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Medullary Carcinoma of the Breast: About A Case

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ABSTRACT

Breast Medullary carcinoma, is a histologic form with inflammatory stroma requiring strict histological criteria for its definition. It represents less than 5% of breast tumors. The aim of this work is to analyze the epidemiological, clinical, evolutive characteristics and therapeutic results, through a retrospective study of medullary breast carcinoma histologically confirmed and treated in Aile 8, department of the university hospital of Casablanca.

Keywords

Breast, Carcinoma, Medullary, Surgery, Radiotherapy, Chemotherapy, Hormonotherapy.

Introduction

It is about a 67 years old patient, single, nulligest, menopaused since 9 years without particular pathological antecedent, whose history of disease goes back to 4 months by the autopalpation of a left mammary nodule, without inflammatory sign nor nipple discharge the whole evolving in a state of conservation of the general state.

The clinical examination revealed asymmetrically sized breasts, with a mass in the upper quadrants of the left breast measuring 6x5 cm, without any mammary discharge or inflammatory signs, and the rest of the clinical examination was normal.

Mammography found breasts with type B density, with opaque lesion in the upper left quadrant without any other abnormality (Figure 1). Ultrasound showed a hypoechoic tissue lesion in the left upper quadrants, containing microcalcifications, vascularized by color Doppler, measuring 61 x 48 mm in diameter, with bilobed contours and bilateral axillary lymph nodes of preserved architecture (Figure 2). This paraclinical examination was classified as BIRADS 4 by the ACR on the left.

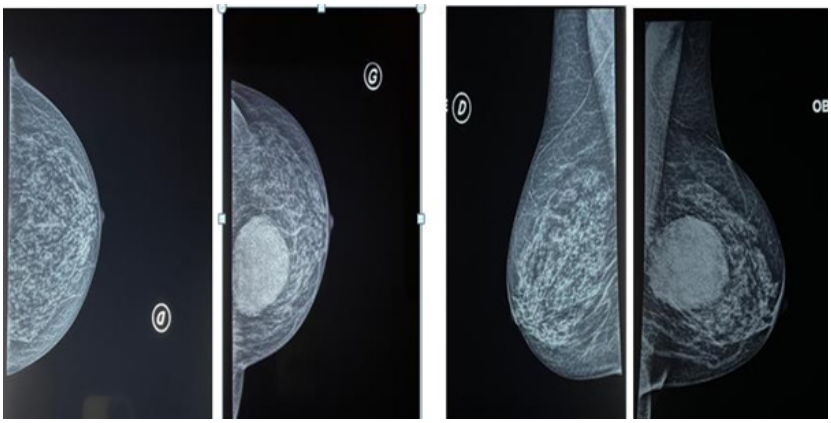

Figure 1: Well-limited dense opacity on mammography [(A) - front view; (B) - side view].

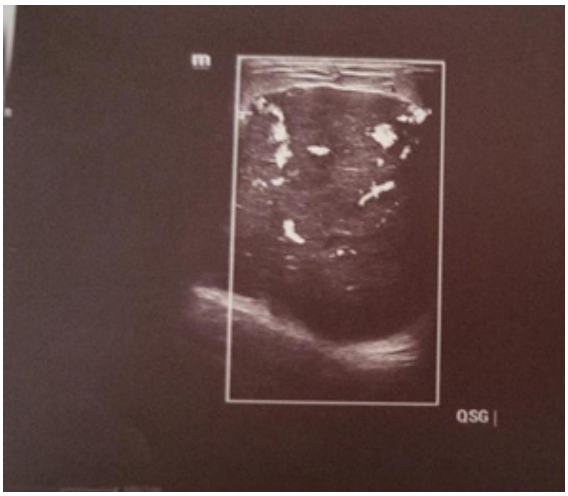

Figure 2: Hypoechoic tissue lesion containing microcalcifications, vascularized on color Doppler.

A trucut biopsy was performed confirming the presence of an invasive breast carcinoma of nonspecific type NOS grade SBR II, without in situ component or peri-tumoral vascular emboli with an immunohistochemistry study in favor of a Luminal A.

The patient had undergone a left mastectomy with a homolateral axillary curage.

The final pathological study showed an invasive breast carcinoma with a medullary aspect of grade SBR II, measuring 6 cm long axis and remaining within 1 mm of the deep border, o.7 cm from the upper limit, a healthy nipple, no in situ component, no peri-tumoral vascular emboli and no lymph node metastasis: 0N+/10N and on the immunohitochemical study, a Luminal A molecular profile with ER at 90%, RP: 90%, Ki67 at 15%, and negative HER 2. The patient was referred to the oncology department for further adjuvant management.

Discussion

Medullary carcinoma represents 5 to 7% of breast carcinomas. It was described in 1949 by Moore and Foote as a particular variety of infiltrating ductal carcinoma, but it was after 1977 that Ridolfi asserted the specificity of the typical medullary carcinoma, as an anatomoclinical entity with a favorable prognosis compared to the breast malignancies [1].

Medullary carcinoma is characterized by its particular clinical aspect, which deserves to be clarified as it is often misleading and suggestive of benignity. It is a well limited tumor, histologically constituted of poorly differentiated cells without associated glandular edification in a sparse stroma with an important lymphoplasmacytic infiltrate [2].

Histologically, medullary carcinomas of the breast are classified into two groups: typical medullary carcinomas defined by the five Ridolfi histological criteria and atypical medullary carcinomas [1-4].

Typical medullary carcinoma requires all of the following criteria:

- Predominantly syncytial growth (>75%).
- Tumor margin completely circumscribed on microscopy.
- Absence of intracanal component.
- Moderate to large diffuse mononuclear stromal infiltrate.
- Grade 1 or 2 nuclear abnormalities.
- Absence of microglandular character.

Atypical medullary carcinoma requires 2 to 3 typical criteria, including predominantly syncytial growth; combined with one of the following atypical criteria:

- Tumor margins showing localized or predominant infiltration.
- Ductal component present or predominant.
- Weak or negligible mononuclear stromal infiltrate.
- Grade 3 nuclear abnormalities.
- Presence of microglandular character.

Medullary carcinoma can occur at any age, but it is usually seen in relatively young women compared to invasive carcinomas [5]. According to a study at the Oncology Center of Marrakech about 53 patients admitted to the service in 2014, it reports an average age of 53 years with extremes ranging from 30 years to 58 years. This phenomenon is probably explained by an increasingly short time between the onset of symptoms and the first consultation [3].

The frequency of medullary carcinoma in families is similar to other histologic of breast cancer subtypes.
According to Erdeich and Claus's research on the relationship between histological subtypes of breast cancer and the incidence of a family history, there is no specificity for medullary cancer [3].

However, Burki and al found a high frequency of family history of malignancies excluding breast cancer related to medullary carcinoma, in particular stomach cancer, uterine cancer and malignant melanoma [3]. Ridolfi demonstrated a relationship between medullary breast cancer and family history in 14% of cases [1,4].

Medullary breast carcinoma is associated with family history of breast cancer because of the presence of susceptibility genes in patients with medullary carcinoma. Multiple studies have demonstrated a higher incidence of BRCA 1 and 2 mutations in this histologic subtype of breast cancer compared to other subtypes.

BRCA1 mutations have also been directly correlated with p53 positivity and low or negative hormone receptor (ER/PR) levels [7,8,10].

These findings provide valuable information about the origin and inheritance of this type of tumor. According to the World Health Organization, it is a well-limited carcinoma composed of poorly differentiated cells in a sparse stroma with intense lymphoid infiltration. The tumor cells are large, with vesicular nuclei, large nucleoli and unclear cytoplasmic boundaries. Histological diagnosis by microscopy requires the five rigorous criteria (Ridolfii) [4].

Most authors agree that the tumor is often discovered by the patient herself in the presence of a breast nodule Clinically, medullary carcinoma usually appears as a unilateral mass, often located in the upper quadrants, especially in the superior-external quadrant, rounded, well limited, and mobile, suggesting a benign formation. Radiologically, medullary carcinoma of the breast is characterized by its misleading benign appearance, evoking in particular an adenofibroma or a benign phyllodes tumor. It presents as a well circumscribed opacity, rarely with a stellate appearance, thanks in particular to a careful examination which often detects fine irregularities of contour. Most often, medullary carcinoma is a solid, hypoechoic nodular development with regular boundaries and posterior enhancement in 64% of cases [6].

In medullary breast cancer, magnetic resonance imaging is not particularly effective and is indicated when the tumor cannot be easily examined by routine imaging and in cases of suspected multifocality or multicentricity that would challenge a conservative treatment option. Homolateral axillary lymph node progression is a component of locoregional disease. Other methods for determining lymph node status include the sentinel node technique, CT, and mammography scans, which have acceptable sensitivity but are less commonly used. Only after the likelihood of visceral metastases has been assessed is the visceral metastatic extension workup undertaken.
It includes:

- A chest X-ray, which allows the diagnosis of pleuropulmonary metastases; if it is not conclusive, it can be completed by a CT scan, which is more efficient for the detection of early lesions.
- An ultrasound of the liver to detect secondary hepatic lesions.
- A bone scan to detect metastatic bone disease.
- A tumor marker: CA 15-3 indicates a more aggressive tumor, with higher levels in medullary tumors than in ductal breast carcinomas.

In terms of immunohistochemistry, medullary cancers are in the majority of cases triple negatives [11]. According to the majority of authors, the treatment of medullary breast carcinoma is similar to that of invasive carcinomas based on conservative treatment and radiotherapy as locoregional treatments, hormonal therapy and chemotherapy as systemic treatments being indicated in the forms of poor prognosis.

Surgery for medullary breast cancer can consist of either conservative treatment or radical surgery if conservative surgery is not indicated.

In case of conservative surgery, axillary lymph node dissection should always be performed. In case of absence of adenopathy clinically and small tumor, the sentinel lymph node technique should be performed. Adjuvant chemotherapy has gained interest in the treatment of breast cancer. The benefits have been enhanced by the use of more effective agents such as anthracyclines and, more recently, taxanes, which are now the 2 most important drug families in the treatment of breast cancer. In contrast, the rationale for chemotherapy in medullary breast cancer is questionable because it has no effect on survival and the risk of relapse. Targeted therapy: Trastuzumab (Herceptin®) is a recombinant humanized Ig G1 monoclonal antibody with cytostatic characteristics, directed against the HER-2 transmembrane receptor, used in cases of HER2 expression. Hormonal treatment is given in all cases where hormone receptors are positive on the tumor. The typical treatment for postmenopausal women is tamoxifen (20 mg/d), which is given for up to 5 years. As well as anti-aromases are given to menopausal women. Radiation therapy is recommended to reinforce the localized control offered by surgery.

The medullary carcinoma is characterized by a better survival rate than other breast carcinomas, this is demonstrated in most studies, and more specifically for the typical form. The good prognosis of medullary breast cancer is due to the almost constant presence of the lymphoplasmacytic infiltrate (T+ lymphocytes and inflammatory plasma cells), which plays an early role in both the cellular and humoral immune response, as well as the extensive role of the apoptic process, which allows the slowing of local and metastatic development [5,9].

The occurrence of distant metastasis is more frequent in atypical medullary carcinoma. According to Martinez and al. the 10-year survival rate for medullary carcinoma compared to invasive ductal carcinoma is up to 84%. The metastatic sites are identical to the rest of the carcinomas, dominated by bone, lung, liver, brain.

Conclusion

Medullary carcinoma is a tumor that is distinguished by particular epidemiological, clinical and radiological characteristics and often aggressive anatomo-pathological contrasting with its favorable evolution.

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