



# The Clinical, Diagnostic, and Therapeutic Characteristics of 22 Male Patients with Breast Cancer

Serdar Gökay Terzioğlu<sup>1</sup>, Murat Özgür Kiliç<sup>1\*</sup> and Gül Dağlar<sup>1</sup>

<sup>1</sup>Department of General Surgery, Numune Training and Research Hospital, Ankara, Turkey.

## Authors' contributions

This work was carried out in collaboration between all authors. Authors SGT and MÖK designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors MÖK and GD managed the literature searches. Authors SGT and MÖK wrote the manuscript. Authors SGT and GD analyzed the study. All authors read and approved the final manuscript.

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## ABSTRACT

**Aim:** The aim of this study is to evaluate the clinicopathological, diagnostic, and therapeutic features of male breast cancer.

**Study Design:** This is a retrospective clinical study.

**Methodology:** Twenty-two male patients who underwent surgery for breast cancer in a tertiary reference hospital in Ankara between 2010 and 2015 were included in this retrospective study. Patient characteristics, clinical findings, diagnostic and therapeutic features were recorded.

**Results:** Among the 22 patients with a mean age of 59.6 years, 3 (13.6%) had a family history of BC. Painless breast mass was the most common (95.5%) presenting symptom. Hypoechoic breast mass with irregular margins was the most frequent sonographic finding (90.9%) while mammography revealed asymmetric density or poorly defined mass in the majority of cases (75%). Modified radical mastectomy was the most performed surgical type (n= 21, 95.5%). In one patient, simple mastectomy was performed for a diagnosis of ductal carcinoma in situ. Twelve (54.5%) patients received adjuvant chemotherapy while 3 (13.6%) cases had radiation therapy. Hormonal

\*Corresponding author: E-mail: [murat05ozgur@hotmail.com](mailto:murat05ozgur@hotmail.com);

therapy was given to 17 (77.2%) patients with receptor positivity. Median follow-up time of the patients was 31.2 months, and 3 recurrences was observed.

**Conclusion:** The incidence of male breast cancer has been increased in the recent years. Since the management of male breast cancer is still based on the rules of female breast cancer, large scale clinical studies are urgently needed to develop an international guideline for of this rare cancer.

**Keywords:** Breast cancer; diagnosis; male; treatment.

## 1. INTRODUCTION

Breast cancer (BC) is one of the most diagnosed malignancies in the world, with a female predominancy [1]. Male breast cancer (MBC) is seen less frequently than female breast cancer (FMC), accounting for approximately 1% of all breast malignancies [2]. Owing to its rarity, the clinical, epidemiological, etiological, pathological, and genetic properties of MBC have been less investigated compared with FBC. In fact, male breast tissue has different structure than female mammarian tissue, in terms of the small size, lack of lobules, and physiological functions. Thus, the management of MBC should be different from FMC. Unfortunately, there is no large randomized clinical trial on MBC, and therefore its management is largely based on clinical data obtained from the researches on FBC [3].

In this study, the clinicopathological features and oncological outcomes of 22 male patients with BC were presented and discussed with the relevant literature.

## 2. MATERIALS AND METHODS

### 2.1 Patients and Study Design

A total of 22 MBC patients who underwent breast surgery in a tertiary reference hospital in Ankara between 2010 and 2015 were included in this retrospective study. Patients' characteristics such as age, family history of BC, and comorbid systemic diseases, the initial clinical symptoms and findings, imaging methods including breast ultrasonography (US), mammography (MG), abdominal US, and bone syntigraphy, type of operation, perioperative complications, histopathological findings, neoadjuvant and adjuvant therapies such as chemotherapy, radiotherapy, and hormonal therapy, recurrences were recorded.

### 2.2 Statistical Analysis

The Statistical package for social science (SPSS 21.0 software, IL-Chicago- USA) was used for

data analyses. Descriptive analysis was done for demographic and clinical features. The results were presented as mean $\pm$ SD/percentages for continuous variables, and number/percentage for categorical variables.

## 3. RESULTS AND DISCUSSION

### 3.1 Results

Twenty-two MBC patients with a mean age of 59.6 years were included in the study. Among those, only 3 (13.6%) patients had a family history of BC. Painless breast mass was the most common (95.5%) presenting symptom, and axillary enlarged lymph nodes were detected in 7 (31.8%) cases at the initial physical examination. All patient characteristics were presented in Table 1.

**Table 1. Patient characteristics and clinical findings of the study group**

Characteristics	n (%)
Age (y)	59.6 $\pm$ 13.4 (32-77)
Family history of BC	3 (13.6%)
Comorbidity	9 (40.8%)
<b>Initial clinical symptoms and findings</b>	
Breast mass	21 (95.5%)
Pain	7 (31.8%)
Axillary LAP	7 (31.8%)
Skin/nipple retraction	7 (31.8%)
Nipple discharge	2 (9%)
<b>Side of tumor</b>	
Left	11 (50%)
Right	11 (50%)
<b>Quadrant of tumor</b>	
Retroareolar (central)	18 (81.8%)
Upper-outer	3 (13.6%)
Upper-inner	1 (4.5%)
Clinical suspicion of malignancy	16 (72.7%)
Duration of symptoms prior to surgery (mo)	75.2 $\pm$ 62.9 (15-300)

\* Age and duration of symptoms prior to surgery were presented as mean $\pm$ SD (range); other variables were presented as number (percentage). y: year, mo: month

US was the first diagnostic step in all patients, and hypoechoic breast mass with irregular margins was the most frequent sonographic finding (90.9%). MG was performed in 20 patients, and asymmetric density or poorly defined mass was the most common finding (75%). Fine needle aspiration cytology (FNAC) was performed in 20 cases, with a diagnosis of infiltrative ductal carcinoma in all. All diagnostic tools were summarized in Table 2.

**Table 2. Sonographic and mammographic findings of the patients (n= 22)**

Radiological findings	n (%)
<b>Ultrasonographic findings (n=22)</b>	
Hypoechoic mass with irregular border	20 (90.9%)
Axillary lymphadenopathy	10 (45.4%)
Inflammatory skin changes	3 (13.6%)
Increased fibroglandular tissue	2 (9%)
Well-defined mass	1 (4.5%)
<b>Mammographic findings (n=20)</b>	
Asymmetric density or poorly defined mass	15 (75%)
Axillary lymphadenopathy	9 (45%)
Spiculated mass	5 (25%)
Microcalcification	3 (15%)
Distortion	2 (10%)

Modified radical mastectomy (MRM) was the most performed surgical type (n= 21, 95.5%). In one patient, simple mastectomy was performed for a diagnosis of ductal carcinoma in situ (DCIS). There was no intraoperative or postoperative complication in the study group. At the final histopathological examination, 21 patients were diagnosed with ductal carcinoma (19 had infiltrative ductal carcinoma and 2 had invasive papillary carcinoma) while one patient had a diagnosis of DCIS. Estrogen receptor (ER), progesterone receptor (PR), and Her2neu positivities were found in 17 (77.2%), 16 (72.8%), and 6 (27.2%) patients, respectively. The majority of cases (16, 72.8%) had low (1 and 2) grade tumors while only 6 (27.2%) patients had high (3 and 4) grade cancers.

Twelve (54.5%) patients received adjuvant chemotherapy while 3 (13.6%) cases had radiation therapy. Most of the patients (n=10) received a chemotherapy regimen containing cyclophosphamide, methotrexate and 5-fluorouracil (CMF) while the remaining 2 patients had taxane-based chemotherapy protocol. The 3 patients had boost radiotherapy (total 66 Gy) due

to the involvement of pectoral muscle. Hormonal therapy was given to 17 (77.2%) patients with receptor positivity. Median follow-up time of the patients was 31.2 months, and 3 recurrences was observed. All recurrences were at the mastectomy region, and re-excision was performed for those. The operative data, postoperative complications, neoadjuvant and adjuvant therapies, recurrences were presented in Table 3.

**Table 3. The perioperative data, neoadjuvant and adjuvant therapies, recurrences of the patients**

Findings	n (%)
Follow-up time	31.2±15.2 (9-60)
<b>Type of surgery</b>	
MRM	21 (95.5%)
Simple mastectomy	1 (4.5%)
Intraoperative complication	Nil
Postoperative complication	Nil
Neoadjuvant chemotherapy	5 (22.7%)
Adjuvant chemotherapy	12 (54.5%)
Postoperative radiotherapy	3 (13.6%)
Hormonal therapy (tamoxifen)	17 (77.2%)
Recurrence	3 (13.6%)

### 3.2 Discussion

In recent years, an alarming increase in the incidence of MBC has been reported by several reports [2,4-6]. Rising of human life-span, recent advances in diagnostic modalities, and increased awareness of MBC among people and physicians are the main reasons of this upward trend. MBC differs from FMC in many respects. For example, male patients usually have a late onset of BC than women, with a median age of 63 years [7]. Painless breast lump is the most common clinical finding as in women, and is usually subareolar. However, nipple retraction and ulceration, skin involvement, and nipple discharge are seen more frequently in men than in women, probably due to the anatomic features of male breast [8]. Axillary lymph nodes are palpable in approximately half of the patients. Similarly, most of the patients presented with painless subareolar mass and palpable axillary LAP in the present study.

Several risk factors such as advancing age, family history of BC, obesity, physical inactivity, high alcohol intake, exogenous oestrogen or anti-androgens therapy, liver cirrhosis, Klinefelter's syndrome, testicular disorders,

androgen gene mutation, and BRCA mutation have been documented to date [7,9-11]. Among those, obesity, exogenous oestrogen or anti-androgens therapy, liver cirrhosis, Klinefelter's syndrome, and testicular disorders are associated with relatively increase in oestrogen level. The presence of BC in first degree relatives increases the risk of MBC as in FBC, and approximately 15% of all cases is familial [9]. BRCA2 mutation is the most well-known genetic risk factor for MBC while BRCA1 mutation has a limited role [4]. Family history of BC was found in 3 patients of the study group, but there was not any associated risk factor of BC.

The diagnostic algorithm in MBC is similar to FBC. A detailed physical examination, imaging methods including US and MG, and FNAC or core biopsy should be the standard diagnostic tools in patients with suspected breast mass. In case of nipple retraction, ulceration or bloody nipple discharge without a palpable breast mass should be also alarmed the physicians for the possibility of cancer. Although male breast has a small volume, MG should be a routine part in diagnostic workup [12]. Cancer is usually demonstrated as irregular, lobulated or spiculated subareolar lesion in MG. Microcalcification is infrequent in comparison to FBC, and is usually round and scattered. In a study, microcalcifications were found in approximately 2% of patients with MBC [13]. Similarly, subareolar mass was the leading sonographic and mammographic finding; however, microcalcification was found only in 3 patients in the present study. The combination of clinical examination, US, and MG can reduce the incidence of unnecessary biopsy [14]. FNAC should be performed for the suspected lesions prior to surgery. Its specificity and sensitivity for detecting malignancy was reported up to 100% [15]. However, larger tissue is obtained by trucut biopsy, which can provide more information on the receptor status. In our study, FNAC was the most performed biopsy technique, and was consistent with the final pathology in all cases. Similar to FBC, most of MBCs are ductal in origin. In our study, infiltrative ductal carcinoma was the most common type, and papillary carcinoma was seen in two patients. DCIS was found in 4 MBC patients, consistent with the literature [16].

The therapeutic approach is based on the data of FBC. Modified radical mastectomy with axillary dissection is the standard surgical treatment in MBC. However, some authors reported that breast conserving surgery (lumpectomy plus

radiation therapy) could be an alternative surgical approach for small and early stage MBC [17,18]. The results of the two surgical types were reported to be similar to those seen in FBC [4,17]. The management of axillary region is challenging. Although sentinel lymph node biopsy was proposed for MBC with T<2 cm and clinically negative axilla, most surgeons performed MRM as a primary standard surgery [19]. In the present study, MRM was the standard surgical approach for infiltrative ductal carcinoma.

Although there are no randomized controlled studies regarding the adjuvant treatment options in men with BC, the oncological responses are not different from FBCs [20]. Axillary involvement is found more than half of the patients, and adjuvant chemotherapy is indicated for such patients. CMF regimen is the most used protocol. However, cyclophosphamide plus doxorubicin plus fluorouracil (CAF) and taxane-based regimens are the other chemotherapy protocols used in MBC. It has been clearly shown that chemotherapy increased the survival [21]. In the absence of axillary metastasis, adjuvant chemotherapy is based on the rules of FBC. Similarly, most of our patients were at advanced stages of tumor and had axillary metastasis, thus standard CMF and taxane-based regimens were applied for those cases. Hormonal therapy is usually indicated in patients with MBC, due to the high incidence of ER/PR receptor positivity. In a recent study, ER/PR positivity was found in the majority of MBC patients in our study, consistent with previous reports [22]. Actually, MBC is similar to postmenopausal FBC in terms of some pathological features including high ER/PR receptor positivity. Therefore, most MBC patients can be treated with 5 years of adjuvant tamoxifen therapy. Two thirds of patients in the present study also had tamoxifen therapy. Contrary to ER/PR receptor status, HER2 expression is less than FBC [22]. The rate of HER2 positivity was also in parallel to literature, with a value of 27%. Other hormonal modalities include aromatase inhibitors, progesteron, anti-androgens, and corticosteroids, and should be used according to the therapeutic response, the recurrence of the cancer or metastatic disease [5,8,9]. Orchiectomy and other ablative surgical treatment modalities including adrenalectomy and hypophysectomy have replaced to modern hormonal therapies.

Radiation therapy is generally indicated for local advanced disease, involvement of breast skin and pectoral muscle, and the presence of axillary

metastasis. The primary aim of radiotherapy is to reduce the risk of locoregional recurrence; however, there is not a general consensus on the optimal radiation dose [5]. In the present study, postoperative radiotherapy was needed in 3 patients with involvement of pectoral muscle.

Overall survival of MBC patients is generally believed to be similar to that of women with BC. However, in a recent study by Yu et al, it was shown that men with BC were twice as likely to die of cancer in comparison to female patients with BC [23]. Although our patient sample size was small to make an accurate statistical analysis for survival of the patients, there no death was observed during the mean follow-up period of 31 months.

#### 4. CONCLUSION

In this paper, we tried to present clinical, diagnostic and therapeutic features of MBC in a small scale study. Although the incidence of MBC has been increased in the recent years, the management of this cancer is still based on the rules of FBC. However, MBC differs from FBC in many respects. Therefore, large prospective clinical studies are urgently needed to develop an international guideline for the management of this rare cancer.

#### CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this clinical study.

#### ETHICAL APPROVAL

It is not applicable.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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