CLINICOPATHOLOGICAL CHARACTERISTICS OF TRIPLE NEGATIVE BREAST CANCER

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ABSTRACT

Objective: To analyze the clinicopathological characteristics of triple negative breast cancer.
Study Design: Descriptive case series.
Place and Duration of Study: Armed Forces Institute of Pathology (AFIP), from Jan 2014 to Dec 2014.
Material and Methods: All cases of triple negative breast cancer diagnosed on histopathological examination followed by immunohistochemistry were retrieved from AFIP tumour registry. Patient's gender, age, tumour laterality, tumour size, histological tumour type, histologic grade, lymphovascular invasion, involvement of surgical margins and lymph node status were noted. The data were analyzed by using computer software program SPSS version 19. Descriptive statistics, frequencies and percentages were calculated.
Results: A total of 35 cases of triple negative breast cancer were included in the study. The age at presentation ranged from 32-79 years with mean age of 50.9 ± 11.7 years. Most of the patients were females (n=34, 97.1%), out of which 51.4% cases (n=18) belonged to premenopausal age group. Right sided breast tumours were more common (n=17, 54.8%). The most common T stage at presentation was p T2 (n=20, 57.1%), while the mean tumour size was 5.2 ± 2.2 cm. The most common histological type was invasive ductal carcinoma, NOS (n=32, 91.4%) while the commonest histological grade was Grade II (n=22, 67.7%). Lymphovascular invasion was observed in 54.3% (n=19) of the cases while lymph node metastasis was seen in 74.1% (n=20) of the cases. Five cases (14.3%) had positive surgical margins.
Conclusion: Triple negative breast cancer was more common in premenopausal females. Most common tumour type was invasive ductal carcinoma, NOS (Grade II) with a pT2 stage at presentation. Lymphovascular invasion and lymph node involvement was also seen in a large number of cases.

Keywords: Clinicopathological characteristics, Triple negative breast cancer.

INTRODUCTION

Breast cancer is the most common cancer affecting the females worldwide[1]. Its incidence in Pakistani women is 24.4% making it the commonest cancer in women in our country as well[2]. Breast cancer is a heterogenous group of diseases which comprises a spectrum of natural history, clinical presentations, pathologic and molecular characteristics of each subtype associated with different prognostic and therapeutic implications[3].

The recent advances in the field of DNA microarray technology has enabled further subdivision of breast cancer into molecular subgroups based on gene expression profiling[4]. Breast cancer can be divided into five subtypes by incorporating molecular markers namely estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER 2): luminal A (ER+, PR+, HER 2-), luminal B (ER+, PR+, HER 2+), basal-like (ER-, PR-, HER 2-), human epidermal growth factor receptor 2-overexpressing (ER-, PR, HER 2+) and normal breast like (ER+, PR+, HER 2-) subtypes. The normal breast like subtype is considered as an artefact. Whereas the basal-like subtypes is of particular importance because majority of basal-like breast cancers exhibit a "triple-negative" phenotype[5].

Triple-negative breast cancer (TNBC) is a relatively new entity, mentioned for the first time in 2005[6]. It is a subtype of breast cancer which is

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Received: 04 Jan 2016; revised received: 20 Jun 2016; accepted: 13 Dec 2016

characterized by the lack of expression of estrogen receptor, progesterone receptor and human epidermal growth factor receptor[7]. TNBC accounts for 10-20% of all breast carcinomas world wide,[8] while its proportion in Asian population is up to 25-30%[9].

TNBC is unresponsive to hormonal and anti-Her2/neu therapy and has different clinical course, morphological features, higher frequency of metastasis and low overall survival as compared to non-TNBC[10]. A large number of TNBC harbor BRCA1 mutations[11]. More than 90% of TNBCs exhibit an invasive ductal, no special type histology, while others may show metaplastic elements and medullary/atypical medullary features. Most of TNBC are high grade (Grade 3) tumours with areas of necrosis[12]. The proliferative index determined by Ki67 and p53 immunostaining is also higher in TNBC as compared to high grade non TNBC[13]. These tumours in addition also express basal markers like cytokeratin 5/6 (CK 5/6) and/or Epidermal growth factor receptor (EGFR)[14]. Unlike breast tumors that are hormone receptor and/or Her2/neu positive, triple negative tumors lack a targeted therapeutic target, with adjuvant therapy being the only treatment option[10]. Several biologically targeted agents are currently being explored for this group.

Although the clinicopathological characteristics of TNBC have been studied in other parts of the world, these features have not been elucidated widely in our population. Thus our study aimed to investigate the clinicopathological characteristics of TNBC in the Pakistani population reporting to our center.

MATERIAL AND METHODS

This retrospective study was carried out at Armed Forces Institute of Pathology, from 1st January 2014 to 31st December 2014. All cases of triple negative breast cancer diagnosed on histopathological examination followed by immunohistochemistry were retrieved from AFIP

Table-I: Clinical characteristics of triple negative breast cancer.

Clinical characteristics	Number of cases (n)	Percentage (%)
Gender		
Female	34	97.1
Male	1	2.9
Age (years)		
Mean ± SD	50.94 ± 11.77	
Range	32-79	
Age specific groups		
Premenopausal women	18	52.9
Postmenopausal women	16	47.1
Tumour laterality		
Right	17	48.6
Left	14	40.0
Missing	4	11.4
Tumour size (cm)		
Mean ± SD	5.24 ± 2.23	
Range	1.8 - 10.5	
T stage		
p T1	3	8.6
p T2	20	57.1
p T3	12	34.3

tumour registry, irrespective of the age and gender of the patients. Cases with incomplete clinicopathological data, recurrent tumours and cases diagnosed on trucut/incisional biopsies were excluded from the study. A total of 35 cases fulfilling the criteria were included in the study. Patient's gender, age, tumour laterality, tumour size in centimeters, histological tumour type, histologic grade, lymphovascular invasion, involvement of surgical margins and lymph node status was noted. The data was analyzed by using computer software program SPSS version 19. Descriptive statistics were calculated. Frequencies and percentages were recorded for categorical variables while mean and standard deviation were calculated for the quantitatve variables.

RESULTS

The tumour registry record from 1st January 2014 to 31st December 2014 showed that a total of 563 cases were subjected to immunohistochemical analysis for estrogen receptor, progesterone receptor and human epidermal growth factor receptor at AFIP, Rawalpindi. During this period, 19% of the cases (n=107) were diagnosed as triple negative breast cancer. The clinicopathologic characteristics of 35 cases of TNBC with complete clinicopathological data were analyzed and are summarized in table-I and II.

The gender distribution showed that 34 patients were females, accounting for 97.1% (n=34); while 1 case was male (2.9%). The female to male ratio was 34: 1.

Table-II: Pathological characteristics of triple negative breast cancer.

Pathological Characteristics	Number of cases (n)	Percentage (%)
Type		
Invasive ductal carcinoma, NOS	32	91.4
Medullary carcinoma	1	2.9
Metaplastic carcinoma	1	2.9
Invasive lobular carcinoma	1	2.9
Histological grade		
Grade I	0	
Grade II	22	62.8
Grade III	10	28.6
Not applicable	3	8.6
Lymphovascular invasion		
Present	19	54.3
Absent	16	45.7
Surgical margins		
Positive	5	14.3
Negative	30	85.7
Lymph nodes		
Positive	20	57.2
Negative	7	20.0
None identified	8	22.8

All the diagnosed cases presented between the age of 32-79 years with mean age of 50.9 ± 11.7 years. A slightly higher prevalence was seen in the premenopausal females (n=18/34, 52.9%) as compared to postmenopausal females (n=16/34, 47.1%).

In our study, the laterality was unknown in 11.4% of the cases. Among the tumours with known laterality, right sided breast tumours were

more common (n=17/31, 54.8%) as compared to left sided tumours. Twenty cases (57.1%) had stage p T2 at presentation, followed by p T3 (n=12, 34.3%). However, the mean tumour size was 5.2 ± 2.2cm with a range of 1.8-10.5 cm.

The most common histological type was invasive ductal carcinoma, NOS (n=32, 91.4%) followed by medullary, metaplastic and invasive lobular carcinoma (n=1, 2.9% each).

Among the cases of invasive ductal carcinoma, 67.7% of the cases belonged to Bloom Richardson Grade II (n=22/32) followed by Grade III (n=11/32, 33.3%). None of the tumours had a Grade I histology on microscopic examination. Grading was not applicable to three tumours; these being medullary carcinoma, metaplastic carcinoma and invasive lobular carcinoma.

Lymphovascular invasion was observed in 54.3% (n=19) of the cases and lymph node involvement was seen in 20 cases (74.1%). Five cases (14.3%) had positive surgical margins.

DISCUSSION

The mean age in our study was 50.9 years. This is in concordance with a study conducted by Rakha et al in Nottingham, the mean age in their study was 49.9 years[10]. Our mean age was 7.6 years younger as compared to study carried out by Spitale et al in Switzerland (58.5 years)[15], 7.2 years younger as compared to the mean age in the study conducted by Onitilo et al in Wisconsin, United States (58.1 years)[13], 5 years younger than Turkish population in a study conducted by Pala et al (55.9 years)[16] and 4.1 years younger than a study carried out in Peurto Rico by Giraldo-Jiménez et al (55 years)[17]. It is 1.5 years older than the study conducted in Malaysia by Kanapathy et al (45.3 years)[18]. Comparing the age with a local study by Sajid et al (46.2 years), conducted at Armed Forces Institute of Pathology, Rawalpindi in 2010, the mean age in our study was 4.7 years older[19]. These differences may be attributable to the larger sample sizes in the above mentioned studies as compared to the current study.

TNBC was slightly more prevalent in premenopausal women (51.4%) in our study. However it was more common in postmenopausal females in studies carried out by Spitale et al[15] in Switzerland and Giraldo-Jiménez et al[17] in Peurto Rico; The percentages being 63.3% (n=90) and 55.6% (n=54) respectively in postmenopausal females (p>0.001).

The mean tumour size in our study was 5.2 ± 2.2cm as compared to 2.6 ± 1.8 cm, reported by Spitale et al in Switzerland (n=90) (p<0.001)[15]. This difference might be due to late presentation of patients to health care units in our population.

Majority of our patients presented with stage p T2 at the time of diagnosis. This observation was in concordance with that of Kanapathy et al[18] in Malaysia (35.7%, n=15/42) and Giraldo-Jiménez et al[17] in Peurto Rico (46.3%, n=25/54). However, stage p T1 was more common in study carried out by Spitale et al[15] in Switzerland (48.1%, n=39/90) (p<0.001). This difference might be due to the early cancer detection among the patients in that part of the world.

The most common histological type in our study was invasive ductal carcinoma, NOS (n=32, 91.4%). These results are almost similar to those of Giraldo-Jiménez et al[17] from Peurto Rico (96.3%, n=52/54), Spitale et al[15] from Switzerland (91.9%, n=80/90), Pala et al[16] from Turkey (90.2%, n= 41), Kanapathy et al[19] from Malaysia (83.3%, n=35/42) and Onitilo et al[19] from USA (82.2%, n=125/152) (p>0.001).

Grade II tumours were the commonest in our population (n=22, 67.7%). This is in contrast to studies carried out by Giraldo-Jiménez et al[17] in Peurto Rico (88.9%, n=66/90), Spitale et al[15] in Switzerland (66.6%, n=48/54), Onitilo et al[13] in USA (76.3%, n=116/152) and Kanapathy et al[18] in Malaysia (76.2%, n=32/42), where Grade III was the predominant histological grade (p<0.001).

Lymphovascular invasion was observed in 54.3% (n=19) of the cases in the current study where as 20.3% cases (n=11/54) showed lymphovascular invasion in a study carried out

by Giraldo-Jiménez et al[17] from Peurto Rico (p<0.001).

Lymph node involvement was seen in 74.1% (n=20) of the cases as compared to the studies done by Kanapathy et al[18] (40.5%, n=17/42) and Onitilo et al[13] (32.2%, n=49/152) (p>0.001). The reason this might be due to the late presentation and larger tumour size in our study.

CONCLUSION

In our population, triple negative breast cancer was more common in premenopausal females. The patients presented with a larger mean tumour size and invasive ductal carcinoma (NOS), Grade II was the commonest tumour type. The tumours showed higher frequency of lymphovascular invasion and lymph node involvement.

As this study was carried out in a small number of patients, further studies on a large sample size may be undertaken to substantiate these fundings.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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