportion with distant metastasis 5(17.2%) and mainly to brain metastasis 3(10.2%) compared with other breast cancers 15(7.3%), early recurrence less than one year occurred in the triple negative 4(80%) while 2(13%) in non triple negative, there is no statistical significant in the local recurrence between triple negative breast cancer and others 2(6.8%), 13(6.4%) respectively.

Table -2 Show patterns of metastasis and local relapse in Triple negative compare with others

Categories		Triple negative	Other types of breast cancer	p-value
Distant recurrence	Total	5(17.2%)	15(7.3%)	0.02
	brain metastasis	3(10.2%)	7(3.4%)	
	Lung metastasis	2(7%)	6(3%)	
	Other sites	0	2(0.9%)	
Time of recurrence	<1year	4/5(80%)	2/15(13%)	0.0001
	≥year	1/5(20%)	13/15(87%)	
Local recurrence		2(6.8%)	13(6.4%)	0.9

Discussion

Triple-negative breast cancer had recently been recognized as an important subgroup of breast cancer with a distinct outcome and therapeutic approach when compared with other subgroups of breast cancer. It is characterized by its unique molecular profile, aggressive behavior, distinct patterns of metastasis, and lack of targeted therapies onset at a younger age, higher mean tumor size, higher-grade tumors, and a higher rate of node positivity[7,8] and our study supported these studies. Other studies represented triple negative more likely to occur among premenopausal women of African-American descent[9,10].This study showed the high BMI are more associated with triple negative breast cancer like other study but differed in the study that done in Boston University which showed the triple negative tumors was associated lower BMI (p=0.02)[11].In this study the majority of BRCA1 associated breast cancers are triple-negative similar to other many preclinical and clinical studies that showed tumors with BRCA1 dysfunction harboring deficient double-stranded DNA break repair mechanisms are sensitive to agents that cause DNA damage, such as platinum agents (cisplatin and carboplatin)[12,13]. Patients in our study with triple-negative category had relatively large tumors more than 5 cm and also found in study by Foulkes et al.[14,15]. The increased incidence of brain metastasis among patients with HER2-positive metastatic breast cancer had been documented for several years, and targeted therapeutics lapatinib (Tykerb) have shown promise in the treatment of HER2-positive trastuzumab (Herceptin) refractory, and progressive brain metastasis[16,17] More recent studies highlight the frequency and aggressiveness of brain metastasis in triple-negative breast cancer[5] same result in this study .Our presentation had interesting in regard that (65.5%) of triple negative had history of contraceptive pills while (32%)in the other type of breast cancer.

Conclusions

Triple-negative breast cancers have a more aggressive clinical course with ayounger age groups than other forms of breast cancer and the majority of those patients had history of smoking, but with noclear explain till now and need further researches .Current

research strategies are aimed at better understanding both the risk factors and the out come of triple-negative breast cancer.

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