Male breast cancer – own experience

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KEY WORDS

male breast cancer ◗ chemotherapy ◗ hormone therapy ◗ radiotherapy

ABSTRACT

Introduction. Male breast cancer comprises about 1% of all breast cancer cases. The advanced stage of the disease at the time of diagnosis is connected with shorter overall survival rates when compared to female patients. We estimate 1, 2, 3, and 5-year overall survival rates in male breast cancer patients treated in the Institute of Oncology in Gliwice between 1996 and 2007, and to evaluate potential prognostic factors influencing patients' survival rate.

Material and methods. We retrospectively analyzed the data of 61 males treated due to breast carcinoma in the Institute of Oncology between 1996 and 2007. The median age was 61 years. The majority of patients were diagnosed in an advanced stage: T3-4 51%, N1-3 46%, M1 11%. The most represented histological type was invasive ductal carcinoma (46%). Tumors were estrogen-receptor positive in 46% and progesterone-receptor positive in 41% of cases. Of the 45 patients who were treated radically, surgery was performed in 84%. Neoadjuvant chemotherapy was performed in 20% and adjuvant in 36% of patients. Adjuvant hormonal therapy was administered to 62%. Palliative treatment was administered to 26% of patients.

Results. The 5-year overall survival rates in the palliative and radical group were 35% and 59%, respectively ($p = 0.01$). In radically-treated patients 5-year disease-free survival was 48%. The variables with the strongest positive influence on the total survival rate included adjuvant hormonal therapy ($p = 0.006$) and radical surgery ($p = 0.01$). The use of chemotherapy had no significant influence on overall survival ($p = 0.06$). Radiotherapy ($p = 0.8$) had no influence on overall survival.

Conclusions. Radical mastectomy is the treatment of choice for male breast cancer patients. Negative receptor status has the most significant negative influence on survival.

Table 1. Clinical characteristics of patients, clinical disease stage and results of the histopathology examination.

Median age (range)	61 (40-90)
Median follow-up in months (range)	5 (1-60)
Side	
left	37 (61%)
right	24 (39%)
The TNM Staging system	
T1	5 (8%)
T2	6 (10%)
T3	3 (5%)
T4	28 (46%)
N 0	15 (25%)
N 1	18 (29%)
N 2	9 (15%)
N 3	1 (2%)
M 0	54 (89%)
M 1	7 (11%)
Histopathological diagnosis	
Infiltrating ductal carcinoma	28 (46%)
Infiltrating lobular carcinoma	1 (2%)
Infiltrating ductolobular carcinoma	2 (3%)
Invasive cancer (undetermined)	13 (21%)
Other	2 (3%)
Estrogen receptor status	
Positive	28 (46%)
Negative	10 (16%)
Progesterone receptor status	
Positive	25 (41%)
Negative	13 (21%)
HER-2 receptor status	
Positive	2 (3%)
Negative	14 (23%)
1 positive receptor was detected in seven patients	

INTRODUCTION

Male breast cancer is a rare neoplasm and constitutes approximately 1% of all cases of breast cancer [1]. Similarly as in women, an increased incidence has been recently seen. According to research conducted in 2005 in the USA male breast cancer accounted for 0.7% of all breast cancer cases, and 1.1% in 2007 [2,3]. Due to the fact that it is a rare disease, data regarding its characteristics come from retrospective studies and case reports. Treatment of men and women are similar, however, biological differences between these neoplasm`s have to be taken into account [4]. Prognosis in men is similar to that in women [1, 5]. Shorter overall survival in men in comparison to women is associated with a more advanced stage of the disease at the diagnosis [1].

The aim of the work was to evaluate updated survival rates after 1, 2, 3, and 5 years in men with breast cancer treated at the Institute of Oncology in Gliwice in the period from1996-2007 and to identify prognostic factors for patients' survival.

MATERIAL AND METHODS

A retrospective analysis was conducted in a group of 61 men treated for breast cancer in the period from 1996-2007 in the Institute of Oncology. Clinical data was taken from medical records located in the Department of Registry of Medical Archives and Patient Service. Data regarding patients' deaths were taken from an electronic registry of patients in the Epidemiology Department. Table 1 presents detailed characteristics of clinical material. The group included 61 men aged from 40 to 90 years, the median was 61. The median follow-up time was 2.9 years (the longest follow-up time was 11 years). Clinical symptoms before diagnostic tests were initiated had 5 months on average (from 1 to 60 months). In three patients breast cancer was likely to have developed as a result of long-lasting gynecomastia. In all patients the tumor was clinically palpable, more frequently on the left side. Synchronous bilateral breast cancer was not observed in any patients.

The microscopic diagnosis of breast cancer was based on the examination of material collected using a fine-needle biopsy (19 patients), core biopsy (4 patients), or post-operative material (38 patients).

45 patients were treated with radical intent. In 29 patients treatment was initiated with a surgical procedure, in 9 patients the surgery was preceded by chemotherapy. Seven patients received radical radiation and systemic therapy. Table 2 presents therapeutic methods.

In the group of patients receiving radical treatment a relapse was observed in 15 (33%) patients, local relapse in 2 (4%), and metastases were observed in 13 (29%) patients.

The group of patients receiving palliative treatment included 16 cases. Metastases were observed in seven of them, and most frequently they were observed in solid organs (in the lungs in four cases and in the liver in two).

In the remaining patients the initial diagnosis was III B (8 patients) and III C (1 patient). In the group of patients receiving palliative treatment, chemotherapy was administered to 9, hormone therapy to 5 and palliative radiation therapy only to one patient. One patient did not give his consent for treatment.

The Kaplan-Meier method was used to analyze overall disease-free, metastasis-free, and relapse-free survival (local relapse or metastases) in the group of patients. The log-rank test was used to evaluate the effects of different variables on survival.

RESULTS

The analysis of overall survival using the Kaplan-Meier method indicated that 1, 2, 3 and 5-year survival rates in the group of patients receiving radical treatment were 100, 80, 80 and 60%, respectively. And in the group of patients receiving palliative care they were 52, 35, 35 and 35%, respectively. Survival rates in the group of patients receiving radical treatment were significantly longer than in the group of patients receiving palliative care, p = 0.01 (Fig. 1).

Table 2. Type of treatment in radically treated patients.

Radical treatment N = 45 (74%)	
Type of surgery:	
A Halstead radical mastectomy	10 (22%)
A Patey/Madden modified radical mastectomy	27 (60%)
BCT (breast conserving therapy)	1 (2%)
Non-operated	7 (16%)
Chemotherapy	
Neoadjuvant	9 (20%)
Adjuvant	16 (36%)
Radiotherapy	
Postoperative	22 (49%)
Alone	7 (16%)
Complementary (adjuvant) hormonotherapy	28 (62%)

The analysis of disease-free survival rates revealed that 1, 2, 3 and 5-year disease-free survival rates in the group of patients receiving radical treatment were 94, 72, 64 and 48%, respectively; and 1, 2, 3 and 5-year local relapse-free survival rates were 100, 97, 97 and 87%, respectively; and metastasis-free survival rates were 95, 75, 67 and 58%, respectively.

In patients receiving surgical treatment, 3-year overall survival was 90%, and 25% in patients who did not receive surgical treatment, p = 0.01 (Fig. 2).

In the group of patients receiving adjuvant hormonal therapy, 5-year overall survival was 87%, and 30% in the group of patients who were not treated with hormonal therapy, p = 0.002 (Fig. 3).

The use of adjuvant chemotherapy had an insignificant influence on overall survival rates, p = 0.06. The use of adjuvant radiation therapy had no influence on survival rates, p = 0.8.

DISCUSSION

Male breast cancer etiology is unknown. High levels of estrogens and prolactin are thought to be risk factors [3, 6]. It is estimated that patients

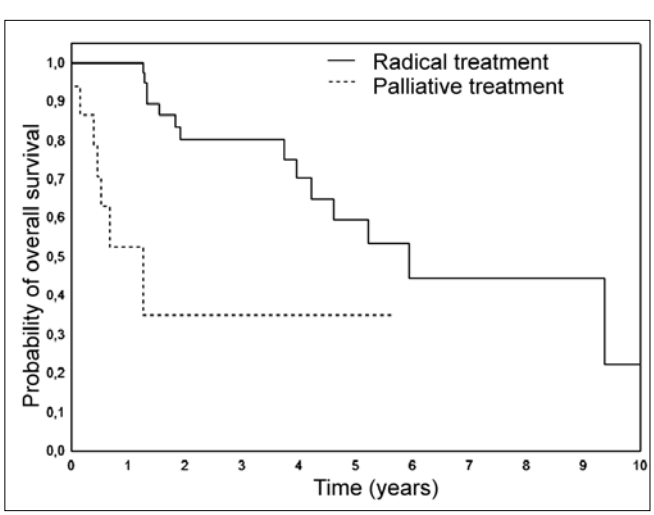

Fig. 1. Overall survival in palliatively and radically treated patients.

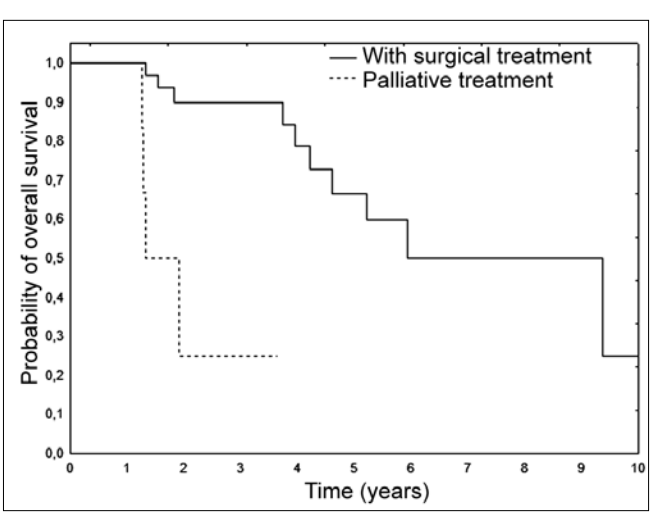

Fig. 2. Overall survival in the group of radically-treated patients with and without surgery.

with Klinefelter's syndrome (XXY genotype) may constitute about 3-7% of all men with breast cancer [2]. The risk of breast cancer is higher in men with testicular abnormalities (undescended testicles, congenital inguinal hernia, testectomy or testitis) [3, 7, 8, 9]. Gynecomastia is often listed as a risk factor [2, 6], although some publications state otherwise (3), and variables such as breast cysts, diseases of the mammilla, chest trauma are reported more rarely [7]. A history of radiation therapy administered to the chest, ionizing radiation, liver diseases, chronic alcohol disease, obesity and a diet rich in animal fat are all risk factors for breast cancer, similarly as in women [3, 6, 10, 11,12, 13, 14, 15, 16, 17].

According to available documents, gynecomastia was recorded in three patients from the studied group.

Familial breast cancer is demonstrated in 5% to 20% of affected men [6, 7].

In our work malignancies in relatives were found in 26% of cases, and in 1/3 it was breast cancer.

Some authors suggest that genetic mutations may correlate with a younger age of disease manifestation and shorter overall survival [2, 7, 18]. Contrary to the female population BRCA1 gene mutations are present in approximately 4% of men, whereas BRCA2 gene mutations are present in 40% [2, 19, 20, 21, 22]. According to some researchers only BRCA2 gene mutations should be regarded as risk factors for male breast cancer [7].

BRCA1/BRCA2 gene mutations were not determined in the studied material.

The diagnosis of male breast cancer increases the risk of other primary neoplasms, and the most common is bilateral breast cancer [23]. In the studied group metachronous bilateral breast cancer occurred in two patients (3%), in one after 42 months, and in the second after 33 months of from the initial diagnosis. In three patients (5%) other primary malignancies were diagnosed.

The mean age of men diagnosed with breast cancer is higher than in women, namely 60 vs. 53 years [3]. The physical examination usually reveals a unilateral painless tumor beneath the nipple. Most publications reported the tumor on the left side of the body [7, 24]. In 15-30% of patients nipple ulceration or bleeding is present at the diagnosis, in 25-50% the tumor cannot be moved and is accompanied by skin ulcers [2, 6]. Bilateral synchronous breast cancer is diagnosed in less than 5% of patients [6].

The clinical characteristics of the studied group is similar to the literature data both in terms of the mean age at the diagnosis, advanced disease stage, and the side of primary tumor location.

Ductal carcinoma *in situ* is present in approximately 10% of patients. Lobular carcinoma *in situ* is observed extremely rarely, and in the majority of cases it coexists with invasive cancer [2, 6]. Ductal carcinoma is the most frequent invasive cancer (70-90% of cases), whereas lobular cancer accounts for 1.5% of cases [2, 3]. The steroid receptor status is usually positive: 80-90% for estrogen receptor and 75-80% for progesterone receptor [2, 6, 7]. HER-2 receptor hyperexpression is significantly more rarely observed than in women, namely in 5% of cases [2, 25]. Infiltrating ductal carcinoma was diagnosed in the majority of cases (46%, with positive ER and PgR receptors in 49% patients). Differences regarding the histopathological characteristics are likely to be the result of the fact that it was not possible to identify the cancer type or to determine the steroid receptor and HER-2 statuses in some histopathological material as the diagnosis had been made based on cytological smears of material collected using a fine-needle biopsy.

Treatment for male breast cancer, both local and systemic, is introduced according to the guidelines valid for the treatment of breast cancer in women [2, 7, 24, 26]. The Halsted radical mastectomy was a standard method in surgical treatment for many years; however, now a modified radical mastectomy by Madden is more frequently performed [24]. Breast-saving procedures are performed rarely [3, 7, 26].

Adjuvant treatment is similarly beneficial as in women [7, 27]. Adjuvant chemotherapy is administered if a microscopic examination reveals axillary lymph node metastases or when the tumor diameter is more than 1 cm [7]. Adjuvant hormonal therapy with tamoxifen is administered steroid receptors in cancer cells are present. A 5-year therapy is recommended [2, 3, 7]. Data regarding therapy with aromatase inhibitors are scarce and controversial [3, 26]. Some authors suggest that adjuvant radiation therapy, which has the same indications as in the case of women [3], should also include radiation therapy to parasternal lymph nodes [7].

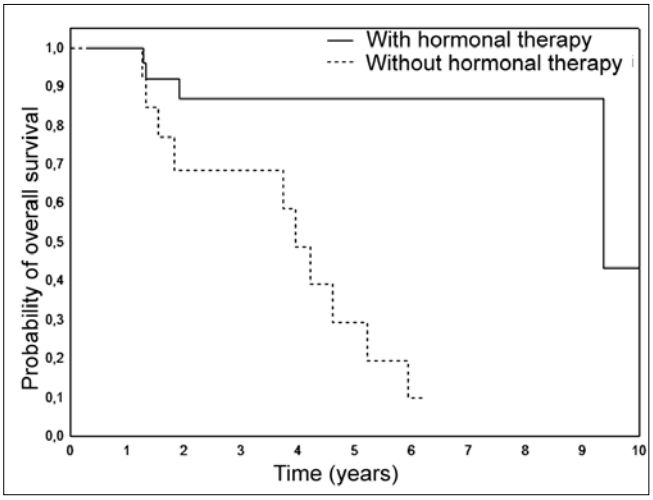

Fig. 3. Overall survival in the group of radically-treated patients with and without hormonal therapy.

In the studied material, 5-year overall survival in the group of patients receiving radical treatment was 59% and was lower than in other publications [27, 28]. This difference may be due to the fact that in this studied group patients had more advanced disease at the diagnosis. Overall survival rates were significantly higher for men receiving adjuvant hormonal therapy ($p = 0.006$), which is in accordance with other publications [27].

CONCLUSIONS

Male breast cancer is a rare neoplasm. Radical mastectomy is the treatment of choice. The negative steroid receptor status is variable with the strongest negative influence on survival. More detailed research should be performed to create a central registry of men with breast cancer.

Acknowledgements:

For the Department of Neoplastic Epidemiology Center of Oncology – Maria Skłodowska-Curie Memorial Institute, Branch in Gliwice for collecting data about patients' deaths available.

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