

## MEDULLARY CARCINOMA OF THE BREAST-EPIDEMIOLOGY, THE PATTERN OF CARE, AND TREATMENT OUTCOME: EXPERIENCE FROM THE TERTIARY CANCER CARE CENTER

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Received: 18 May 2022, Revised and Accepted: 21 June 2022

### ABSTRACT

**Objectives:** Medullary breast carcinoma is a very rare subtype of invasive ductal carcinoma breast which accounts for about 1–7% of all breast carcinoma. The natural history of this uncommon histological subtype is unknown because of the lack of adequate reported data in the literature and the rare variety of this tumor. In our retrospective analysis, we have tried to identify demographic clinicopathological features and treatment outcomes of this rare subtype.

**Methods:** Between January 2012 and December 2017, total of 1271 breast carcinoma cases were identified, and clinic pathological, demographic profile, and treatment received were recorded from the medical records file. American joint committee on Cancer tumor, node, and metastasis system was used for staging.

**Results:** Out of 1271 breast carcinomas, 19 histologically confirmed medullary carcinoma cases were identified and constitute about 1.5% of the total case. About 78% of patients were with Stage II and Stage III disease at the time of diagnosis. Eleven patients were initially treated with MRM followed by adjuvant chemotherapy and radiotherapy. Eight patients received neoadjuvant chemotherapy followed by surgery and radiotherapy. In addition to cytotoxic chemotherapy, two patients received trastuzumab also. None of the patients received hormone therapy as all the patients were hormone receptor-negative.

**Conclusions:** Out of all invasive carcinoma, approximately 1.5% of cases were medullary carcinoma. About 90% of cases were triple-negative. Triple-negative breast cancer is usually associated with poor outcomes but medullary carcinoma despite being triple-negative, patients with medullary carcinoma have a good chance of long-term survival.

**Keywords:** Medullary carcinoma, Breast, Triple-negative.

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### INTRODUCTION

Worldwide, About 63% of death in the year 2008 was due to non-communicable disease (NCDs) and in India, NCDs account for 53% of deaths [1]. Malignancy is one of India's leading causes of death among NCDs and accounts for 6% of mortality in the year 2008 [1]. For both sexes, according to GLOBOCAN 2018, breast cancer second most common cancer after lung cancer accounting for 11.6% of total cases [2]. Breast cancer is a major public health problem for women throughout the world. Because of inadequate screening and lack of appropriate medical facilities, most of the cases are diagnosed at an advanced stage and thereby increasing breast cancer mortality [3]. Medullary breast carcinoma (MdBc) is a very rare subtype of invasive ductal carcinoma breast which accounts for about 1–7% of all breast carcinoma and is a very soft and fleshy mass, resembling the medulla of the brain; this tumor is called medullary carcinoma [3,4]. MdBc is characterized by well-circumscribed borders, syncytial growth, large cells, and dense lymphocytic infiltration. Typical medullary, atypical medullary, and medullary-like invasive ductal carcinoma are considered single entity as "carcinoma with medullary features" or simply "medullary breast cancer [5]" and lacking estrogen receptor (ER), progesterone receptor (PR), and HER2-Neu expression [6]. The natural history of this uncommon histological subtype is unknown because of the lack of adequate reported data in the literature and the rare variety of this tumor. In our retrospective analysis, we have tried to identify demographic clinicopathological features and treatment outcomes of this rare subtype.

### METHODS

Between January 2012 and December 2017, total of 1271 breast carcinoma cases were identified, and clinic pathological, demographic

profile, and treatment received were recorded from the medical records file. Along with history and physical examination, complete blood count, liver function test, renal function test, serology (HIV-I,II; HBsAg; anti HCV), electrocardiogram, echocardiography, chest X-Ray-PA, ultrasonography of the whole abdomen, immunohistochemistry for ER, PR, and HER2neu were performed. American joint committee on Cancer tumor, node, and metastasis system was used for staging. Whole-body PET CT scan was performed in selected cases presented with locally advanced breast carcinoma. All the data were collected from the record section of the department of radiotherapy and before collection of data, we have taken the informed consent of the patient and/or patients relatives, stating the nature of this study and no harm and no financial burden would occur and that further management of the patients would not be hampered.

### RESULTS

Out of 1271 breast carcinomas, 19 histologically confirmed medullary carcinoma cases were identified (Figs. 1 and 2) and constitute about 1.5% of the total case. The median age of diagnosis is 46 years with a range of 38–64 years. All the demographic details are summarized in Table 1. The most common presenting feature is awareness of breast lump followed by axillary swelling and breast lump (clinical features depicted in Table 2). About 78% of patients were with Stage II and Stage III disease at the time of diagnosis (depicted in Table 3). All the Histopathologic characteristics are summarised in Table 4. Eleven patients were initially treated with MRM followed by adjuvant chemotherapy and radiotherapy. Eight patients received neoadjuvant chemotherapy followed by surgery and radiotherapy. Chemotherapy regimens were six cycle TAC (Taxen-docetaxel, A-Adriamycin,

**Table 1: Baseline patients characteristics**

Age at diagnosis	Years
Median	52 years
Mean±SD	52.58±9.62 years
Range	38–70 years
Age at menarche (Mean±SD)	12.2±1.7 years
Age at first childbirth (Mean±SD)	26.3±2.9 years
Positive family history	2 (10.53%)
Parity	
0	1 (5.26%)
1–2	11 (57.89%)
≥3	7 (36.84%)
Residential area	
Rural	8 (42.1%)
Urban	11 (57.9%)
Menopausal status	
Premenopausal	6 (31.58%)
Postmenopausal	13 (68.42%)
Body Mass Index (Mean±SD)	30.37±2.43
Addiction	
Smoking	1 (5.26%)
Alcohol	0
Tobacco chewing	2 (10.53%)

**Table 2: Clinical features at presentations**

Symptoms	n (%)
Breast lump	18 (95)
Axillary swelling	7 (37)
Breast lump+axillary swelling	8 (42)
Local Pain	5 (26)
Site of breast lump	
Right breast	9 (47)
Left breast	10 (53)

**Table 3: Stage at presentation**

Stage	n (number of patients) %
Stage I	3 (16)
Stage II	8 (42)
Stage III	8 (42)
Stage IV	0

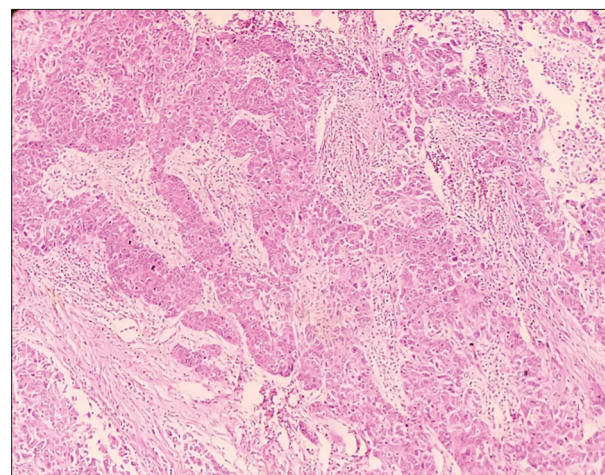
**Table 4: Histopathological characteristics**

IDC, NOS	1220 (96%)
Lobular	25 (2%)
Medullary	19 (1.5%)
Other rare type	7 (0.5%)

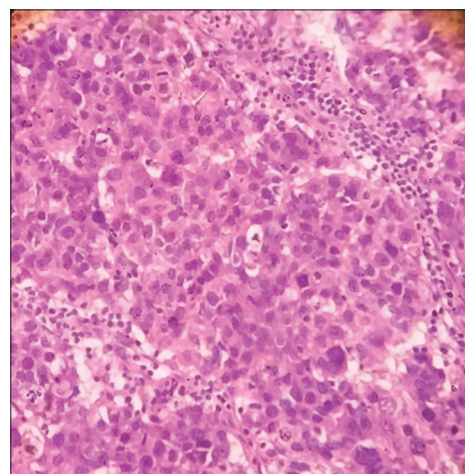
C-cyclophosphamide), four cycles AC followed by T (12 cycles weekly paclitaxel). In addition to cytotoxic chemotherapy, two patients received trastuzumab also. None of the patients received hormone therapy as all the patients were hormone receptor-negative.

## DISCUSSION

In the year 1977, Redolfi *et al.* first described medullary carcinoma of the breast (MdBc), which very rare type of tumor and accounts for 1–7% of all breast carcinoma [7]. In our study, of all diagnosed invasive carcinoma, only 1.5% of cases were MdBc, which corresponds to the reported literature [8]. MdBc is more common in African Americans than Japanese women and an extremely rare type of breast cancer in males (<0.5%). In our study, all MdBc patients were female [9-11]. Although MdBc can occur at age, in the reported literature, the mean age of diagnosis of IDC is around 60 years, the mean age of diagnosis of MdBc is 45–54 years, [12] and in our study mean age at the time of presentation of MdBc is



**Fig. 1: Photomicrograph (low power view): Sheets of large pleomorphic tumor cells diffusely spread in the stroma which is infiltrated by lymphocytes**



**Fig. 2: Photomicrograph (400×): Tumor cells having large nuclei and prominent nucleoli grow in a syncytial fashion and are sharply separated from the surrounding stroma. The frequent mitotic figure was also noted**

52.51 years with a range from 38 to 70 years. None of the patients in our study were below 35 years. BRACA 1 and BRACA two mutations have been associated with the development of breast carcinoma at a younger age.

In comparison to IDC, despite being triple-negative and having aggressive histological and cytological features, most MdBc has a good clinical outcome. In other words, MdBc is usually high grades in appearance but low grades in their behavior. A well-known prognostic and predictive factor was ER, PR, and HER2Neu receptor status (hormone receptor expression profile). In most reported literature, the majority of MdBc cases were triple-negative and lower incidence of hormone receptor expression [4,10]. In the present study, 17 (90%) patients were triple-negative, and only 2 (10%) patients were HER2 positive.

## Limitations

However, the major limitation of our study is that the results may not be a true representative of the entire Indian community as our study is a single institutional retrospective study and shows the analysis of the past 10 years only.

## CONCLUSIONS

Out of all invasive carcinoma, approximately 1.5% of cases were medullary carcinoma. The majority of the medullary breast carcinoma (MdBc)

patients presented with Stage II and III disease. About 90% of cases were triple-negative. Triple-negative breast cancer is usually associated with poor outcomes but MIBC despite being triple-negative, patients with MIBC have a good chance of long-term survival, that is, MIBC is usually high grades in appearance but low grades in their behavior.

#### ACKNOWLEDGMENT

The authors express their appreciation to Prof. Srikrishna Mandal, Head of the Radiotherapy Department for independent reviewing of our manuscript and DR. Nipamanjari Barman, Associate Professor, Dept. of Pathology, DH Medical College and Hospital, Diamodharbour for providing two photomicrographs.

#### AUTHOR'S CONTRIBUTION

All authors contributed equally to this article including data collection, writing, and reviewing the manuscript.

#### CONFLICT OF INTEREST

All authors declare no conflict of interest for the publication of this article.

#### AUTHORS FUNDING

None.

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