Original article

Breast cancer in women aging 35 years old and younger: The Egyptian National Cancer Institute (NCI) experience

A.D. Darwish [a, *], A.M. Helal [a], N.H. Aly El-din [b], L.L. Solaiman [c], A. Amin [d]

[a] Medical Oncology, National Cancer Institute, Cairo University, Cairo, Egypt
[b] Biostatistics & Epidemiology, National Cancer Institute, Cairo University, Cairo, Egypt
[c] Medical Oncology, Beni Suef University, Egypt
[d] Radiation Oncology and Nuclear Medicine, National Cancer Institute, Cairo University, Cairo, Egypt

ABSTRACT

Objective: The aim is to identify the epidemiological and clinicopathological features associated with young breast cancer (BC) patients and to discuss factors affecting tumor recurrence and DFS.
Patients & methods: A retrospective analysis was conducted based on medical records from young females patients aged ≤35 years with pathologically confirmed primary breast cancer treated during 2008−2010 at NCI. Cases with non invasive cancer and non carcinoma histology are excluded.
Results: Of the 5408 cases diagnosed with breast cancer, 554 were young. Four hundred & fifty eight patients representing 9.2% were within our inclusion criteria. Almost half of the patients (45.9%) presented with stage III. Axillary nodes involvement was in 63.9%, 83.3% were grade 2. More than one quarter of tumors was hormone receptors negative (28.8%) & Her2 was over-expressed in 30%. Mastectomy was offered in 72% while conservative breast surgery in 26%, 69.2% received chemotherapy either adjuvant, neoadjuvant or both, 82.5% received adjuvant radiotherapy, 68.6% received hormonal therapy. Metastatic disease developed in 51.3%, with 31% having more than one site of metastases. After a median follow up period of 66 months, the median DFS of patients was 60 months. The median DFS was significantly shorter among patients with positive lymph nodes ($P < 0.0001$), ER negative disease ($P = 0.045$) and stage III disease ($P < 0.0001$).
Conclusion: Breast cancer in young women is aggressive from the time of diagnosis. Our results provide baseline data of young BC in the Middle East & North Africa region; thus, contributing to future epidemiological and hospital-based researches.

© 2016 Elsevier Ltd. All rights reserved.

Introduction

Breast cancer (BC) is the second most common cancer in the world and, by far the most frequent cancer among women. Incidence rates vary nearly fourfold across the world regions, with rates ranging from 27 per 100,000 in Middle Africa and Eastern Asia to 96 in Western Europe [1]. In USA about 19% of breast cancers are diagnosed in women ages 30−49 years, and 44% occur among women who are age 65 years or older [2]. In Japan, BC in women aged younger than 35 years old comprises approximately 3% of Japanese breast cancer patients [3]. In most African countries, BC among young women comprises a high proportion of cases than among older women. This is a demography driven phenomenon rather than a true intrinsic biologic significance, because the African population has a low median age; generally 20 years and below [4]. Nevertheless in North Africa, the incidence among women aged 15−49 is lower than in Western countries, but the very low incidence among women aged more than 50, combined to the young age pyramid of North-Africa, makes the relative proportions of young patients substantially higher (50−60% versus 20% in France). Such epidemiological features result mainly from peculiar risk factor profiles, which are typical for many developing countries and include notably rapid changes in reproductive behaviors [5]. In Arab women the average age at presentation of BC is a decade earlier than in US and European women. The median age at diagnosis in Arab populations, is about 48 years, and about two-third of women with BC are younger than 50 years [6]. In Egypt the incidence rate of breast cancer is 29.9/100,000 population in the age

group of 30—34 years [7]. In a study comparing Egypt's Gharbia Cancer Registry (GCR) and the United States Surveillance, Epidemiology, and End results (SEER) registries, Egyptian GCR cases were, on average, over 10 years younger than US SEER cases, with nearly 19% of GCR cases ≤40 years of age as compared to only 6% of US SEER cases [8].

Although many studies considered young age as an independent prognostic factor with worse outcome the reasons are still controversial [9]. Many reports showed that breast cancer at young age carries more aggressive features as lymphovascular invasion, grade 3 histology, HER2 oncogene over expression, absence of the estrogen receptors, higher triple negative subtypes and more advanced presentation [10,11]. While other studies have supposed that breast cancer in young patients is unique biologically with gene expression that is different from the older patients [12,13]. Several reports showed higher rates of local recurrence and lower survival when young women with breast cancer are compared with older patients [14].

In addition to considerations related to presentation of disease and prognosis, young patient population less than 35 years face some specific problems that are less relevant for older patients. These issues may include disruption of career in its early phase, child bearing and ongoing family responsibilities, impact of therapy on sexuality and body image, and the psychosocial stress of facing a life threatening illness at a young age [15]. Fertility, genetics, psychological and emotional factors are particularly important in young patients while taking treatment decisions [16].

In the current retrospective study we document the clinicopathological features & treatment outcome of breast carcinoma in a relatively large cohort of young women originating from a region where BC in young women is very high. There is very limited published literature on experiences of treating BC in young Middle East or North Africa population. It isn't clear whether the disease is different than that reported in the west? Some studies have argued that but not yet confirmed [17]. In our analysis, we had two objectives [1]: to identify the epidemiological and clinicopathological features associated with young BC patients and [2] to discuss factors affecting tumor recurrence and disease free survival.

Patients and methods

This is a retrospective study that included young female patients with primary breast cancer aged ≤35 years treated at NCI, Cairo University from January 2008 to December 2010. The study received approval from ethical committee of NCI. Early, locally advanced and metastatic breast cancer cases were included. The analyses were based on 5408 cases of invasive breast carcinomas who were diagnosed and/or treated at NCI. Five hundred and fifty four cases were ≤35 years. Subjects with non-invasive cancer (2 cases) other non carcinoma histology (53 cases) or unspecified malignancy (2 cases) were excluded. In 39 patients record no data but the histopathology are found so finally 458 are included.

Data collection

Data were collected jointly by 2 team members (LS & AA) and reviewed jointly by two other members (AD & AH). To avoid inconsistencies, all the study members discussed the abstraction items and had them written in a data collection sheet. Data sheet used for data extraction included the following information:

➢ Patient's identifiers (name-hospital number-phone number-date of entry).
➢ Patient's demographics including (age — marital status — parity - number of children).

➢ Family history, oral contraceptive pills intake history
➢ Tumor related data including laterality, presenting symptoms, histopathological data of the tumor (size-histological type-grade-lymph node status-number of positive nodes—metastasis status-site of metastasis (if any) — staging according to AJCC system-ER status-PR status-HER 2neu status-recurrence (if any) and its site).
➢ Breast cancer subtypes were identified based on immunohistochemical surrogates for ER, PR & HER2 status.
➢ Treatment (Surgery type, chemotherapy, radiotherapy & hormonal therapy).
➢ Time related data including date of entry, date of diagnosis, surgery date, chemotherapy starting and ending date, date of recurrence, date of last follow up and date of death if any and mentioned.

Statistical analysis

All analyses were performed using SPSS version 17.1IL Chicago. A code book was created to keep different categories for each variable. Every effort was done to avoid missing data. Survival was estimated using the Kaplan—Meier method and groups were compared using the log-rank test. Univariate analysis was done of clinicopathological factors &treatment modalities (patient age, pathological type, tumor grade, tumor stage, ER status, PR status, lymph nodes, IHC based subtype, type of surgery, adjuvant &/or neoadjuvant chemotherapy) through the time-to-event endpoints. Time to distant metastases (TDM) was defined as the time between surgery and first documented distant metastases. Time to local recurrence (TLR) was defined as the time between surgery and the first documented local recurrence. Disease free survival was defined as the time interval between surgery and the first documented relapse, death, or last follow-up, which ever occurred first. A probability (P) < 0.05 is considered statistically significant.

Results

This retrospective cohort study included 458, representing 9.2% of the 5408 cases of pathologically proven breast cancer who presented to NCI Cairo at the period of the study.

Patients' characteristics

The patients' characteristics are outlined in (Table 1). The median age at diagnosis was 32 years. About two thirds of patients aged >30—35 years.

Tumor characteristics

The most common pathological type was invasive duct carcinoma presented in 340 patients (83.7%), other types (including papillary carcinoma, mucinous carcinoma, medullary carcinoma, metaplastic carcinoma, tubular carcinoma, invasive cribriform carcinoma were encountered in 31 cases (7.7%)). Tumor grade was documented in 370 cases and grade 2 was the most common grade (83.3%). Almost 2/3 of our patients had positive ER receptors and positive PR receptors (68%, 62.7%) respectively. From 183 patients, HER2 was over expressed in 55 patients (30.1%). On reviewing the files, almost 2/3 of patients (62.1%) presented with (T2) followed by 23.5% (T3). Four percent presented with Stage I, 39.6% with stage II, 45.9% stage III. Thirty six patients (10.2%) presented at first by metastatic disease, 12 patients had bone only metastasis while 6 patients had bone and visceral metastasis, 8 patients had liver metastasis, 6 patients had lung and only one patient presented