RESEARCH COMMUNICATION

Breast Cancer in Tunisia: Clinical and Pathological Findings

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Abstract

Introduction: The aim of this study was to survey the clinical and pathological features of breast cancer in the Center of Tunisia. Design: Characteristics of all breast cancer cases diagnosed in the Pathology Department, Farhet Hached Hospital, Sousse, Tunisia during a 15-year period (1993-2007) were analyzed. Results: A total of 2,404 new cases of breast cancer were recorded, only 48 being diagnosed in men. The age-standardized incidence rate was 0.7 and 29.2 per 100,000 in men and women, respectively, with median ages of 48.0 and 64.5 years. Invasive ductal carcinoma was the most common (2,012 cases). Stage II was the most frequent (47.7%) followed by advanced stages (Stage III and IV, 41%). Conclusion: Cancer of the breast remains the most common cancer in the absence of specific screening measures among Tunisian women. Our study justifies the need to plan and develop effective programs aiming at the control and prevention of the spread of breast cancer in Tunisia.

Keywords: Breast cancer - clinicopathological findings - Tunisia

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Introduction

Breast cancer is the most common form of malignancy affecting women worldwide and therefore a major public health concern (Curado et al., 2007; Ferlay et al., 2010). Breast cancer is now the leading female cancer in most developing countries with around 690,000 new cases (Braunwald et al., 2001; Parkin et al., 2003; Curado et al., 2007; Ferlay et al., 2010). Incidence rates are high (greater than 80 per 100,000) in developed regions of the world (except Japan) and low (less than 40 per 100,000) in most of the developing regions (Ferlay et al., 2010).

In Tunisia, breast cancer remains the most common cancer in women (Maalej et al., 1999; Parkin et al., 2003; Curado et al., 2007; Maalej et al., 2008; Ben Abdallah et al., 2009; Missaoui et al., 2010; Missaoui et al., 2010). Several studies have been carried out about breast cancer in order to establish its clinical, pathological and epidemiological patterns, mainly at the Salah Azeiz Cancer Institute (Maalej et al., 1999; Maalej et al., 2008; Ben Abdallah et al., 2009). Recently, we described the epidemiological profile of breast cancer in the Center of Tunisia (Missaoui et al., 2010). Nevertheless, data on clinical and pathological patterns of breast cancer in the Center of Tunisia are limited. The purpose of the present study was to report the clinical and pathological features of all breast cancer cases diagnosed in the Center of Tunisia during a 15-year period (1993-2007), based on the database of the population-based Cancer Registry of the Center of Tunisia.

Materials and Methods

We carried out a retrospective study of 2,404 cases of breast cancer diagnosed in the Pathology Department of the Farhet Hached University Hospital, Sousse and registered in the Cancer Register of the Center of Tunisia during 15-year period time (January 1993-December 2007). The cancer registry has provided important information on cancer patterns over the previous years (Parkin et al., 2003; Curado et al., 2007; Missaoui et al., 2010). The study was approved by the Human Ethics Committee at the Farhet Hached University Hospital of Sousse (Tunisia) and it conformed to the provisions of the Declaration of Helsinki.

The International Classification of Diseases, 10th revision (ICD-10) was used for cancer classification (Percy et al., 1992). In the present study, the inclusion criteria were new cases of breast cancer (C50) diagnosed between the 1st January 1993 and the 31st December 2007.

We reviewed the medical records for data on age, sex, origin, delay to diagnosis, signs and symptoms, paraclinical data at time of diagnosis, histopathology, Scarff-Bloom-Richardson (SBR) grade, tumor stage, and treatment. Patients with bilateral breast cancer were recorded only one time. Clinical and pathological features

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including age at diagnosis, tumor size, tumor stage, and SBR grade were also analyzed across three phases: phase 1: 1993-1997, phase 2: 1998-2002, and phase 3: 2003-2007. The SPSS program, version 17 (SPSS Inc., Chicago, IL) was used for statistical analysis and probability values of 0.05 or less were considered statistically significant.

Results

Clinicopathology

A total of 17,238 cases were registered in the Cancer Registry of the Center of Tunisia during the study period (1993-2007). The Cancer Registry counted 2,404 new cases of breast cancer. Most of the patients were women, with 2356 women versus 48 men. The median age at diagnosis was 48 years (ranging, from 22 to 91 years). At the time of their breast cancer diagnosis, 15.2% of patients were nulliparous and 1.3% of the women were pregnant. The age-standardized incidence rate (ASR) was 29.2 per 100,000 during the study period. Detailed characteristics of breast cancer in this survey (phase 1, 2, and 3) are demonstrated in Table 1.

The mean diagnostic time was 7 months and 45.4% of the patients consulted after a time interval of 3 months. The major cause of consultation was a tumor with or without associated symptoms (85.8%). The tumor was more frequently located in the left breast (51% versus 48% in the right breast). The disease was bilateral in 1% of the cases. Contiguous localizations were the preferential site of the tumor (32.9%) followed by the upper and external quadrant (31.7%) and the upper and internal quadrant (8.8%). Mammography showed opacity with malignant features in 84.2% of the cases. The tumor size was higher than 2 cm in 81.2% and than to 5 cm in 33.9% of cases. According to the American Joint Committee on Cancer (AJCC) staging system, stage II was the most frequent (47.7%) followed by advanced stages (stages III and IV) with 41% of cancer cases. Early stages (stages 0 and I) represented only 11.2% of breast cancer (Table 1). Invasive ductal carcinoma was the most frequent histopathological type (2012 cases) followed by lobular carcinoma (132 cases). Non invasive carcinoma represents only 2.4% of cases with in situ ductal carcinoma as the most frequent (79.2%). According to the SBR grading system, grade II was the most frequent grade (846 cases) followed by grade III (38.5%) and grade I (16.1%). Over the study period, the rate of SBR I tumors increased from 8.3% in phase 1 to 17.8% in phase 3 (p=0.02) (Table 1).

Table 1. Characteristics of the Breast Cancer in the Center of Tunisia, 1993-2007

	1993-1997	1998-2002	2003-2007
Age at diagnosis Mean(years)	50.6	49.8	50.5
Median	49	47	48
Female ASR (/10^5)	23.4	29.8	29.7
Male ASR (/10^5)	0.6	0.9	0.4
Tumor size (n = 2257)	322	860	1075
< 2 cm	66 (20.5%)	110 (12.8%)	160 (14.9%)
≥ 2 cm	256 (79.5%)	750 (87.2%)	915 (85.1%)
≥ 5 cm	102 (31.7%)	310 (36%)	260 (24.2%)
≥ 10 cm	15 (4.6%)	44 (5.11%)	35 (3.2%)
SBR grade (n = 1875)	208	711	956
I	29 (8.3%)	104 (14.6%)	170 (17.8%)
II	92 (44.2%)	305 (42.9%)	449 (46.6%)
III	86 (41.3%)	301 (42.3%)	336 (35.1%)
IV	1 (0.4%)	1 (0.1%)	1 (0.1%)
Stage at presentation (n = 2355)	344	900	1111
0	3 (0.9%)	22 (2.4%)	29 (2.6%)
I	34 (9.9%)	74 (8.2%)	103 (9.3%)
II	160 (46.5%)	417 (46.3%)	547 (49.2%)
III	107 (31.1%)	262 (29.1%)	312 (28.1%)
IV	40 (11.6%)	125 (13.8%)	120 (10.8%)

Calculated according to valid (none missing) cases; ASR, Age-standardized rates; SBR grade, Scarff-Bloom-Richardson

Therapeutics

Among our patients, 81.6% received a surgical treatment (1961 cases). Surgery consisted of a mastectomy in 1565 patients (79.8%) and 396 patients (20.2%) were treated by a conservative surgery. For 672 patients (56.8%), adjuvant treatment (radiation therapy, chemotherapy, and/or hormone therapy) had been indicated. Among these patients, 16% of cases were handled by the three adjuvant modalities; 51.1% of patients received chemotherapy associated to radiation therapy; 24.1% of cases received chemotherapy and 8.8% received radiation therapy. Hormone therapy was indicated for 705 patients (29.3%). Surgery was the only treatment for 265 patients. An exclusive chemotherapy has been indicated for 283 patients. Radiation therapy was the only local treatment after chemotherapy for 23 patients. An exclusive radiation therapy has been indicated for only 2 patients. Unfortunately, 135 patients had received no treatment.

Breast cancer in men

Breast cancer was diagnosed in only 48 men during our study period, which represents 2% of all breast cancer cases and 0.5% of all cancers in men. The crude incidence rate of the male breast cancer was 0.5 per 100,000 with an ASR of 0.7 per 100,000. In this group of patients, the median age was 64.5 years (ranging from 31 to 88 years) with 33.3% of cases were aged 60-70 years. Time interval between first consultation and care was 9.2 months. According to the AJCC staging system, 78.7% of the tumors were of stages II and III. The most frequent histopathological type was invasive ductal carcinoma (79.2%). According to the SBR grading system, grade II was the most frequent grade (57.2%) followed by grade III (31.4%) and grade I (11.4%).

Discussion

The current study investigated clinical and pathological features of breast cancer in the center of Tunisia, diagnosed in the Pathology Department of Farhet Hached University Hospital, Sousse (1993-2007). The cancer of the breast remains the most common cancer among Tunisian women and constitutes a real problem of public health. According to Globocan 2008, the incidence of the breast cancer was of 30.3 per 100,000 women in Tunisia (Ferlay et al., 2010). The incidence rate was widely weaker than the rates observed in the most developed countries, such as United

States (ASR: 122.9) (Altekruse et al., 2010), Europe (ASR: 66.6), Canada (ASR: 83.2), Australia (ASR: 84.8), and Denmark (ASR: 89.1) (Ferlay et al., 2010). Nevertheless, the incidence rate reported here remains superior to rates reported from Asia (Ferlay et al., 2010). We reported recently significant increasing trends of the incidence of breast cancer among Tunisian women (Missaoui et al., 2010; Missaoui et al., 2010). Increasing trends were also described in Eastern Asian countries (China, Japan, the Republic of Korea, and Taiwan) and Southeastern Asia (the Philippines, Singapore, and Thailand) (Shin et al., 2010). The increasing trends seemed to be related to a number of risk factors including the events of reproductive life and lifestyle factors, such as early menarche, late menopause, low parity, late age at first live birth, and low prevalence of breastfeeding, that modify endogenous levels of sex hormones (Key et al., 2002; Missaoui et al., 2010; Missaoui et al., 2010), and certainly to the absence of an effective screening program for breast cancer among Tunisian women. In Tunisia, there was only one experience of breast cancer screening program organized in the Ariana province (North of Tunisia) by the Family and Population National Office (Bouchlaka et al., 2009; Bouchlaka et al., 2009; Chelli et al., 2009; Zaanouni et al., 2009). The study was initiated in 2003 and lasted 5 years. A total of 8244 women were screened and 50 women presented a cancer. This study showed that an early diagnosis can lead to a dramatic reduction of the tumor size, more better prognostic features, more conservative surgery and slight improvement of survival (Bouchlaka et al., 2009; Bouchlaka et al., 2009; Chelli et al., 2009; Zaanouni et al., 2009). Thus, a structured extended screening program must be installed in Tunisia to achieve these objectives but requires an important financial and human investment.

In the current study, male breast cancer accounts for 0.5% of all cancers in men, similar to that reported from developed countries (Weiss et al., 2005; Fentiman et al., 2006). As female breast cancer, the incidence of male breast cancer varies greatly in different geographical areas and ethnic groups with higher rates in North America and Europe and lower rates in Asia (Weiss et al., 2005; Fentiman et al., 2006). A substantial high proportion of male breast cancer cases have been reported in Africa (Giordano et al., 2002; Giordano et al., 2004). These relatively high rates have been attributed to endemic infectious diseases, such as bilharziosis and hepatitis B/C that, by chronic liver infection, may cause liver damage leading to hyperoestrogenisms (Ottini et al., 2010). The incidence of male breast cancer increases with age with a peak incidence in the sixth decade (Giordano et al., 2002; Ottini et al., 2010). In our study, men were older at the time of diagnosis compared to women, with a median age at diagnosis of 64.5 years compared to 48 years for women (Missaoui et al., 2010). The median age at onset was higher than that reported from other North African counties, such as Morocco (60 years) and Libya (61 years) (El Omari-Alaoui et al., 2002; El-Habbash and Alwindi, 2009). Several studies have reported that men tended to be older than women at the time of a breast cancer diagnosis (Ottini et al., 2010). In the United States, the median age at diagnosis of male breast cancer was 67 years (Giordano et al., 2002; Giordano et al., 2004; Altekruse et al., 2010). The absence of screening programs in men may explain the advanced age of male breast cancer diagnosis (Giordano et al., 2004; Ottini et al., 2010).

According to AJCC staging system, stage II was the most frequent similar to the rate reported previously in the global Tunisian population (46.9%) (Maalej et al., 2008). As we reported recently (Missaoui et al., 2010), the breast cancer remains diagnosed at advanced stages over time. Moreover, the tumor size remains higher than 2 cm in most cases diagnosed during the study period. This can be attributed mainly to the absence of specific screening measures for breast cancer among Tunisian women. However, recently, Harirchi et al. (Harirchi et al., 2010; Harirchi et al., 2010) reported decreasing trends of tumor size as well as downstaging of female breast cancer without a formal screening program among Iranian women. The authors attributed these trends to the overall improvement in the level of health in Iran and also educational activities that teach women when and why to ask for breast examination (Harirchi et al., 2010; Harirchi et al., 2010).

Invasive ductal carcinoma was the most common histological type of breast cancer diagnosed in the Center of Tunisia. Data from the Salah Azeiz Institute and the Cancer Registry of Northern Tunisia described similar rates (Maalej et al., 1999; Maalej et al., 2008; Ben Abdallah et al., 2009). Over the whole study period, SBR II grade tumors remains the most frequent in the Center of Tunisia similar to results described previously (Maalej et al., 1999; Maalej et al., 2008; Ben Abdallah et al., 2009).

In conclusion, although the relatively low incidence rate compared to that reported from developed countries, breast cancer remains the most common cancer diagnosed at advanced stages among women in the Center of Tunisia. Our findings justify the need to plan and develop effective programs aiming at the control and prevention of the spread of breast cancer in Tunisia.

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