Medullary carcinoma experience in the Breast Oncology Unit of Hospital Juárez de México

ABSTRACT

Background: Medullary breast cancer is a rare type of cancer with a good prognosis. Determining the demographic characteristics of our population would allow us to know if the proposed treatments internationally are applicable in our hospital.

Methods: We performed a retrospective analysis by reviewing clinical files with a histopathological diagnosis of medullary breast cancer from February 1993 to February 2011. We found 41 patients who had been treated in the Oncology Unit of the institution.

Results: We report an incidence of 3.04%, originating in 11 Mexican states. Patients demonstrated a low to middle socioeconomic level in 39.02%. The average age at the time of diagnosis was 50 years. No family history was reported but some patients had a medical history for type 2 diabetes, hypertension and previous breast cancer; 63.41% were menopausal. The average clinical size of the tumor was 58 mm. In 63% of the cases, tumors were located in the left breast; 53.1% were clinical stages I and II, 46.3% were clinical stages III and in 9.6% of the cases primary tumor could not be assessed. Only 47% of the patients had positive axillary lymph nodes at diagnosis. Immunohistochemistry was only reported in 14/41 patients. According to the molecular classification of breast cancer, eight were triple negative, two luminal A, one luminal B and three were Her2neu.

Conclusions: The Mexican population presents epidemiological and clinical characteristics similar to those patients described in other international studies.

Key words: carcinoma, medullary, breast cancer, incidence.
INTRODUCTION

Medullary breast carcinoma (MBC) is uncommon and has a better prognosis than the more common forms of infiltrating ductal carcinoma.¹ ² According to Geschickter,³ Ewing referred to some carcinomas such as medullary and it was not until 1940 when this term was applied to a specific disease. Moore and Foote defined the lesion in a report published in 1949 and noted that during many years these patients were referred to at the Memorial Hospital as bulky carcinomas. According to the articles by Bloom⁴ and Wilson,⁵ specific histopathological criteria were proposed to determine the prognosis.

MBC represents 3% of the infiltrating ductal carcinoma variants except in women with mutation of the BRCA-1 gene for whom it is reported in 13% of the cases.⁶ ⁷ From the macroscopic point of view, it is a spherical, soft tumor with a friable surface, which seems to be encapsulated and is mistaken with benign tumors.⁸-¹⁰ Microscopically, the growth pattern is syncytial with large leaf-shaped cells and pleomorphic nuclei with marked lymphocytic infiltrate and well-encapsulated margins.⁸ ⁹

Although MBC has an anaplastic morphology, a higher nuclear grade correlated with aneuploidy of the DNA and elevated mitotic index in relationship with the elevated fraction of the S phase by flow cytometry. According to the world literature, it is reported as a separate entity with a better prognosis due in part to its immunophenotypic profile and investigations that report better clinical results when diagnosed in early clinical stages.⁹ ¹¹

In the Hospital Juárez de México (HJM), breast cancer represents the first cause of cancer, which is more frequent in women 41 to 65 years of age, with an annual growth rate of 9.4% in a 10-year follow-up (unpublished data). It is important to determine the epidemiological and clinical characteristics of our population to know if they are similar to those described in other countries, and if the proposed treatments internationally are applicable in our hospital center. With this as a goal, this study was conducted.

MATERIALS AND METHODS

We carried out a retrospective and descriptive study in the HJM. All pathology reports between February 1, 1993 and February 28, 2011 of patients with a diagnosis of breast cancer were reviewed. From a total of 1677 women, 51 were found with pathological confirmation of medullary carcinoma and who were admitted due to diagnosis of breast cancer during this period to the Oncology Service of the institution.

Of the 51 patients with MBC, ten were excluded because they were missing a medical record. At the final selection, only 41 patients were included in the study. The information was obtained from the clinical records and the pathology reports. From there the different study variables were obtained: origin, socioeconomic status, age, personal and family medical history, hormonal status, average clinical size of the tumor, clinical stage at the time of diagnosis, lymph node metastasis, histological grade, immunohistochemistry, survival and sites of metastasis.

RESULTS

Of 1677 women treated for breast cancer at the Oncology Department of the HJM during an 18-year period, 51 were found with a histological diagnosis of MBC according to the records from the Pathology Service, which represents an incidence of 3.28% (51/1677); however, there were ten cases excluded due to lack of a medical record. For representation of the final percentage, only 41 cases were counted, changing the global percentage to 2.4% (4100/1677).
Of the 41 patients studied, 11 were from 11 Mexican states; 34.15% were from the Federal District (DF) (Figure 1). The socioeconomic status was low/medium in 39.02% of the cases (Figure 2). The average age at the time of the diagnosis was 50 years (range: 30-80 years).

Only one patient had a family history of breast cancer. With respect to personal medical history, 21.9% reported having type 2 diabetes mellitus, systemic arterial hypertension, and breast cancer; one patient had a previous meningioma and colloid goiter (Figure 3). With respect to hormonal status, 63.41% were menopausal, 34.15% non-menopausal and in 2.44% the hormonal state was unknown (Figure 4). The average tumor size was 58 mm (range: 10-190 mm) (Figure 5). For tumor location, 51.2% of the cases were located in the upper outer quadrant, 63% in the left breast and 37% in the right breast.
In 47% of cases, there was histopathological confirmation of the surgical specimen obtained from the mastectomy. Immunohistochemistry was only reported in 14 patients and according to the molecular classification of breast cancer, eight were triple negative, two luminal A, one luminal B and three were Her2neu positive. There was metastasis reported in 17.1% of the patients and the site most affected was the lung (14.6% of the cases) followed by the central nervous system, liver and mediastinum.

There were 12.2% of the women studied who had a second primary tumor. Anatomic sites were three cases in the breast, and one each in the ovary, kidney and endometrium.

For clinical stages, 53.7% were reported in stages I and II and 46.3% in stage III. There were no cases in stage IV, and 9.6% were unable to be stratified according to the AJCC (Figure 6). Axillary lymph nodes were identified clinically in 60% of the cases. In only 47% of the cases was there histopathological confirmation of the surgical specimen obtained from the mastectomy.

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With respect to survival, the majority of the patients were lost to follow-up when found to be disease free. For this reason the 5-year survival rate was 39%. Of these women, 56% are alive and without tumor activity (up to the
time of the study) and 7% died as a result of tumor activity.

**DISCUSSION**

Geschickter described these lesions as neoplastic mammary carcinoma and concluded that “the grade of malignancy in this group of cancers is less than expected for its size and microscopic appearance.”

Moore and Foote defined the lesion and noted that these tumors had been referred to for years at the Memorial Hospital as “bulky carcinoma.” The 5-year survival of 52 patients with MBC was 82.7%, a result considerably better than the 50% obtained for patients with nonspecific infiltrating ductal carcinoma (CCI-NE). Axillary metastasis was present at the time of the mastectomy in 43% of the cases.

On performing a 5-year follow-up, Moore and Foote found that 11.5% of the patients died due to breast cancer and concluded that “the poor adjustment between the tumor and the host is responsible for a better survival in these patients.”

In 1956, Richardson reported MBC in 117 patients and arrived at the conclusion that Moore and Foote were correct with respect to their reports. Also, they proposed radical mastectomy as the ideal treatment for these patients and reported a 10-year survival rate of 64%. They also described that the survival of patients with axillary metastasis was better than patients without axillary metastasis (72 vs. 87%). They also reported that patients with tumors <1 inch had a better prognosis.

In the last 15 years there have been various publications questioning the conclusions of Moore and Foote and Richardson because the statistics obtained showed that patients with MBC did not have a better prognosis; however, on reviewing the study not all patients met the criteria for histologically defining MBC.

Schwartz reported 80 patients with well-circumscribed MBC and concluded that the 10-year survival in patients with negative axillary lymph nodes was >60%. The results of this study report that the incidence of MBC is 2.4%, a percentage similar to the international literature (3%). Of the 41 patients analyzed, the following were observed.

**Age and Hormonal Status**

In the majority of the populations reported, patients with MBC are menopausal at the time of diagnosis except in Japanese women, although there is no satisfactory explanation for this observation. We observed in our population that 63.41% of the patients were menopausal, perhaps because the average age in our study at the time of diagnosis was 50 years of age.

**Tumor Size and Survival**

Reports by Moore and Foote in 1949 focus on bulky tumors. However, in 1959 Foote noted that MBC tended to be smaller than those previously reported and the term of “bulky” could not be applied. In the study by Ridolfi et al., it was found that carcinomas <3 cm in diameter have a significantly better prognosis.

The results obtained in our study show that patients had an average tumor size of 58 mm, perhaps because 46.3% are found in advanced stages at the time of diagnosis. This was reflected in a poor 5-year survival reported at 39%; however, many of our patients are lost to follow-up when found to be free from manifestations, a circumstance that prevents determining a proper Kaplan-Meier curve.
**Immunohistochemistry**

These tumors share the CCI-NE markers that are almost always triple negatives. In our study only on 14 patients was an immunohistochemistry done and a triple negative pattern was observed in eight.

**Second Primaries**

According to Schwartz, 12.5% of the patients have contralateral breast cancer. Flores et al. described a metachromatic contralateral carcinoma in nine patients. Six were CCI-NE and three were MBC. In our study 12.2% had a second primary, 7.3% of these were contralateral breast cancer.

The most frequent non-breast neoplasms according to Ridolfi et al. are ovarian and there were 6/192 patients found. For our analysis we found only three non-breast neoplasms in 41 patients: one case of ovarian cancer; another case of endometrial cancer and one case of renal cancer.

**Recurrence**

According to Ridolfi et al., the initial recurrence occurred locally: in the thoracic wall, axilla or supraclavicular in 25% of the cases; in the other 75% it would be a distant recurrence. In our study only 17.1% of the cases had a recurrence; the most common site of metastasis was the lung in 14.6% of the cases followed by the central nervous system, liver and mediastinum.

There were local recurrences reported in our patients, perhaps due to the multimodal treatment provided to these patients consisting of chemotherapy, surgery and radiotherapy.

In conclusion, the Mexican female population has epidemiological and clinical characteristics similar to patients described in other international studies. We consider that the treatments described in these populations are applicable to Mexican patients.

**REFERENCES**


