



Breast Cancer in Men: Characteristics Epidemiological, Clinicopathological and Therapeutic

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Abstract

Background: Breast cancer is the leading malignancy in women, but it is relatively rare in men, accounting for 1% of all breast cancers. In Morocco, its incidence is 0.8/100,000 in men. This condition epidemiology, therapeutic and prognostic remains unknown given the scarcity of reported series. The objective of this work is to identify the epidemiological, clinical, pathological and therapeutic of this cancer in men. **Results:** Six patients were diagnosed with breast cancer with a ratio of 6/1277 cases. The mean age of patients was 63.3 ± 9.7 ans; the most common histological type was invasive ductal carcinoma (83.3%). The grade 2 SBR has a majority (66.7%), while that of SBR 3 is less represented (33.3%). A positive estrogen receptor (66.7% of cases) and progesterone (50.0% of cases) was noted. The HER2 receptor is overexpressed in 25% of cases. The treatment was essentially surgical (83.3%). Additional treatment included adjuvant chemotherapy (50.0%), radiotherapy (50.0%) and hormonal therapy (16.7%) was administered. **Discussion/Conclusion:** Breast cancer in men is rare and appears to have a very close clinical, histological characteristics and prognosis to those of elderly women. The diagnosis is usually late and tumors are treated in advanced stages. An improved prognosis requires better awareness for early detection.

Subject Areas

Oncology

Keywords

Breast Cancer, Men, Epidemiology, Clinical, Therapeutic

1. Introduction

Breast cancer is the most common cancer in women in both the developed and developing countries.

However, this typically “female” disease can also affect males. Male breast cancer is a rare disease. It represents approximately 1% of breast cancers and 0.6% of the malignant disease in humans [1] [2]. Its incidence increases gradually, from 0.86/100,000 to 1.06/100,000 inhabitants in the last three decades [3].

In Morocco, according to the Cancer Register of the Region of Greater Casablanca (RCRC), its incidence is 0.8/100,000 in men [4]. It is a disease diagnosed more often at an advanced stage, making prognosis worse [5]. The only way to study the characteristics of this disease in males is the retrospective analysis of several small series of patients over several years. Several risk factors have been implicated such as direct family history, some metabolic and endocrine disorders, particularly real or relative hyper-oestrogenism [6].

Breast cancer in men is a little known pathology of the public and the discovery of a breast lump in a man does not raise the same concern as in women. Most studies show a more advanced stage at diagnosis and a poorer prognosis in men [7] [8]. Treatment recommendations for breast cancer in men are extrapolated from those used for breast cancer in women. Men are treated as postmenopausal women. However, until now no study made on the male population showed the modalities of care in terms of affects survival [9] [10]. The objectives of this study are to investigate the epidemiological, clinical, histological, therapeutic and prognosis of breast cancer in men treated at the Mohammed VI center for the treatment of cancer.

2. Patients and Methods

2.1. Type of Study

This is a cross-sectional study at the Mohammed VI center for the treatment of cancers Hospital IBN ROCHD (One of the two major centers for the care and treatment of cancers in Morocco treating 3000 - 3500 cases of cancers including breast cancer represents 20% of cases and breast cancer in men is 0.4% of cases).

2.2. Study Population

We included in our study consecutively all cases of male breast cancer that has been treated at the Center from January first 2013 until 30 December 2014. Data collection was done retrospectively, from patient medical records.

The data collected focused on:

- Socio-demographic data: Age at diagnosis, marital status, number of children and the concept of breast cancer family history.
- Clinical data: The stage at diagnosis, tumor size, lymph node involvement, distant metastasis, histological type, histological grade, laterality with quadrant or tumor region, the hormone receptor status, HER2 receptor (Human Epidermal growth factor) and proliferation index Ki-67.
- Therapeutic Data: Neoadjuvant chemotherapy, radiotherapy, adjuvant chemotherapy, hormone therapy and targeted therapy.

The variables studied were all well documented in all patients. Agreement of the ethics committee has been proven to this study. Data entry was conducted by Microsoft Office Excel (2007) and analysis of variables by the Epi Info software. The study association by crossing the variables between groups was evaluated by the test of chi-square. The test is considered significant when $p < 0.05$.

3. Results

3.1. Epidemiological Aspects

Between January 2013 to December 2014, six cases of male breast cancer have been supported in the Mohammed VI center for cancer treatment, CHU Ibn Rochd Casablanca. Epidemiological, clinical, histological and therapeutic patients are summarized in **Table 1**. The mean age at diagnosis was 63.3 ± 9.7 ans.

3.2. Histopathological Aspects

The most common histological type was invasive ductal carcinoma, it was observed in 83.3% of cases and invasive carcinoma in 16.7% of cases. Tumors were localized in 50% of cases. Lymph node involvement was described in 33.3% of cases. In our series, male breast cancer was high grade (grade II and III). The SBR grade II was found in 66.7% of cases and grade III in 33.3% of cases. Hormone receptor positivity was found to estrogen in 66.7% of cases and progesterone in 50.0% of cases. Overexpression of HER2 was observed in 25.0% of cases over 66.7% of cases. The molecular profile of male breast cancer was essentially luminal; luminal A was found in 50.0% of cases while luminal B in 16.7% of cases.

3.3. Treatment

Out of all of our series, 83.3% of patients underwent mastectomy and one patient had not undergone any surgery after the diagnosis of ductal carcinoma by biopsy. Of all mastectomies, 50.0% of cases were associated with axillary dissection and 16.7% of cases a simple mastectomy. Chemotherapy was performed in 50.0% of cases. The average age of patients in our series who received adjuvant chemotherapy was 59.0 ± 8.1 years. The additional irradiation was performed in 50.0% of cases. Of all irradiated patients, 55.5% of cases had lymph node involvement. Only one case (16.7%) had a tumor over 2 cm and 100% of the cases had grade II tumors (**Table 1**).

Table 1. Epidemiological, clinical, histological and therapeutic features.

Features	Number (N=6)	Percentage (%)
Average age	63.3 years	
Smoking	2	33.3
Breast cancer antecedent	0	0
BMI		
<25	4	66.6
25 - 30	0	0
>30	1	16.6
NP	1	16.6
Call sign		
Nodule	2	33.3
Isolated retraction	1	16.6
Isolated flow	1	16.6
Isolated ulceration	2	33.3
TNM Stage		
T0	0	0
T1	0	0
T2	4	66.6
T3	0	0
T4	2	33.3
N0	3	50.0
N1	1	16.6
N2	1	16.6
N3	1	16.6
M0	5	83.3
M1	1	16.6
SBR grade		
SBR I	0	0
SBR II	4	66.6
SBR III	2	33.3
Histological Type		
infiltrating ductal carcinoma	5	83.3
Invasive carcinoma	1	16.6
invasive lobular carcinoma	0	0
Treatment		
Mastectomy	2	33.3
lumpectomy	3	50.0
No surgery	1	16.6
Chemotherapy	3	50.0
Hormonotherapy	1	16.6
Radiotherapy	3	50.0

4. Discussion

4.1. Epidemiology

Breast cancer is a rare condition in men. It represents less than 1% of cancers in men and only 0.6% of all breast cancer [6] [9]. It is the first cancer in women with a rate of 23% and is the leading cause of female cancer mortality [1] [2] [3]. The incidence of breast cancer has been increasing in recent years. Moreover, Harlan *et al.* showed an

increase in breast cancer incidence in men by 26% between 1973 and 1998 in the United States [11]. The incidence of this cancer varies by country. This variation suggests the impact of the environment on the incidence [12]. This pathology appears 10 years later in men than in women, with an average age ranging between 59 and 66 years [3] [6] [8] [10] [13]. In our study, the mean age at diagnosis was 63 years, 5 years younger in literature but remains higher than in women.

4.2. Risk Factor

The etiology of breast cancer in men is not clearly established and the small number of cases does not allow the realization of a prospective study. However, some risk factors seem to be implicated.

Several studies have shown the involvement of direct family history of breast cancer [5] [7] [9] [10] and constitutional mutations of BRCA 1 and BRCA2 [14] [15]. The most frequent cases that were observed were related mutations of the BRCA2 gene [15].

The US network of cancer (National Comprehensive Cancer Network current) recommends providing education and encouragement to self-examination and conduct biannual clinical breast exams for men with gene mutations BRCA1 and BRCA2 [16]. This type of cancer could also have an endogenous cause, such as chronic conditions responsible for anti-androgenic or hyperprolactinémants effects such as liver failure, diabetes, obesity and kidney failure. Hormonal imbalance such as real hyperoestrogenism or relative or abnormalities of metabolism and excretion of endogenous steroids can also affect.

Hyperoestrogenism could also have an exogenous origin, in connection with certain medications [17] [18]. Some authors observed a hormone-dependency with hormone receptor-positive in 65 to 90 cases depending on the series, those with estrogen in 65% - 86% of cases and those with progesterone in 65% - 80% of cases [9] [13] [15] [19]. In our series, it was positive to estrogen in 66.6% of cases and progesterone in 50% of cases. Most authors have shown that adjuvant hormonal therapy improved the prognosis for survival and complete remission rate and recommend a systematic hormone therapy for all stages N1 and metastasis [6] [7] [8] [9] [13] [19].

In our series, 16.7% of cases had severe obesity. As in women, overweight and obesity are risk factors implicated in breast cancer. Similar results have been observed by several authors [20].

A second cancer may be associated with breast cancer in humans. Moreover, Cutuli and al., by conducting a multicenter study found the association with various cancers, anteriorly, synchronous or Metachronous [18]. Associated cancers are various such as prostate cancer, colorectal, bronchopulmonary, esophageal, or blood disorders [18] [21]. Moreover, Satram-Hoang and al., found on a series of 1921 men with breast cancer, 221 or 11.4% developed a second metachronous malignant tumor [21].

4.3. Diagnosis

Breast Cancer diagnosis in men is usually done at later stages and tumor size is often

superior to breast tumors in women [16]. In our series, stage at diagnosis was mostly stage II and III and all cases had T2 or T4 tumors, averaging 23 to 30 mm. Korde and al., have shown that tumor size in men is an average of 2.4 cm versus 2.2 cm in women [16]. Mammography and ultrasound are used to help diagnosis with the same criteria of malignancy in women. Male breast cancer screening cannot be considered. Moreover, Hines *et al.*, in a retrospective study from 2001 to 2004, have found only 4% of suspect images, and only 1% of cancers identified by biopsy on 212 patients with a mammography [22]. These authors showed the futility of imagery in male breast cancer and the diagnosis is in most cases clinical [22].

4.4. Histology

In our series, invasive ductal carcinoma was found in 83.3% of cases, this is the most common histological type, as in women. Similar results have been observed by several authors [6] [9] [10] [13].

Breast cancer in men rarely presents lobular carcinoma, unlike women where it occupies the second histology after invasive ductal carcinoma.

Male Breast cancer is characterized by a high expression of hormone receptors. In our study, we found positive hormone receptors in 80.0% of cases to estrogen and 60% to progesterone. HER2 overexpression is less common; our study showed that 25.0% of cases showed that overexpression. However, Giordano and al., in their study reported HER2 overexpression in 37% of cases [23].

We also noticed that in our study tumors were of high histological grade, 66.7% of grade II and 33.3% of grade III. Our results confirm those of Oger and al., which showed a high grade (grade II and III) in 72.0% of cases of breast cancer in men [24].

4.5. Treatment

Breast cancer treatment in humans based on mastectomy associated with an ipsilateral axillary dissection [25]. While in women, the standard treatment is a conservative or radical surgery in healthy margins, coupled with an analysis of the sentinel node [26]. In our series, 83.3% of patients underwent a mastectomy and 50% an ipsilateral axillary dissection. Axillary lymph node involvement is important in men and has been observed in 50% - 60% of cases by some authors [27]. Our study revealed a lymph node in 50% of cases.

Radical surgery is completed with adjuvant treatments. Adjuvant radiotherapy reduces the risk of local recurrence, but is controversial, as some studies have shown no benefit in overall survival [28]. In our study, the indication of the irradiation was applied in 50.0% of cases; similarly, for chemotherapy. In literature, its use is beneficial in younger patients with nodal involvement or in high-risk patients with poor prognostic factors, such as lack of expression of hormone receptors [29].

Hormone therapy has an important place in the adjuvant treatment of breast cancer, given the high frequency of hormone receptor positivity [6] [8] [15] [30] [31]. The reference molecule is tamoxifen. In our series, 16.7% of patients received hormone thera-

py with tamoxifen. Furthermore, Ribeito and al., noted in a series of 38 cases, a decrease in the risk of recurrence and death, after hormone treatment of patients [32].

Like any other study our study has its strengths and its limitations. This study presents the place of status the breast cancer in men is a particular entity at the center, but the information is limited and relates only to breast cancer in men cases in the public sector consultant and does not concerncases treated privately.

5. Conclusions

Male breast cancer is a rare disease and has its own characteristics. Considering all these observed differences, we cannot consider it as comparable to that of women.

The particularity of breast cancer in men is in its discovery at a late stage and high hormone receptor positivity. Besides, diagnosis and screening are the most important points to be developed to improve the prognosis. A large prospective study would improve knowledge regarding both diagnostic and therapeutic.

Author Contributions

Ahmadaye Ibrahim Khalil: data collection, data entry, data analysis, results interpretation, writing of the manuscript, Houriya Mestaghanmi: Data analysis, results interpretation, writing of the manuscript, Fadwa Qachach: interpretation of results, writing of the manuscript, Rachid Saile: interpretation of results, writing of the manuscript, Kariima Bendahhou: data analysis, results interpretation, writing of the manuscript, Abdelatif Benider: therapeutic management of patients and the writing of the manuscript.

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