Journal of the Egyptian National Cancer Institute xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Journal of the Egyptian National Cancer Institute

journal homepage: www.sciencedirect.com

Full length article

Metaplastic breast carcinoma: Analysis of 31 cases from a single institute

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ARTICLE INFO

Article history:
Received 13 March 2017
Received in revised form 24 April 2017
Accepted 8 May 2017
Available online xxxx

Keywords:
Metaplastic
Breast
Cancer
Clinicopathological
Outcome

ABSTRACT

Purpose: Metaplastic carcinoma of the breast (MBC) accounts for less than 1% of all mammary tumors. This study aimed at revision of the clinico-pathological features, treatment strategy and outcome for MBC patients presented to the Kuwait Cancer Control Center to define the clinical behavior and prognostic factors of these neoplasms in our population.

Patient and methods: Thirty-one patients were retrieved from our surgical pathology registry between January 2005 and December 2014. Medical records were revised regarding the clinico-pathological features and treatment outcome.

Results: MBC represented 1% of our breast cancer patients. The median age was 50 years (32–70 years). Two patients presented with metastatic disease. Mastectomy was done for 24 patients and 7 had conservative surgery. The median tumor size at the time of surgery was 5.5 cm (1.5–12 cm). Axillary nodes were negative in 21 patients (N0), 5 patients were N1, 4 patients were N2 and one Nx. Three histological subtypes were presented: carcinosarcoma (7 cases), squamous cell carcinoma/IDC with squamous differentiation (15 cases), high grade IDC with metaplastic differentiation (9 cases). Immunohistochemically, 26 were negative hormone receptors and all were negative for Her2/neu overexpression. Chemotherapy was used in 28 patients, and adjuvant radiotherapy in 24 patients. The median follow-up was 47 months (7–126 months), six patients lost follow-up. The 5-year OS was 69% and 5-year PFS was 50%.

Conclusion: MBC is a rare entity among breast carcinoma in Kuwait. Most of the cases present with poor prognostic indicators and often show lack of expression of ER, PR and Her2/neu.

Introduction

Metaplastic carcinoma of the breast (MBC) is a histologically distinct group of breast cancer in which adenocarcinoma co-exists with a mixture of spindle cell, squamous, chondroid or bone-forming neoplastic cells [1–3]. These non-adenocarcinoma elements may be present as a microscopic focus or may dominate the histologic pattern. MBC is considered a rare breast neoplasm that accounts for less than 1% of all mammary tumors [4]. It was officially recognized as a distinct pathologic diagnosis only in 2000. Molecular studies suggested that both epithelial and mesenchymal components of MBC are derived from a single stem cell and further mutations led to the clonal evolution of the metaplastic component as a heterologous element [5]. The molecular mechanisms that advances the metaplastic carcinogenesis might be different from those associated with other breast cancer subtypes including basal-like cancers [6]. It is suggested that upregulation of epithelial-mesenchymal transition genes (EMT) might play a crucial role in the pathogenesis of MBC [7].

MBC often manifests with a rapidly growing palpable mass with high density on mammography [8]. Despite less frequent axillary lymph nodes involvement [9], MBC is associated with other poor prognostic indicators being mostly negative for hormone receptors and Her2/*neu* over-expression [10]. Its outcome was reported to be worse compared with matched typical invasive ductal carcinoma or triple negative ductal carcinoma [11–15] even with routine aggressive multidisciplinary care, being a chemoresistant variant [16].

Aim of the study

The present work aims at revision of the clinico-pathological features, treatment strategy and outcome for MBC patients

Peer review under responsibility of The National Cancer Institute, Cairo University.
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http://dx.doi.org/10.1016/j.jnci.2017.05.002
1110-0362/

Please cite this article in press as: Fayaz S et al. Metaplastic breast carcinoma: Analysis of 31 cases from a single institute. J Egyptian Nat Cancer Inst (2017), http://dx.doi.org/10.1016/j.jnci.2017.05.002

presented to the Kuwait Cancer Control Center (KCCC) to define the clinical behavior and prognostic factors of these neoplasms in our population.

Patients and methods

Thirty-one patients were retrieved from the surgical pathology registry of the KCCC between January 2005 and December 2014. KCCC is the multidisciplinary cancer center in Kuwait to which cancer patients are referred from different provinces in Kuwait. Treatment protocol of MBC in our center follows the same principles of classical adenocarcinoma of the breast. Patients who presented with early disease (T1/T2 and N0/N1) were treated with surgery (lumpectomy with negative margins or mastectomy + axillary staging with either sentinel lymph node biopsy or axillary clearance) followed by the appropriate adjuvant treatment (chemotherapy, radiotherapy and hormonal treatment). Patients presented with locally advanced (T3/T4 or N2/N3) or those who needed tumor downstaging for breast conservative surgery were treated with neoadjuvant chemotherapy followed by the appropriate surgery then adjuvant radiotherapy ± hormonal treatment (according to the hormonal receptor status).

Retrieved database included the epidemiological data (patients' age, menopausal status); clinico-pathological features (tumor type, stage, grade, size, Ki67, hormone and Her2/*neu* receptor status); local and systemic treatment given; disease recurrence and survival. The pathological material including the immunostained paraffin blocks were meticulously reviewed in KCCC.

Epidemiological and clinicopathological features were summarized using descriptive statistics. Overall survival (OS) and progression free survival (PFS) were estimated using Kaplan Meier method. OS was defined as the time from diagnosis to death and PFS was defined as the time from diagnosis to the date of first progression. Patients without documented disease progression were censored at the last date of their follow up. Statistical significance was calculated by using the log-rank test and defined as $P < 0.05$.

Immunohistochemical (IHC) assays were performed using monoclonal antibodies against ER and PR (Dako, Glostrup, Denmark) and Her2/neu (Labvision, Fremont, California, USA). We followed the ASCO and the CAP recommendations for reporting the results of the IHC assays for ER&PR and Her2/*neu*. For ER&PR, all cases with at least 1% positive cells are considered as receptor positive [17]. The Allred score, which combines the percentage of positive cells and the intensity of the reaction, is used for ER&PR evaluation [18]. HER2 status can be determined by assessing protein expression on the membrane of tumor cells using IHC or by assessing the number of HER2 gene copies using in situ hybridization (ISH). The results for Her2 testing by IHC are reported according to the intensity and the percentage of positive staining in tumor cells (0, 1+, 2+, or 3+). Score 0 and 1+ are considered negative for Her2 amplification. Score 3+ is considered positive. Score 2 is considered equivocal and ISH is ordered for confirmation. Her2 is considered to be amplified if the average Her2 copy number is ≥ 6 signals/cell or Her2/CEP17 ratio ≥ 2 [19].

Results

Clinicopathological features and treatment charcteristics

The characteristics of the 31 MBC patients are detailed in Table 1. MBC represented 1% of 2970 registered patients who were diagnosed with breast cancer in 10 years period. All patients were

Table 1
Clinicopathological characteristics of 31 patients of MBC.

Age	
Median (range)	50 years (32–70 years)
Clinical T-stage	*No. (%)*
cT1	3 (10)
cT2	5 (16)
cT3	10 (32)
cT4	13 (42)
Site of the tumor	
UOQ	17 (55)
LOQ	2 (6.5)
UIQ	5 (16)
LIQ	2 (6.5)
Central	5 (16)
Pathological T-stage	
pTx	1 (3)
pT1	3 (10)
pT2	8 (26)
pT3	10 (32)
pT4	9 (29)
Pathologic N-stage	
pN0	21 (68)
pN1	5 (16)
pN2	4 (13)
pNx	1 (3)
M stage	
M0	29 (94)
M1	2 (6)
Overall clinical stage	
Stage I	3 (10)
Stage II	13 (42)
Stage III	13 (42)
Stage IV	2 (6)
Pathology subtype[*]	
Carcinosarcoma	7 (23)
Squamous cell	15 (48)
High grade IDC with mesenchymal differentiation	9 (29)
Hormone Receptor Status	
Negative	26 (84)
Positive	5 (16)
Her2/neu overexpression	
Negative	31 (100)
Positive	0 (0)
Ki67	
Negative	1 (3)
Positive	27 (87)
Missing	3 (10)
Surgery	
Mastectomy	24 (77)
Conservative surgery	7 (23)
Axillary clearance	19 (61)
Sentinel Lymph node biopsy	12 (39)
Chemotherapy	
Neoadjuvant	13 (42)
Adjuvant	13 (42)
Palliative	2 (6)
No chemotherapy	3 (10)
Type of chemotherapy[**]	
FEC	3 (11)
TE	2 (7)
FEC/Taxotere	3 (11)
AC/Taxol	12 (43)
TC	5 (17)
Others	3 (11)
Radiation Therapy	
Adjuvant	24 (77)
Palliative	3 (10)
Not used	4 (13)