CANCER OF THE MALE BREAST: A REVIEW

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A review of 20 cases of male breast cancer in 17 patients from 1959 to 1990 was performed. The median age at presentation was 53.3 years (range: 29 to 79). At the time of diagnosis, 30% (6) patients were stage I, 65% (13) stage II, and 5% (1) stage IV. Surgery was the initial form of therapy in all cases either as a radical mastectomy, modified radical mastectomy, or total mastectomy. The median disease-free survival was 4.8 years with a 5-year disease-free survival of 41%, and with a 5-year overall survival of 47%. Seven patients are alive with no evidence of disease, two are alive with disease, five have died of disease, and two died of other causes. Estrogen receptor (ER) and progesterone receptor (PR) assays were performed on the tumors of 10 patients, with 80% being ER positive and 70% PR positive. The median disease-free survival for ER positive patients was 6 months with a 5-year disease-free survival of 12.5%. The overall median survival for this group was 2.9 years with an overall 5-year survival of 25%. In this review there was a high percentage of patients who were ER positive. The positive receptor status had value in predicting decreased survival. *(J Natl Med Assoc. 1996;88:439-443.)*

Male breast cancer is rare and accounts for approximately 1% of all breast malignancies. It corresponds to less than 1% of all malignancies in men. It is estimated that there will be 1400 cases of male breast cancer in 1996. It is also estimated there will be 300 deaths from male breast cancer in 1996. This represents 0.75% of the deaths of the estimated total cases of breast cancer and 0.58% of the deaths of the estimated deaths for 1996.[1] Male breast cancer is considered to have a poorer prognosis than female breast cancer.[2]

Treatment regimens have been extrapolated from the experience with female patients. However, these experiences are not necessarily applicable. Due to its small incidence, most studies in the treatment of breast cancer do not include male patients. Hormone receptor status and endocrine therapy have been described as playing a role in the treatment of male breast cancer.[3,4] Use of adjuvant therapy in the form of systemic chemotherapy or tamoxifen has been shown to reduce the risk of death in female breast cancer patients. However, data describing the use in male breast cancer are lacking. Therefore, treatment must rely on the analysis of individual institutional experience.

MATERIALS AND METHODS

The records of 17 male patients with breast cancer, treated over a period of 31 years (1959 to 1990), were reviewed. Twenty cases of male breast cancer were retrieved from the Tumor Registry at the City of Hope National Medical Center (COH). These patients were either initially diagnosed at COH or referred for treatment. These 17 cases represent 0.5% of all the cases of breast cancer treated at COH during this time period. The charts were reviewed in a retrospective manner. Staging was based on the TMN staging system of the American Joint Committee on Cancer.[5] Follow-up was obtained by direct contact with the patient and his family at COH. The overall and disease-free survivals were calculated using the Kaplan-Meier product-limit survival analysis method.

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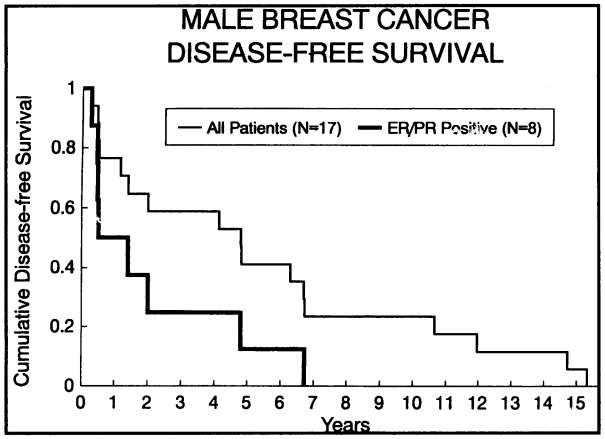

Figure 1. Comparison of disease-free survival of the patients who were ER positive and all patients.

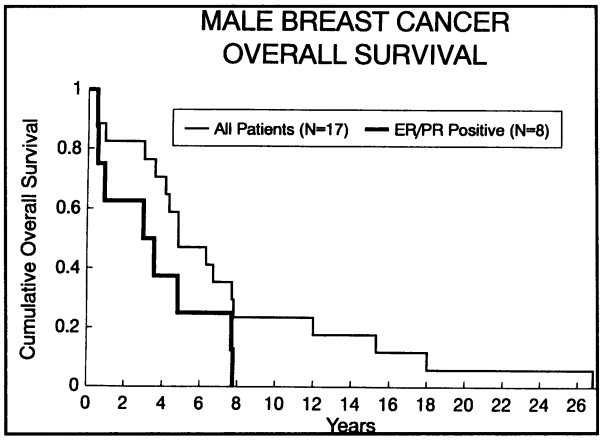

Figure 2. Comparison of overall survival of ER-positive patients and all patients.

RESULTS

Patient ages ranged from 29 to 87 years (median: 53.3 years). One patient had a family history of male breast cancer in a paternal uncle. There were no other reports of a family history of breast cancer (male or female). The ethnic classification of the male breast cancer patients consisted of 2 Hispanic and 15 white males.

A palpable breast mass was the most common presenting sign (13 patients) followed by nipple retraction (6 patients) and nipple discharge (6 patients). In nine cases, a palpable breast mass was the sole sign. The only other sign to present alone was nipple retraction (1 patient) (Table). Axillary nodes were palpable in three patients. One patient had peau d'orange skin changes and one patient had diffuse breast enlargement (gynecomastia). The most common location of the breast mass was beneath the nipple. Eleven patients had left-sided breast tumors and three patients had right-sided tumors. Three patients had bilateral breast cancer, and two of these were synchronous lesions.

A mammogram was performed at the time of initial evaluation on five patients. All five mammograms had findings that were consistent with cancer. Six patients had fine-needle aspiration of a palpable breast mass. Five documented a cancer diagnosis and one was a false negative.

Primary treatment was radical mastectomy (1 patient), modified radical mastectomy (18 patients), or total mastectomy (1 patient). The pathologic type of breast cancer was infiltrating ductal carcinoma in 18 of 20 tumors. The two exceptions were cases of mucoid carcinoma and anaplastic carcinoma. A component of ductal carcinoma in situ was identified in three of the specimens. Five patients received adjuvant chemotherapy, four patients received adjuvant hormonal therapy (tamoxifen), and two patients received adjuvant radiation therapy. Three of these patients had a combination of adjuvant therapies. One patient with bilateral synchronous breast cancer was treated with adjuvant high-dose chemotherapy and an autologous bone marrow reinfusion. This patient had a breast cancer with 13 of 14 nodes positive. The nodes were estrogen receptor/progesterone receptor positive, and his tumor had a high S-phase and was diploid. Because of the poor prognostic indicators and having bilateral breast cancer, he was treated aggressively with high-dose chemotherapy followed by autologous bone marrow reinfusion. He had no evidence of disease at 6 months follow-up.

Estrogen and progesterone receptor assays were performed on 10 patients. Eighty percent were ER positive and 70% were PR positive. There was only one patient who was both ER and PR negative.

When the patients were staged, six (30%) patients with stage I and 13 (65%) patients had stage II disease. No patients had stage III disease and one (5%) patient had stage IV disease. Among the 13 patients with stage II disease, 10 had positive axillary nodes. Of the stage II patients, five had T2N1 disease, five had T1N1 disease, and three had T2NO disease.

Five patients died of disease. Four of these had stage II and one had stage I disease. The one patient with stage IV disease is alive with disease at 3.5 years after primary treatment.

The Kaplan-Meier method was used to calculate disease-free survival and overall survival. The median disease-free survival and overall survival were 4.8 years and 4.8 years, respectively, for all patients. The median 5-

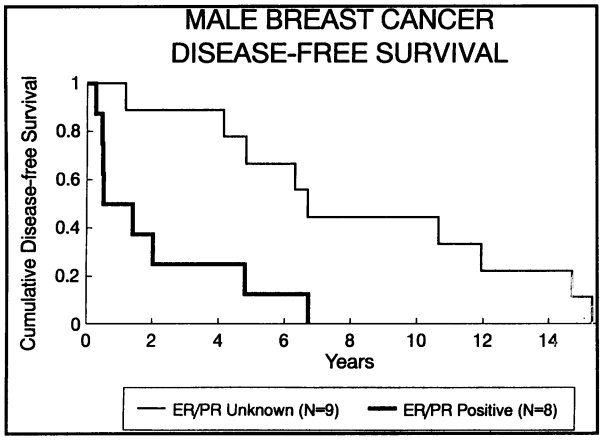

Figure 3. Comparison of disease-free survival of ER-positive patients and patients with unknown receptor status.

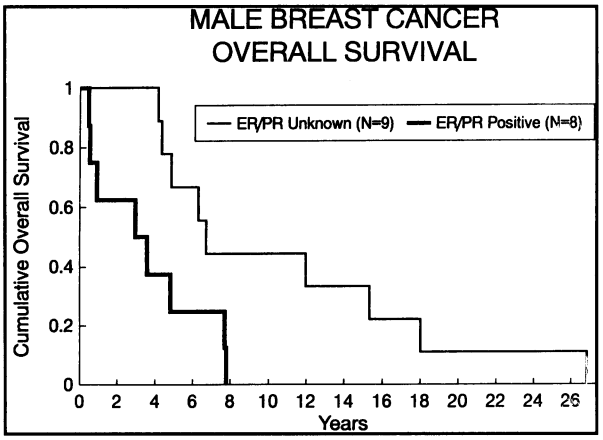

Figure 4. Comparison of overall survival of ER positive patients and patients with unknown receptor.

year disease-free survival and overall survival were 41% and 47% (Figures 1 and 2). For the eight patients that were estrogen receptor positive the median disease-free survival was 6 months with a 5-year disease-free survival of 12.5% (Figure 1). The overall median survival for this group was 2.9 years with a 5-year survival of 25% (Figure 2). The median disease-free survival of those patients who were ER negative or unknown was 6.7 years with a 5-year survival of 65% (Figure 3). The median overall survival of this group was 6.7 years and 5-year survival 65% (Figure 4). The differences in disease-free survival and overall survival showed a trend but statistical analysis of survival curves was not performed due to small sample sizes.

TABLE. CANCER OF THE MALE BREAST PRESENTING SIGNS AND SYMPTOMS

Signs & Symptoms	No. of Patients
Breast mass	13
Nipple retraction	6
Nipple discharge	6
Palpable axillary nodes	3
Inflammatory changes	1
Skin nodule	1
Breast enlargement	1

DISCUSSION

In this series, the incidence of male breast cancers was 0.5% of all breast cancers treated at COH during this time period. It has been reported that when breast cancer occurs in men, it is usually detected in the 60-year age range, about 10 years later than in women.[6,7] In our series, the median age of diagnosis was 53.3 years, which is close to the median age of diagnosis in females. Also, the reported incidence for men <40 age group is 7%,[8] whereas in our series it was 24%. Male breast cancer shows a slight and unexplained predilection to the left breast as does female breast cancer. There were 14 cases of left breast cancer with 3 cases being bilateral. We found that the presenting signs and symptoms were similar to that of female breast cancer.

The causes of male breast cancer are no better understood than that of female breast cancer. There are several etiologic factors that have been implicated in the development of male breast cancer. These include: Klinefelter's syndrome, hyperestrogenism, radiation, trauma, and gynecomastia. Patients with Klinefelter's syndrome approach a risk of developing breast cancer close to females with an incidence of 6%.[9] Patients with Klinefelter's syndrome develop hypertrophic breast, which not only demonstrates gynecomastia but also the development of acini and lobules as seen in females. The administration of exogenous estrogens to male patients leads to the development of acini and lobules identical to those of the female breast. In male patients with prostate cancer who were treated with estrogens, there was thought to be an increase in male breast cancer. The apparent increase in male breast cancer was subsequently shown to be metastatic prostate cancer to the breast.[10,11] The evidence to link hormonal stimulation to the development of male breast cancer is weak.

There are reports of 11 male patients who developed breast cancer after radiation exposure.[12,13] These men developed breast cancer 12 to 36 years after exposure to the radiation. There is also a report of development of male breast cancer following repeated fluoroscopy for pulmonary tuberculosis.[14] This patient developed breast

cancer 38 years after receiving a cumulative minimal dose of 100 cGy. The dose of radiation that is reported in these patients ranges from 100 cGy to 1000 cGy. The history of recent trauma to the breast has been elicited from several patients, but this association may be more of the traumatic event bringing notice to an already present breast cancer than coincide with the development of breast cancer.

Gynecomastia is the principal differential diagnosis in men with breast masses. A history of drug usage (digoxin, ketaconazole, and cimetidine), alcohol use, hormone ingestion, bilateral synchronous presentation, or a testicular mass favor the diagnosis of gynecomastia. The preexistence of gynecomastia in men who develop breast cancer is uncommon. However, the microscopic appearance of gynecomastia (fibroepithelial hyperplasia and stromal hypertrophy) may be more common and has been found in 40% of pathologic material reviewed in one series. There was no difference in the prevalence of gynecomastia related to age. The presence of gynecomastia was independent of the proportion of intraductal carcinoma present.[15]

Mammograms are diagnostic in men with breast cancer. Mammograms were diagnostic of carcinoma in 100% (5/5 patients) of our patients. Even though the most common presentation is a breast mass, mammography could be useful in detecting and confirming contralateral breast cancer. Therefore, it should be attempted in all men when the diagnosis of breast cancer is made and in the follow-up period.

The primary approach for treatment of male breast cancer is surgery. This is in the form of total mastectomy and axillary node dissection that has replaced radical mastectomy in most cases. The role of adjuvant chemotherapy has been established in female breast cancer patients but not in male breast cancer patients. Adjuvant chemotherapy in male breast cancer may reduce the risk of recurrence and favorably influence survival.[16,17] The addition of adjuvant systemic therapy is advised when there are pathologically positive axillary nodes. A treatment regimen similar to that of female patients may be appropriate for treatment of male breast cancer.

Estrogen receptor status has been used in female breast cancer to predict response to hormonal therapy. In female breast cancer, approximately 60% contain positive estrogen receptors. Positive estrogen receptors are found in approximately 80% to 85% of the male breast cancers.[3,4,18,19] The incidence of estrogen receptor-positive tumors appears to be higher in male breast cancer compared with females. Hormonal therapy in the form of orchiectomy and adrenalectomy has been used for the treatment of metastatic male breast cancer. The response rate to hormone therapy has varied and may be related to the positivity of estrogen receptors. It has been suggested that a relationship between low estrogen receptor and unfavorable orchiectomy response may exist.[4] As more data are accumulated, may emerge as so. Because of the high rate of estrogen receptor tumors, it has been suggested that tamoxifen may be useful in these patients.[20] In this study, there were 10 patients who had hormonal receptor assays performed. The ER were positive in 80%.[10] The patients who were ER positive had a decreased disease-free survival and overall survival compared with the overall and disease-free survival of all patients. Three patients who were ER positive received tamoxifen and had progression of disease. One patient had bilateral orchiectomies and then had a 2-year period without progression of disease. Orchiectomy alone was performed on one patient who was ER positive when he developed metastases, and he did not have a response.

Patients who have had no response to one form of hormonal therapy have responded to a second-line hormonal therapy (ie, antiestrogens, estrogens, and androgens).[21,22] The correlation of ER status with response to hormonal manipulation in male breast cancer is not conclusive. Even though it has been suggested that less positive estrogen receptors have unfavorable response to some hormonal therapy, the tumor growth may still respond to second-line hormonal therapy. The response to hormonal therapy cannot be predicted consistently based on the receptor status in male breast cancer patients. In female breast cancer patients, the receptor status can be used to choose treatment modalities and also predict a better survival. In this report, male breast cancer patients who had positive estrogen receptors had a decreased disease-free survival and overall survival. This may be due to a paradoxical effect on tumor growth by hormonal manipulation.

Even though most information about male breast cancer is obtained in a retrospective fashion, this still provides valuable information about the natural history of the disease.

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