Original Article

Male Breast Cancer in Singapore: 15 Years of Experience at a Single Tertiary Institution

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Abstract

Introduction: Male breast cancer is a rare disease entity, with little data from the Southeast Asian perspective. Hence, this study aims to review the data from our local experience in order to better delineate the disease characteristics in our population. Materials and Methods: Male patients with histologically proven breast cancer were identified from a prospectively collected database. The clinical, histopathological and survival data were reviewed retrospectively and analysed. Results: Twenty-one patients were identified. The median age at diagnosis was 68 years. Eighteen patients underwent simple mastectomy with curative intent, with the remainding patients having metastatic disease at presentation. Almost half of the patients presented with stage III or IV disease. At the time of analysis, median overall survival was 50 months and median disease-free survival was 47.5 months. None of the patients had any documented family history or risk factors for male breast cancer. Conclusion: The disease appears to be a sporadic and rare occurrence in the local male population. A high index of suspicion should be maintained in males presented with a unilateral breast lump so that appropriate treatment can be instituted.

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Key words: Asian, Clinical characteristics, Prognosis, Treatment

Introduction

Male breast cancer is a rare disease entity, traditionally said to represent <1% of all diagnosed breast cancers. Recent statistics, however, suggest that its incidence may be on the rise, although the clinical significance of this is unknown.[1,2] This rarity has precluded large randomised controlled trials, and most treatment recommendations and guidelines, including those for adjuvant therapy, are extrapolated from data derived from female patients.

Most published data on the topic of male breast cancer are derived from retrospective, single-institutional studies, and not much information from the Southeast Asian perspective has been available to date. This study therefore set out to better delineate the characteristics of male breast cancer in our local population, and describe the treatment outcomes and prognosis of these patients.

Materials and Methods

All consecutive male breast cancer patients treated between 1 April 1995 and 31 December 2009 at the Singapore General Hospital were identified from a prospectively collected institutional breast cancer database. Clinical, treatment, histopathological and survival data were then collected retrospectively from the patients' case sheets, outpatient records, pathological reports and operation records, and analysed.

Staging was recorded according to the 2003 AJCC (7th Edition) staging criteria. Tumour, node and presence of metastases (TNM) staging was recorded based on pathological staging performed post-surgery. If the patients did not undergo surgery, clinical TNM staging was applied instead. Follow-up and survival data were calculated from the date of definitive diagnosis to the date of death or till

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31 December 2010 i.e. time of data collection.

In the absence of established protocols for adjuvant treatment in male patients, our institution follows closely those recommendations and guidelines established for the treatment of disease in female patients.

Statistical analysis was conducted using Statistical Package for Social Sciences (SPSS) version 16.0 (Chicago, IL, USA). Overall survival and disease-free survival analysis was performed using the Kaplan-Meier method, and univariate analysis evaluating factors correlating with survival was performed using the log-rank test. A *P* value of <0.05 was considered to be statistically significant.

Results

Twenty-one patients were diagnosed with male breast cancer at our institution during the 15-year period. The median age at presentation was 68 years (range, 42 to 80 years). Figure 1 shows the age distribution at the time of diagnosis. Eighteen of these were Chinese, with 2 Malays and a Vietnamese gentleman making up the remainder. All the patients presented with a painless unilateral breast lump, with only 2 reporting other symptoms i.e. associated skin erythema and ulceration, respectively. None of them reported having a first-degree relative with a history of breast or ovarian cancer, and none had a personal history of any other cancers previously diagnosed. None of the patients had any documented identifiable risk factor for breast cancer.

All but 3 of the patients underwent surgery with curative intent. A breakdown of the details of the surgical interventions is presented in Table 1. The local treatment of choice was a simple mastectomy, which all the patients received. Only 4 patients received a sentinel lymph biopsy, and of these, only one was negative. This patient went on to undergo a low axillary sampling, as at the time the sentinel node biopsy procedure was not yet well-established in male patients. This was ultimately negative for any involved lymph nodes. The rest of the patients who underwent surgery all received a full level I-II axillary clearance.

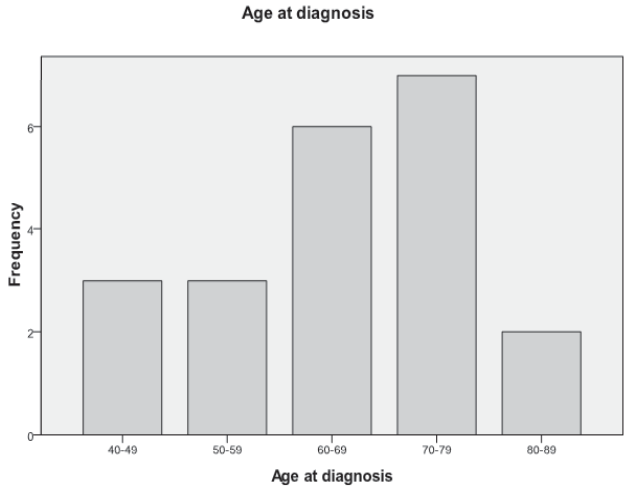

Fig. 1. Age distribution of patients at the time of diagnosis.

Table 1. Treatment and Clinicohistopathological Characteristics of Tumours

Tumour Laterality	Right	14
	Left	7
Palpable axillary nodes	Yes	5
	No	16
Surgery	Yes	18
	No	3
Extent of local surgery	Simple mastectomy	18
	Other	0
SLN biopsy	Yes	4
	No	14
Management of axilla	Axillary clearance	17
	Axillary sampling	1
T stage	T1	7
	T2	13
	T3	0
	T4	1
N Stage	N0	8
	N1	4
	N2	5
	N3	4
M stage	M0	18
	M1	3
Tumour grade	1	3
	2	11
	3	5
	Not Reported	2
ER status	Positive	21
	Negative	0
PR status	Positive	18
	Negative	3
Her2-neu status	Positive	4
	Negative	11
	Not reported	6

Eight patients received adjuvant chemotherapy, 5 received adjuvant radiotherapy to the chest wall, and 10 received hormonal therapy.

Of the 3 patients who did not undergo surgery, 1 had extensive supraclavicular and cervical lymphadenopathy at the time of diagnosis, and was diagnosed 6 months later with metastatic laryngeal cancer. Another presented with

multiple brain metastases causing midline shift died shortly after diagnosis. The last patient presented with metastases to the lung, liver and bone. This patient received palliative chemotherapy and is the only of the 3 who remains alive at the time of writing, 18 months after diagnosis.

The clinicohistopathological characteristics of the patient cohort are shown in Table 1. The mean tumour size at diagnosis was 25.5 mm (SD ±12.2 mm). There was a preponderance of right-sided tumours (14/21), and almost all the tumours were invasive ductal carcinomas (19/21), with the remaining 2 being an invasive lobular carcinoma and a mixed ductal/mucinous carcinoma.

At the time of analysis, the median overall survival was 56 months (range, 1 to 163 months), and the median disease-free survival being 56 months (range, 0 to 163 months). Two patients had been lost to follow-up. Nine patients were alive without evidence of local or distant disease and 5 patients had succumbed to their cancer. One patient (alluded to earlier) was alive with metastatic disease. Four patients died from other causes—2 suffered fatal myocardial infarctions, and the remaining 2 died of metachronous laryngeal and pancreatic carcinoma. Figures 2 and 3 show the Kaplan-Meier survival curves for overall and disease-free survival in our cohort.

Univariate analysis comparing the effect of age, stage, grade, hormone receptor status and treatment was performed, but no statistically significant differences were seen (data not shown).

Four patients presented with recurrence after initial curative surgery. Three of these recurred distally with metastases to brain and lung (at 48 months), bone and brain (at 53 months) and bone, lung and liver (at 36 months) respectively. The other patient presented with axillary recurrence 48 months after mastectomy and axillary clearance, which was locally excised. Unfortunately, he was found to also have liver metastases 2 months later on surveillance imaging.

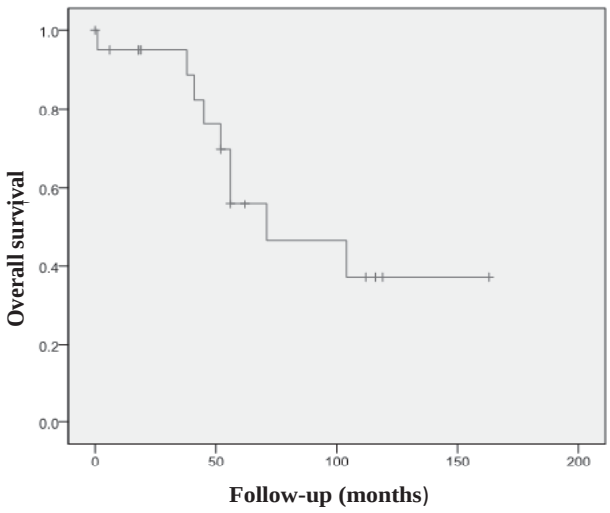

Fig. 2. Overall survival of male breast cancer patients.

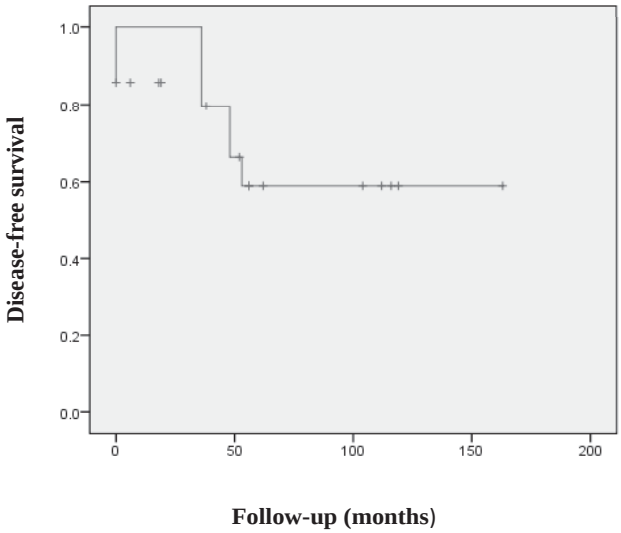

Fig. 3. Disease-free survival of male breast cancer patients.

Discussion

Male breast cancer is a rare disease entity in our local setting, with only 21 cases diagnosed and treated at our institution over a 15-year period, compared with over 500 new cases of female breast cancer diagnosed and treated annually at our institution. It is unclear whether this reflects the true comparative incidence of the disease among males, or whether (as is more likely) the increasing numbers of early stage screening-detected cancers among females contribute to the increasing numbers of female cancers diagnosed and treated.

Locally, we have found that compared to female patients, male patients tend to be older at diagnosis (median age 68 years), and present with advanced disease—almost half (10/21) patients were stage III or IV at diagnosis. In contrast, a median age at diagnosis of 52 years,[3] significantly younger than that of our patient population, has been reported in the local literature on female breast cancer patients. Conversely, 5/21 patients or 23.8% of our cohort had high grade tumours which is similar to the 26.6% reported in a local cohort of female patients.[3] While most international data, including large-scale retrospective studies and meta-analyses agree that male breast cancer patients present at a more advanced age,[4] the data were conflicting with regard to the aggressiveness of male breast cancer. Some studies show that the majority of male breast cancer tend to be high grade, yet others quote an incidence of Grade 1 and

2 tumours of up to 94%.[5,6]

All but one of our patients had T1 or T2 tumours, with 12/20 or 60.0% of these patients being node-positive—4 being N1, 5 being N2 and 3 being N3 at the time of diagnosis. It has previously been suggested that due to the relatively smaller size of the male breast, smaller tumours may tend to metastasise earlier to the axillary lymph nodes. Indeed, in an earlier study of the local female breast cancer population, the incidence of node-positive disease in patients presenting with T1and T2 tumours was noted to be 35%, markedly different from our male breast cancer cohort.[3] This is of significance as axillary nodal status has been consistently shown to be an important predictor of overall survival in male breast cancer.[7] In one early series, the 5-year survival of node-negative patients was 70%, while that of node-positive patients decreased to between 37% and 54%.[8]

No correlation between age, stage, grade, hormone receptor status or treatment with survival was found in our series. However, as it stands to reason that patients with more advanced stage of disease and patients who were treated with curative intent tend to have better outcomes, it is most likely that the patient numbers in our cohort were simply too small to make meaningful comparisons and demonstrate a statistically significant difference.

All the tumours diagnosed in our study cohort were ER positive, 18/21 were PR positive and 4/21 overexpressed cerb-2. The high rates of hormone receptor positivity and low rates of Her2-neu overexpression are well documented and are in concordance with other published data in the literature.[9,10]

Table 2. Established Risk Factors for Male Breast Cancer

Genetics
BRCA2 mutations
BRCA1 mutations
Klinefelter's syndrome
Family history of breast cancer
Ashkenazi Jewish men
Cowden syndrome
Endocrine
Estrogen excess: liver disease, exogenous estrogens
Androgen deficiency: prolactinoma
Others
Chest wall radiation
Testicular disorders: undescended testes, congenital inguinal hernia, orchiectomy, orchitis, infertility
Lifestyle: obesity, alcohol, diet
Occupational and environmental exposures: occupational exposure to heat, high ambient temperature, exhaust emissions, electromagnetic field radiation

Endocrine, genetic and other risk factors for male breast cancer which have been previously identified are shown in Table 2.[11] However, none of these factors were identified in our series, and male breast cancer in our population appears to be a sporadic disease. It must be pointed out, however, that due to the retrospective nature of this study, information on these risk factors might not have been documented during the initial presentation and work-up.

Although male breast cancer has traditionally been associated with a dismal prognosis, this is usually attributable to the late age of presentation and advanced stage at diagnosis. In studies where male and female breast cancer patients were matched by age and stage, equivalent survival has been reported.[9,12] In our study, it is difficult to comment on the effect of these factors due to the small numbers available and variable follow-up data and time. However, it should be noted that there were only 5 cancer-related deaths in our study cohort over the period under review.

Conclusion

Male breast cancer remains a rare disease in the local setting. It appears to be sporadic, with patients presenting at an advanced age and stage of disease. However, good long-term survival has been achieved in our series, in which the treatment protocols follow closely those established for female breast cancer. Attending physicians must have a high index of suspicion in male patients who presented with a unilateral breast lump in order to avoid delays in diagnosis, and to ensure that appropriate treatment is instituted so as to maximise clinical outcomes.

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