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Metaplastic carcinoma of the breast with mesenchymal differentiation: a rare case report and literature review

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ABSTRACT

Metaplastic breast carcinoma with mesenchymal differentiation (MCMD), formerly known as carcinosarcoma, is a very rare and aggressive tumor that has recently been classified as a subtype of metaplastic breast carcinoma. It accounts for 0.08%–0.2% of all breast cancers, with only a few cases reported in the literature. Here we report a case of a 56-year-old woman with a large, hard lump in her right breast, with no history of breast cancer in first degree relatives. Symptoms were present 6 months before presentation. After hospitalization and following physical evaluation, USG, mammography, biopsy and immunohistochemistry, the diagnosis of metaplastic carcinoma with mesenchymal differentiation was established. Two of 11 axillary lymph nodes were positive for metastases. The optimal treatment modality for metaplastic carcinoma is not yet established due to its rarity and heterogeneity. Modified radical mastectomy is the preferred surgical procedure because a large tumor size is a contraindication for breast conserving surgery. In conclusion, a patient with such an enlargement of the breast mass must be carefully evaluated, for the correct diagnosis of a possible metaplastic carcinoma.

Category: Case Presentation

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Introduction

Metaplastic breast carcinoma with mesenchymal differentiation (MCMD), formerly classified as carcinosarcoma, is a very rare and aggressive tumor. Recently, this type of tumor has been classified as a subtype of metaplastic breast carcinoma. It represents about 0.08%-0.2% of all breast cancers (depending on the study), being therefore only a few cases reported in the literature [1].

Histologically, metaplastic breast carcinoma with mesenchymal differentiation is characterized by a biphasic pattern of epithelial and malignant sarcomatous cellular components, with no clear evidence of transitional zones between these two cellular elements. It is described in this article such a rare case of metaplastic breast carcinoma with mesenchymal differentiation, in a 56-year-old woman presented to our clinic for diagnosis and treatment [1,2].

Case Presentation

We report a case of a 56-year-old woman presented to the OPD with a hard lump in her right breast. She has no history of breast cancer in her first-degree relatives. In the last 6 months, she had a painful lump in her right breast, which grew gradually, but without being investigated and treated.

The initial physical examination in the OPD revealed a hard nodule of about 8X8 cm, tenderness over the present mobile nodule, not fixed to the chest wall. She had no palpable ipsilateral and contralateral axillary and supraclavicular lymph nodes at presentation.

The ultrasound described it as a large hypoechoic lesion with an irregular border, measuring 6.5 X 5.6 cm, involving all quadrants of the breast and with increased blood flow on color doppler (BIRADS-4). No enlarged lymph nodes were detected on this USG.

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On mammography, a hypodense lesion measuring 6 X 6.5 cm with a spiculated border was detected with a BIRADS score of 4.

Trucut biopsy from the lump revealed predominantly atypical cells present in groups, as well as scattered slightly admixed with numerous stromal fragments. These atypical cells were round to oval and spindle-shaped, with centrally to eccentrically placed nuclei, with large and variable amounts of nucleoli and cytoplasm, being bipolar that is vacuolated in some places or with eosinophilic granules in other areas. It was classified as malignancy, with the possibility of being metaplastic carcinoma. MRM was planned in view of metaplastic carcinoma and specimen done and sent for HPE. The procedure was performed by the operator and his team, the postoperative period being without notable uneventful.

Histopathology report of specimen showed on glossy examination that it was a right sided mastectomy specimen, measuring 22X15X4 cm in size and with an attached skin flap of 18X7 cm. Microscopical examination revealed metaplastic carcinoma with mesenchymal differentiation. From 11 lymph nodes isolated, 2 presented tumor infiltration. IHC analysis showed a strong and diffuse positive reaction for vimentin and cytokeratin (CK), but negative for BCL-2 and CD -34.

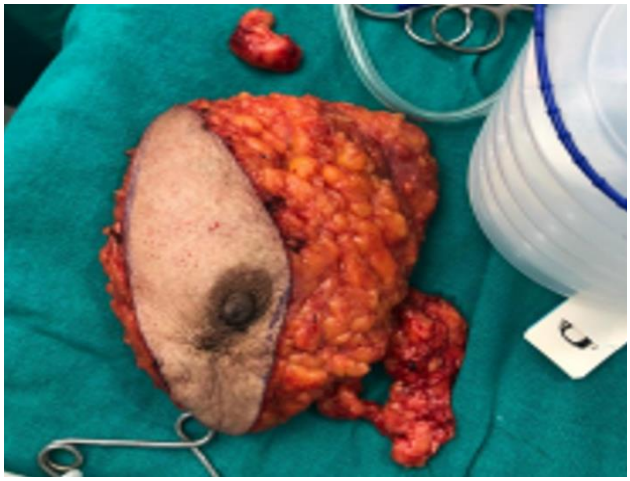

Figure 1. Excised right breast lump following MRM

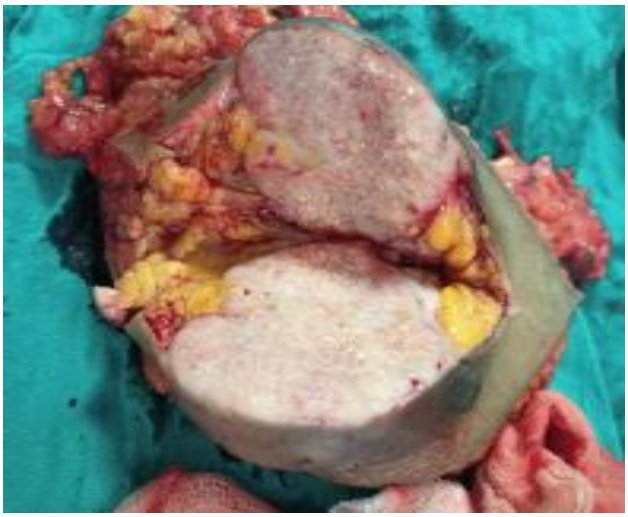

Figure 2. Cut section of breast lump following MRM

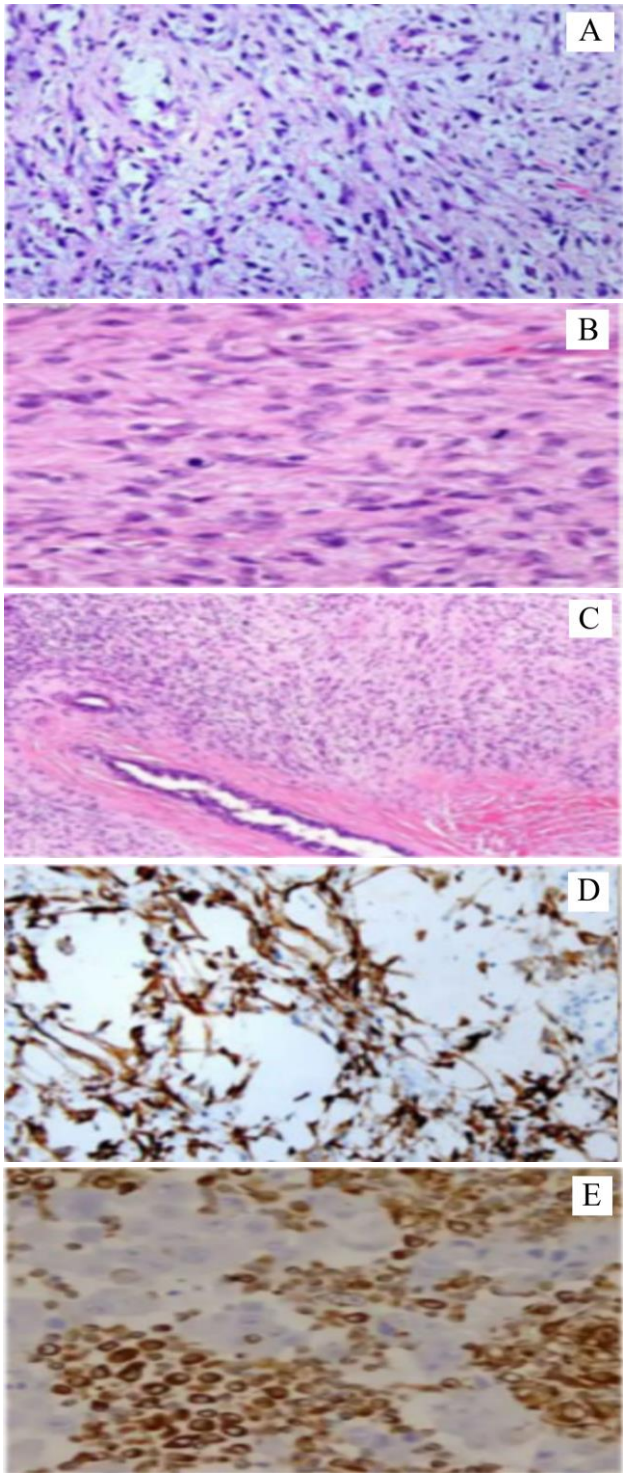

Figure 3. **A** - Atypical cells, OVOID to spindle in safe, arranged in sheets and showing marked cytologic mitotic atypia. **B** and **C** - Atypical cells are infiltrating the ducts and lobules of breast. **D** - Section examined showing that cytokeratin (CK-5) is positive in epithelial cells. **E** - Section examined showing vimentin is positive in mesenchymal cells

Carcinosarcoma is an extremely rare neoplasm that occasionally occurs in organs such as the ovary or uterus. The neoplasm is characterized by a biphasic pattern (carcinomatous and mesenchymal), without a transition zone being present between them [3,4].

The WHO classification of breast tumors, 4th edition classifies metaplastic tumors into metaplastic carcinoma of no special type, low-grade adenosquamous carcinoma, fibromatosis- like metaplastic carcinoma, squamous cell carcinoma, spindle cell carcinoma, metaplastic carcinoma with mesenchymal (chondroid, osseous) differentiation, other types of mesenchymal differentiation (mixed), myoepithelial carcinoma. Metaplastic carcinomas may be either low-grade tumor (e.g. adenosquamous carcinoma or spindle cell carcinoma), or high-grade tumors (e.g. squamous cell carcinoma, or spindle cell carcinoma) [5,6]. Its presentation is similar to other types of breast cancer clinically as well as radiologically. Carter et al. shows an age of presentation of the tumor in the range from 40 to 96 years, with an average of 68 years, while Luini reported that the age varies between 22 and 91 years [7,8]. Tumor size ranged from 1.5 to 15 cm, with a median of 4 cm in a series of 29 cases [7]. The reported incidence of axillary lymph node metastases at diagnosis has ranged from 5% to 56% [9,10]. The most common sites of distant metastasis are the lungs and bones [7]. These variations in lymph node metastasis may be due to the expansion of the epithelial component and the differentiation between different cell types in the primary tumor. In primary breast sarcoma, lymph node metastasis seems to be less common [11,12].

Immunohistochemistry (IHC)

IHC plays a crucial role in establishing the accurate diagnosis of metaplastic carcinoma. It usually stains positive for vimentin and cytokeratin, and negative for ER/PR, HER2/Neu, as similarly observed in the presented study [9,12].

Treatment Modality

The optimal method of treatment for metaplastic carcinoma is not yet precisely established, due to the rarity and heterogeneity of this type of cancer [13-15]. Modified radical mastectomy is usually the preferred surgical procedure because the large size of the tumor is an important contraindication for breast conserving surgery. Carcinosarcomas are poorly differentiated aggressive neoplasms that often tend to be triple negative (ER, PR, and HER-2/neu). Adjuvant chemoradiotherapy is usually required, for locoregional control as much as possible. Hormone therapy is ineffective because these tumors are usually triple negative, as discussed above. Anthracycline-based chemotherapy appears to be more effective than cyclophosphamide, methotrexate and fluorouracil regimens [16-19]. Adjuvant radiotherapy has been shown to reduce the risk of death by up to 33% in mastectomy patients [20]. Overexpression of Her1/epidermal growth factor receptor (EGFR) suggests that several agents like gefitinib and cetuximab, which target the EGFR, may play an important role in the therapeutic approach of metaplastic carcinoma [21-23].

Five years survival

The reported cumulative 5-year survival rate for carcinosarcoma is 49% [24-26]. Metaplastic carcinomas have a worse free-disease interval and overall survival rate when compared with adenocarcinoma [27-29].

Prognostic factors for survival

In a study by Chao et al. it was concluded that duration of symptoms, TNM stage, tumor size and axillary node status were significant prognostic factors for survival [30]. Disease-free survival and overall survival are lower in metaplastic carcinoma compared with invasive ductal carcinoma of the breast and other forms of triple-negative breast cancer [31,32].

Conclusions

Current scientific knowledge about MBC is relatively limited. The rarity and heterogeneity of MBC in terms of biological and morphological features, as well as the different classification and treatment strategies in the literature have limited attempts to obtain satisfactory data and evidence to establish a sound treatment strategy in this unusual breast neoplasm. Although the promising results obtained in small and selected groups of patients (who were treated personalized according to the characteristics of cancer stem cells) are encouraging, more studies should be done in larger groups to find potential molecular targets and test the effectiveness of the approach by targeted therapy.

Contributions

Davinder Kumar: designed and wrote the paper. Anil Kumar: designed/ wrote the paper and collected the data. Gajendra Dandotiya: designed and wrote the paper. Ashish Kumar Yadav: designed and wrote the paper. Ritu Bhukal: performed and interpreted the pathological data of the study.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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