CASE SERIES

Male breast cancer: A 10 year retrospective case series in a tertiary care hospital

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Abstract

Male breast cancer is a rare disease and it differs from breast cancer in women by some characteristics. The incidence of the disease has increased in the last 25 years. The records of male patients who underwent surgery for breast cancer between 2007 and 2017 were retrospectively reviewed in a tertiary care hospital in Istanbul, Turkey. The patients' ages, background, family history, clinical features, histopathological features of the tumour, its stage, the treatment and the survival were investigated. SPSS 15.0 for Windows programme was used for statistical analysis.Survival analysis was performed with Kaplan-Meier method.Determinants were analysed by univariate Cox regression analysis. A total of 15 patients were evaluated in our study. Fourteen patients had invasive ductal carcinoma and one patient had intraductal papillary carcinoma. The median follow-up period of the patients was 36 months The axillary lymph node metastasis positivity rate (number of metastatic lymph nodes/number of lymph nodes dissected) was statistically significantly higher in patients who died than in patients who survived.In univariate Cox regression analysis, the effects of age, tumour size, estrogen, progesterone, the presence of HER2/neu receptor and axillary metastasis on survival were not determined. We believe that raising awareness on male breast cancer in the community, genetic testing and screening mammography in high-risk patients will be useful in early diagnosis of the disease and improvement of its prognosis.

Keywords: Male breast cancer, Genetic testing, Screening mammography.

Introduction

Male breast cancer (MBC) is a very rare disease representing nearly 1% of totalbreast cancer patients. However, the incidence of MBC has increased by 26% over the last 25 years.[1] In 2016, there were approximately 2,400 new cases and estimated 440 breast cancer-related deaths among patients with MBC in the United States.[2]

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The perception of breast cancer in society as a disease associated with only women plays a role in the delay of diagnosis. It has been reported that the duration between the onset of the disease and its diagnosis is in the range of 18 weeks to 6 months.[3]

In the etiology of MBC; family history, hormonal disorders (high levels of estrogen and prolactin), exposure to radiation, liver cirrhosis along with hyperestrogenaemia and Klinefelter syndrome are thought to be effective.[4]

It has been reported in literature that the tumour size and axillary lymph node involvement are important prognostic factors in male breast cancer as well as in female breast cancer.Male and female breast cancers show similarity regarding clinical findings and distant metastasis. However, there are some biological differences between MBC and female breast cancer. Especially histological subtype distribution and receptor expressions differ between males and females.[5] Few prospective studies of treatment in men with MBC have been done, so management is based largely on extrapolation from results in postmenopausal women.[6]

Case Series

Records of 15 male patients who were diagnosed with breast cancer in our clinic between 2007 and 2017 were retrospectively reviewed. The clinical characteristics of patients are presented in Table-1. The mean age was 61.3±15.1 years, with the youngest at 31-years old and the oldest at 82 years of age. All of the patients presented with a complaint of a breast mass. In two patients, the periareolar mass was accompanied by ulceration. In two patients, nipple retraction was detected with mass. Eight patients had palpable lymph nodes in the axilla. In 10 patients, axillary lymph node involvement was detected by ultrasonographic examination. When the patients' histories were examined, one patient had gynecomastia, and no patient had Klinefelter syndrome or exposure to radiation. One patient had a family history of breast cancer.

There was invasive ductal carcinoma in 14 patients and intraductal papillary carcinoma in 1 patient. All patients were diagnosed with ultrasound-guided thick needle biopsy. Histopathological examination revealed estrogen receptor was positive in 14 patients, and progesterone

Tables-1: Patient characteristics.

Characteristics (%)	No. of Patients
Mean Age (Years)	61.3±15.1
Tumor size (cm)	3.0±1.3
Histology	
Invasive ductal carcinoma	14 (93.3 %)
Intraductal papillary carcinoma	1 (6.7%)
Hormone Receptor Status	
ER (-)	1 (6.7 %)
ER (+)	14 (93.3 %)
PR (-)	2 (13.3%)
PR (+)	13 (86.7 %)
HER 2 (-)	13 (86.7 %)
HER 2 (+)	2 (13.3 %)
Triple Negative	1
Surgery	
Modified radical mastectomy	13 (86.7 %)
Simple mastectomy + SLNB	2 (13.3 %)
Axillary Lymph Node Metastasis	
Yes	12 (80%)
No	3 (20%)
Pathologic Stage	
T1N1	1 (6.7%)
T2N0	2 (13.3%)
T2N1	8 (53.3%)
T2N2	1 (6.7%)
T3N0	1 (6.7%)
T4N1	1 (6.7%)
T4N2	1 (6.7%)
Adjuvant Treatment	
Chemotherapy	10 (66.6%)
Radiotherapy	12 (80%)
Hormone therapy	14 (93.3%)

receptor was positive in 13 patients. Two patients were HER2/neu positive. Triple negativity was found in one case.

Modified radical mastectomy was performed in 13 patients. Two patients underwent simple mastectomy and sentinel lymph node biopsy. Histopathological examination revealed a mean tumour size of 3.0±1.3 cm. The mean number of dissected lymph nodes in patients who underwent axillary dissection was 14.9±4.6. Twelve

Table-2: Univariate cox regression analysis.

	p	HR	95 %CI	
Age	0,953	0,999	0,954	1,045
Tumour size	0,829	0,874	0,258	2,966
Estrogen receptor	0,082	0,085	0,005	1,365
Progesterone receptor	0,206	0,333	0,060	1,829
HER-2	0,586	0,654	0,142	3,013
Axillary Lymph node metastasis	0,709	26,631		

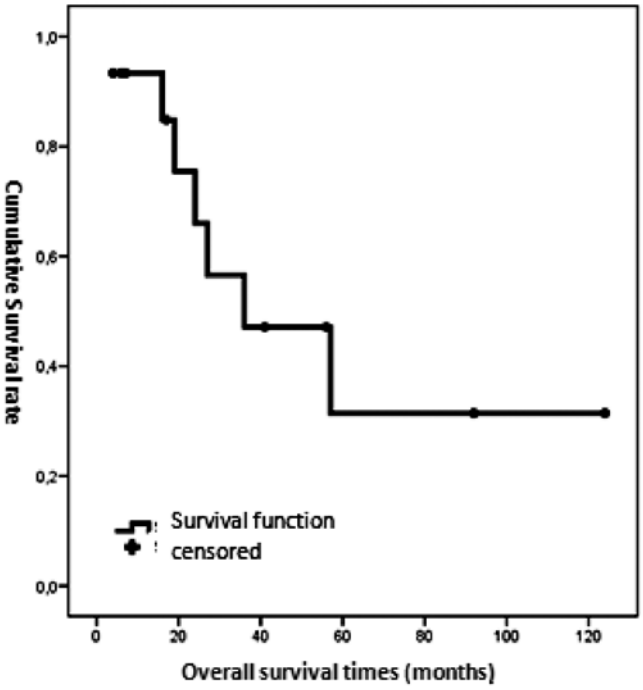

Figure: Overall survival of male breast cancer.

(80%) of the patients had axillary lymph node metastasis. The mean number of metastatic lymph nodes in these patients was 2.8±2.0. According to TNM classification, 3 (20%) patients were Stage 2A, 9 (60%) patients were Stage 2B, 1 (6.7%) patient was Stage 3A, and 2 patients (13.3%) were Stage 3B. There were no patients with metastasis stage 4 at admission.

Neoadjuvant chemotherapy was not administered to any patient. After surgery, 10 patients received adjuvant chemotherapy, 12 patients received radiotherapy, 14 patients received hormonotherapy. Patients were followed up every 6 months for the first 3 years, then with annual controls. Overall survival time in follows up was defined as the period between the diagnosis and the last control or death. The median follow-up time of the patients was 36 months (min 7 months, max 71 months). During the follow-up period, 7 (46.7%) patients were lost. The survival rates were found as 93.3% for 1 year, 66% for 2 years, 47.1% for 3 years and 31.4% for 5 years (Figure).

SPSS 15.0 for Windows programme was used for statistical analysis. Mann-Whitney U test was used to compare two independent groups. Rates in independent groups were tested by Chi-square analysis. Survival analyses were performed with Kaplan Meier Analysis. Determinants were analysed by univariate Cox regression analysis. The statistical significance level was accepted as $p < 0,5$.

Patients with Stage 2A and 2B had a median survival time of 57 months, patients with Stage 3A and 3B had a median survival time of 16 months. The difference was statistically significant. Log-rank p<0.001.

When a comparison was made between the survivors and deceased patients, there was no statistically significant difference with regards to age, tumour size, estrogen receptor, progesterone receptor, CerbB2 positivity, stage of the disease and axillary metastasis. Axillary lymph node metastasis positivity of the patients who died (number of metastatic lymph nodes/number of dissected lymph nodes) was statistically significantly higher than the patients who survived (p= 0.042). In univariate Cox regression analysis, no effect of age, tumour size, estrogen, progesterone, HER2/neu receptor positivity and axillary metastasis was detected on survival (Table-2).

Discussion

Male breast cancer (MBC) accounts for less than 1% of all breast cancers.In United States MBC affects only 1,000 men each year. Most western studies reveal that breast cancer in males has a unimodal age distribution, a later age at onset and poor prognosis compared to their female counterpart.[7,8]

The incidence of MBC increases with age. Studies have reported that the average age of onset is between 67 to72 years and it is seen 5 years later than women with breast cancer.[9] For example, in a high volume study in literature, the rate of male cancer among 53,012 breast cancer specimens was only 51 (0,096 %). It was also frequently seen in the 6th and 7th decades. The ages ranged from 33 to 82 years with a mean age of 56.2 years.[10]

The mean age in our study was 61.3 years and was lower than the literature. However, female breast cancers are also seen at younger ages in our country compared to western countries.[11] We think that the result of our study is parallel to the average age of female breast cancer in our country.

Most cases of MBC are sporadic. Familial history can be detected in 5% to 10% of cases. It has been reported that in cases of familial male breast cancer, BRCA-2 may be useful in detecting men with highrisk of breast cancer.[12] In our study, there was a positive family history in one patient. Treatment strategies are extrapolated from the management of female breast cancer.[13] In parallel to the treatment of female breast cancer, surgical treatment in MBC showed an alteration from radical mastectomy to modified radical mastectomy. However, breast-conserving surgery has not gained popularity as in female breast cancer because of the lack of breast tissue in men, the proximity of the tumour to the nipple-areola complex, and because the safe surgical margin is usually not achieved with adequate resection.[14] Since axillary lymph node involvement is common in MBC, modified radical mastectomy has become the most established intervention. Sentinel lymph node biopsy can be performed instead of axillary dissection for evaluation of axilla in male patients as the axillary lymph node involvement is clinically and radiologically absent in female breast cancer.[15] Similar to the literature, 13 patients were treated with modified radical mastectomy, 2 patients underwent simple mastectomy and sentinel lymph node biopsy in our study. No axillary dissection was performed in these two patients because there was no metastasis in the sentinel lymph node.

Among male breast cancers 85% are invasive ductal carcinoma. Invasive lobular carcinoma, which is the second most common in female breast cancer, is much less common in MBC. In our study, 14 (93%) patients had an invasive ductal carcinoma, whereas no lobular carcinoma was seen in any patient. Unlike females, papillary carcinoma is the second most common histological type seen in men.[16] We also detected papillary carcinoma in one patient.

Adjuvant chemotherapy in MBC is frequently recommended postoperatively, as its positive effect on general survival in female breast cancer is proven, but its use is limited due to advanced age and comorbid diseases. Because of high ER positivity in MBC, hormonotherapy is applied more frequently.[17] Because axillary lymph node involvement, central location, skin and pectoral muscle involvement are common in MBC, adjuvant radiotherapy in men is more common than in female patients.

The median follow-up time of the patients in our study was 36 months. Seven patients (46.7%) died during the follow-up period. In univariate Cox regression analysis, effects of age, tumour size, estrogen, progesterone, Her2/neu receptor positivity and presence of axillary metastasis on survival were not detected; however, in accordance with the literatüre,[18,19] the median survival times of patients with Stage 2A and 2B were statistically significantly longer than those with Stage 3A and 3B patients. Similarly, the number of metastatic axillary lymph nodes in patients who died was statistically significantly higher than in patients who survived.[20] Despite the limited number of patients present in our study,findings suggest that axillary lymph node metastasis and the stage of the disease affect survival significantly.

Conclusion

Male breast tissue is very small compared to female. Therefore breast cancer skin and pectoral muscle invasion spreadmore quickly and likewise axillary lymph node involvement occurs in a short time. In our study, the clinicopathological features of male breast cancer patients who were operated in our clinic were examined and their effects on survival were demonstrated. The size of the tumour and the presence of axillary lymph node metastasis are the most important factors affecting overall survival. It is caused by delay in patient consulting the physician. Little awareness of male breast cancer in the community leads patients to consult their physician long after the symptoms have started and the tumour is in advanced stages.

We propose that raising awareness about male breast cancer in the society, teaching self-examination in men, genetic tests and screening mammography in high-risk patients will be helpful in early diagnosis and improvement of prognosis. Thus, there is a need for more free awareness public programmes to educate men about breast cancer and promote its early detection.

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