

## Male Breast Cancer; Experience with 6 Cases

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**Abstract:** Background /Aim: Generally, Breast cancer is much less common in men than in women. Men tend to present with breast cancer at an older age than women. Liver cirrhosis and prolonged use of diuretics were found among most of cases. Breast cancers that arise in men are more often hormone receptor positive than female breast cancers. The most common clinical presentation is a painless, firm, subareolar mass Methods: The study included 6 patients with male breast cancer that had been managed by the authors at Tanta University Hospital over 3 years duration ; a minimum follow up period of 6 months was undertaken for all cases .All patients included were symptomatic and finally diagnosed by preoperative biopsy. All patients were studied for their clinical and pathological features, presentations, their surgical managements and outcome after surgery. Results: The results of the study revealed that the disease was early in 5 and was locally advanced in one patients. Their ages ranged between 46 and 73 years. All patients were managed surgically with no reported complications. Conclusion: For definitive local therapy for men with breast cancer; we recommend a modified radical mastectomy rather than lumpectomy or more radical surgery. [Nature and Science 2010;8(10):253-259]. (ISSN: 1545-0740).

**Keywords:** Breast cancer, gynecomastia of male breast.

### 1. Introduction:

Male breast cancer (MBC) is rare in contrast to female breast cancer, which is the most common cancer in females and the second leading cause of cancer related deaths in women [1] . Although MBC shares many similarities with cancer of the female breast, there are also important differences [2] .In the United States, approximately 1990 new cases of MBC are diagnosed annually, and 450 deaths occur; this represents less than 0.5 percent of all cancer related deaths in men annually [1] . By contrast, in Tanzania and areas of central Africa, breast cancer accounts for up to 6 percent of cancers in men [3] . In the United States, the ratio of female to male breast cancer is approximately 100:1 in whites, but lower (70:1) in blacks [2], The median age of onset of MBC is 65 to 67, approximately 5 to 10 years older than in women [2,4-9] . Like female breast cancer, the incidence of MBC has been increasing; one report suggests that incidence has increased 26 percent over the past 25 years [10].

The risk was significantly higher in men who had a first degree relative with breast cancer (RR 1.92), a history of a bone fracture after age of 45 years (RR 2.2), obesity (RR 1.79) and low levels of physical activity. Smoking and alcohol consumption was not found to be associated with increased risk.

Gynecomastia may mimic MBC. It is most often related to drugs (e.g. estrogens, digoxin, cimetidine, spironolactone, & calcium channel blockers), liver cirrhosis and testicular diseases (e.g.

orchitis, undescended testes [cryptorchidism] and testicular injury) [4,8] .

With the exception of Klinefelter syndrome (which is associated with gynecomastia in about 80% of cases), no well-established data indicate that gynecomastia predisposes to development of MBC. The unusual feature of this gynecomastia is that the patient may develop lobular structures & this is the only type of gynecomastia that carries an increased risk of MBC which is 10-20 folds greater than normal [38].

Some chronic liver diseases may be associated with increased risk of development of MBC e.g. cirrhosis, alcoholic liver disease, and schistosomiasis [11-17].

Several of the risk factors for MBC involve imbalance in estrogenic versus androgenic influences (i.e. relative estrogen excess or lack of androgen) [3,4] . As an example, men with liver disease have increased production of androstenedione from the adrenal glands, enhanced aromatization of androstenedione to estrone, and increased conversion of estrone to estradiol [18] . On the other hand, androgens may convey a protective effect on breast tissue by inhibiting cell proliferation. The association of MBC with prolactinoma, a condition often associated with low plasma testosterone levels, is consistent with this hypothesis [19,20] .

It is hypothesized that relative changes in endogenous hormones may play a causative role in MBC. However, abnormalities in peripherally detectable hormone levels have not been detected in

affected men [21]. Furthermore, other conditions associated with an increased estrogen-to-testosterone ratio such as obesity, thyroid disease, use of marijuana, and exogenous estrogen use (e.g. transsexuals, treatment of prostate cancer) have a less certain relationship to MBC [4,12].

About 15 to 20 percent of men with breast cancer have a family history of the disease, compared to only 7 percent of the general male population [6]. This disparity implies that some families carry genetic mutations that increase their risk for both male and female breast cancer [22].

Inherited mutations in BRCA gene also increase the risk of MBC, although not to the same absolute level of risk as in women. The risk appears to be higher with inherited BRCA2 rather than BRCA1 mutations [23].

#### Aim of the Work

The aim of this study was to assess the clinicopathological features and management strategy for male patients with non-metastatic breast cancer.

## 2. Patients and Methods:

This study included 6 male patients with breast cancer who were admitted and treated in the Surgical and medical Oncology Departments of Tanta University Hospital over a period of three years (from February 2007 to February 2010) duration with minimal follow up period of 6 months durations .. The least reported age was 46 years and the highest one was 73 years. All patients were informed by this study and written consents were taken from cases who underwent surgery. All patients were subjected to full history taking, thorough clinical examination including tumor staging by the T.N.M. staging system identical to that used for female breast cancer according to the American Joint Committee on Cancer (AJCC) [24], specific laboratory investigation [haematological profile, complete liver, kidney, & adrenal function] to assess patients' fitness for both surgery and chemotherapy, also metastatic work-up in the form of chest X-ray, bone scan, & pelvi-abdominal ultrasonography (& pelvi-abdominal CT if needed).

Mammography was done for all cases. Pathological diagnosis was confirmed by FNAC. If FNAC is not conclusive, core or open biopsy was performed. Assay for hormone receptors (estrogen and progesterone) and HER2 expression was done for all patients.

Five patients were presented by early breast cancer (T1,2 N0, M0, or T0,1,2 N1, M0). Those patients were submitted to modified radical mastectomy. Breast conserving therapy (lumpectomy or quadrantectomy) is generally not performed because of the lack of breast tissue and the central

location of most tumors. Accurate surgical evaluation (of the tumor stage and size) is essential to guide the adjuvant therapy. Complete axillary dissection was done for all patients [24].

Only one patient presented by locally advanced breast cancer (stage IIB: T3 N0 M0). This patient received neoadjuvant chemotherapy in the form of 3 cycles of FAC regimen (5-fluorouracil 500 mg/ m2 I.V. day 1, adriamycin 50 mg/ m2 I.V. day 1, & cyclophosphamide 500mg/ m2 I.V. day 1) with 21 days interval between each two successive cycles [25]. After each cycle of the neoadjuvant chemotherapy, the patient was examined for the size of the tumor (using sono-mammography) & the regional lymph nodes status. After the third cycle of the neoadjuvant chemotherapy, bilateral mammography & breast ultrasonography were done. There was no response to the neoadjuvant chemotherapy according to Dixon et al (1998) classification:

Complete clinical response (CR): complete disappearance of the tumour both clinically & mammographically.

Partial response (PR): decrease of 50% or more in the total tumour size.

No response (NR): decrease of less than 50% or increase of less than 25% in total tumour size.

Progressive disease (PD): increase of 25% or more in total tumour size.

According to this classification, the patient who showed no response was submitted to radical mastectomy due to presence of chest wall invasion that persists after the neoadjuvant chemotherapy.

After removal of the stitches, all patients received 6 cycles of adjuvant chemotherapy.

After completion of chemotherapy, radiotherapy was given starting 1 week after the 6th cycle of chemotherapy. Post-operative chest wall & regional lymph nodes irradiation was given to men who are at high risk of relapse because of four or more involved lymph nodes & locally advanced disease. The total dose of radiotherapy was 50 Gy for every patient divided into 25 fractions, each fraction was 2 Gy given daily for 5 days each week for 5 weeks.

For men with invasive tumors of any size that express steroid hormone receptors, we recommended five years of adjuvant tamoxifen. At present, there are insufficient data to recommend an aromatase inhibitor in the adjuvant setting for MBC. We recommend trastuzumab with chemotherapy rather than chemotherapy alone for men with HER2-positive advanced breast cancer (Grade 1B).

## 3. Results:

A total of 6 male patients with breast cancer were included in the study. The age distribution of

patients was shown in Table (1), that revealed that only one patient were below the age of 50 years and most of the patients were between 50 & 60 years old (could be attributed to the common drug intake and severe degree of liver cirrhosis in this age group) .

**Table 1. Age distribution of all patients (n=6)**

Age	Number	%
-40	0	0
-50	1	16.6
-60	3	50
-70	1	16.6
-80	1	16.6
<b>Total</b>	<b>6</b>	<b>100</b>

Clinical presentation and evaluation: The most common clinical presentation was a painless, firm, subareolar mass. Liver cirrhosis was found in 4 patients. Table (2) summarizes the symptoms in studied patients.

**Table 2. Symptoms at presentation**

Symptom	Number of patients (n. = 6 )	%
<b>Breast mass</b>	6	100
<b>Skin redness</b>	3	50
<b>Skin edema</b>	2	33.3
<b>Nipple discharge</b>	1	16.6

The first step in the evaluation of a suspicious breast mass in a man is mammography. The mammogram was abnormal in 70 percent of MBCs.

Any suspicious mass requires biopsy to confirm the diagnosis and to assay for ER and PR content as well as HER2 status. Although fine needle aspiration (FNA) cytology can provide adequate diagnostic

material in many cases, avoiding open or surgical biopsy, whereas 6 samples were insufficient for diagnosis. a core or open biopsy was performed.

Staging work-up — The staging system developed by the American Joint Committee on Cancer (AJCC) classifies breast malignancies by tumor (T) node (N) and metastasis (M) categories, and stage groupings with similar prognoses are combined [24] . Clinicopathological examination revealed that all cases were invasive duct carcinoma. Table (3) shows the tumour stage in all patients, As regard nodal status; N I nodes was found in 4 patients and NII nodal status found in 2 patients.

**Table 3. Tumour size assessment**

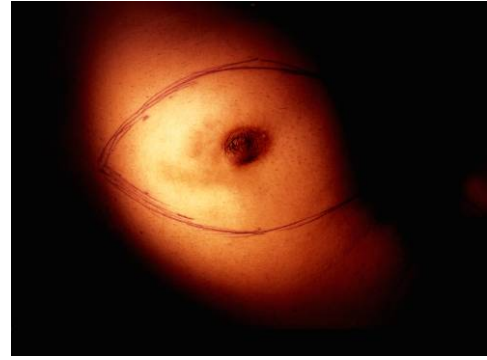
Tumour size (T)	Number Of Patients( n = 6 )	Percent
<b>T0</b>	0	0
<b>T1</b>	2	33.3
<b>T2</b>	3	50
<b>T3</b>	1	16.6
<b>T4</b>	0	0
<b>Total</b>	<b>6</b>	<b>100</b>

Assay for hormone receptors (estrogen and progesterone) was positive in five cases, whereas HER2 was expressed in only two cases. Both studied parameters were negative in the locally advanced case. As regards surgical intervention; modified radical mastectomy was done for 5 cases and the locally advanced that showed no response to chemotherapy. There were no complications related to surgery except seroma reported in one case.

Follow-up of patients [a minimum period of 6 months] revealed that treatment failure in the form of local recurrence was reported in one case who was locally advanced and showed no response to neoadjuvant before radical mastectomy. Distant metastases (lung and vertebral metastasis) was reported in one case that required chemotherapy regimen other than FAC regimens.



(1-A)



(1-B)



(1-C)



(1-D)

**Fig. 1 A-D:** showed photography of a male patient with breast cancer with nipple retraction and skin attachment without muscle or chest wall attachment who underwent modified radical mastectomy.



(2-A)



(2-B)

**Fig. 2 A, B:** Showed photography of another male patient with breast cancer with nipple retraction but without skin, muscle or chest wall attachment who underwent modified radical mastectomy.

#### 4. Discussion:

Male breast cancer is rare. Of all breast cancers, men with breast cancer make up less than 1%. Male compared with female breast cancers occurred later in life with higher stage, lower grade, and more estrogen receptor-positive tumors. In our study, 50 % of the patients were between 50 & 60 years old. This is compatible with the results reported by Atahan *et al.*, who evaluated 42 male patients with breast cancer &

they found that the median age is 55 years ( range 33-77 years) [24].

The first step in the evaluation of a suspicious breast mass in man is mammography. The mammogram is abnormal in 80 to 90 percent of MBCs, and can usually distinguish between malignancy and gynecomastia. In one study, the reported sensitivity and specificity rates of

mammography for the diagnosis of MBC were 92 and 90 percent, respectively [26].

Radiographic features suggestive of malignancy include eccentricity to the nipple, speculated margins, and microcalcifications. In contrast, gynecomastia typically appears as a round or triangular area of increased density positioned symmetrically in the retroareolar region. In rare cases, concurrent gynecomastia can mask a malignant lesion [27].

Any suspicious mass requires biopsy to confirm the diagnosis and to assay for ER and PR content as well as HER2 status. Although fine needle aspiration (FNA) cytology can provide adequate diagnostic material in many cases, avoiding open or surgical biopsy. If inadequate tissue is obtained, or FNA is not feasible, a core or open biopsy should be performed [28].

The traditional surgical approach for localized breast cancer in men is modified radical mastectomy (MRM) (done in 5 cases.) Although randomized studies have not been conducted in men, retrospective data suggest the equivalence of radical mastectomy and MRM in terms of local recurrence and survival [29]. Moreover, randomized studies support the therapeutic equivalence of these two surgical procedures. The only exception is that patient who have extensive chest wall muscle involvement may benefit from a radical mastectomy [30].

Surgical assessment of the axillary nodes is an essential part of primary therapy. Increasing amounts of data support the view that at least in women, surgical assessment of the axillary nodes is associated with a better outcome. In keeping with this conclusion, at least some data suggest that men who have nodal dissection omitted tend to have a worse outcome [30].

SLN biopsy may be successful in men as well, although the available data are scant. Due to the rarity of MBC, large studies establishing the sensitivity and specificity of SLN biopsy in MBC have not been carried out. However, in a total of 143 men reported in seven retrospective series, a SLN was successfully identified in all but one [31]. A combined 11 men with a negative SLN biopsy underwent completion axillary node dissection, and none had additional involved nodes.

Despite the limited amount of data, an expert panel convened by the American Society of Clinical Oncology (ASCO) concluded that the use of SLN biopsy for men with breast cancer was "acceptable" [31].

Because of its rarity, few data in the literature referred to the response of male breast cancer to neoadjuvant chemotherapy. Adjuvant RT — In small retrospective series, post-mastectomy RT appears to reduce loco-regional recurrence in MBC, but the

influence on survival is unknown [32]. RT techniques vary substantially between different series and over time, complicating the clinical assessment of benefit.

Post-mastectomy RT should be applied to both men with breast cancer [33]; possibly because they have a higher incidence of nipple or skin involvement [34]. However, few studies showed that male breast cancer patients with extensive nodal involvement appeared not to have had a significant benefit from post mastectomy irradiation. Post-mastectomy RT is recommended for men with four or more positive lymph nodes, N2/N3 nodal disease, or locally advanced (T3/T4) primary tumors [34].

The low incidence of MBC precludes the development and completion of clinical trials to assess the efficacy of adjuvant systemic therapy, and few prospective data are available to guide treatment. [35].

Because the majority of MBCs are hormone receptor-positive, five years of adjuvant tamoxifen is recommended for most men following mastectomy. Prospective trials to confirm the validity of this approach in men are not available. However, retrospective comparisons support a survival benefit from adjuvant tamoxifen in MBC [36].

As an example, in one report that compared 39 men who received tamoxifen to a group of historical controls who underwent mastectomy alone, the treated group had better five year actuarial survival (61 versus 44 percent) and disease-free survival (56 versus 28 percent) [37].

From this study we concluded that cancer breast can affect cirrhotic patients and male patients receiving certain medication gynecomastia was an association with higher incidence in the age between 50 & 60 years. As regard surgical intervention; modified radical mastectomy was done for nearly all cases (5 out of six patients) and the results were satisfactory. Radical mastectomy was done for locally advanced cases. Chemo radiation is required after surgery to assure complete cure. FAC regimen was effective as an adjuvant therapy. If metastasis developed during follow up; another chemo they is required.

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