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FCO • 13(1) • 2022 •48–52
DOI: 10.2478/fco-2022-0006

Forum of Clinical **Oncology**

A Rare Case of Primary Carcinosarcoma of the Breast

Case report

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Received 14 July 2022; Accepted 22 December 2023

Abstract: Breast carcinosarcoma is a rare malignancy accounting for approximately 0.08-0.2% of all breast tumours. It is a type of metaplastic mammary carcinoma displaying biphasic differentiation with epithelial and mesenchymal cellular characteristics with probable derivation from myoepithelial cells.

A 65-year-old woman presented to our hospital with a two-month history of a rapidly growing mass in her left breast. Neither her medical nor family history was positive for malignancies. Subsequently, she underwent a fine needle aspiration, which was positive for adenocarcinoma, followed by a lumpectomy with axillary lymph node dissection. The histology revealed an undifferentiated neoplasm and the immunohistochemical cell staining was positive for pan-cytokeratin, SMA, Vimentin, and S-100, suggesting the diagnosis of breast carcinosarcoma with a triple-negative immunophenotype. There was no evidence of metastasis except for a positive lymph node, indicating a stage IIIA disease. Thus, she received adjuvant chemo-radiotherapy. However, 16 months later, she presented with metastatic disease, and unfortunately, she died 4 months later due to a systemic infection.

Aggressive behavior, higher staging, chemoresistance, and higher proportion of triple negative breast cancer seem to be the main characteristics of breast carcinosarcoma, which is recognised as a separate entity from common invasive ductal carcinoma, with significantly worse clinical outcomes.

Keywords: *breast cancer • carcinosarcoma • triple-negative • biphasic differentiation • rare histology • poor prognosis*

1. Introduction

Breast cancer is a heterogeneous disease regarding its histological types. Invasive breast carcinoma is the most prevalent type, accounting for about 80%[1]. Metaplastic breast carcinoma (MBC) is categorised in several different subtypes with various clinical behaviors. Carcinosarcoma (CS) of the breast should be carefully differentiated from other subtypes of MBC. Its reported incidence is 0.08-0.2% of all breast malignancies[2-4]. Despite its rarity, it is a very aggressive tumour, related with reduced overall survival and disease-free survival[5]. The strict definition of this mixed tumour requires the presence of biphasic differentiation with epithelial and mesenchymal cellular characteristics with probable derivation from myoepithelial cells[6].

Herein, we present an interesting case of breast carcinosarcoma in a 65-year-old woman. This rare case poses an interesting diagnostic challenge, which merits presentation.

2. Case report

A 65-year-old woman was admitted to our hospital for the investigation of a left breast mass, which grew rapidly within two months. According to her past medical history, she was diagnosed with metabolic syndrome and her family history was free of malignancies.

Upon physical examination, a firm mass of 5 cm in greatest dimension was palpable in the upper-outer quadrant of the left breast but there was no palpable

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axillary lymphadenopathy. The mammography showed a high-density mass with marginal irregularity and pleomorphic calcifications in close contact with the thoracic wall. The ultrasonography revealed a solid hypoechoic mass of 36.4 mm x 27.5 mm displaying irregular boundaries. Subsequently, she underwent a fine needle aspiration, which was positive for adenocarcinoma, followed by a lumpectomy and axillary lymph node dissection. The pathology report revealed a tumour consisting of an epithelial and a sarcomatoid component measuring 7x7 cm. Tumour cells displayed high-grade cellular atypia and mitotic count was high (Figures 1-3). Immunohistochemical staining was positive for pan-cytokeratin (in both components), SMA, Vimentin and S-100. One out of 11 axillary lymph nodes was positive for metastatic infiltration and both the hormone receptors, and the HER2 analysis was negative, indicating a triple negative subtype. These findings confirmed the diagnosis of the breast carcinosarcoma. After an extensive work-up, the pathological TNM staging was pT3N1M0 (stage IIIA). The patient completed adjuvant chemotherapy with doxorubicin, cyclophosphamide and weekly paclitaxel, followed by adjuvant radiotherapy. 16 months later, she presented with metastatic foci in both lungs and sternum. She received first-line treatment with chemotherapy and radiotherapy to her sternum with partial response. Unfortunately, she died 4 months later due to a systemic infection.

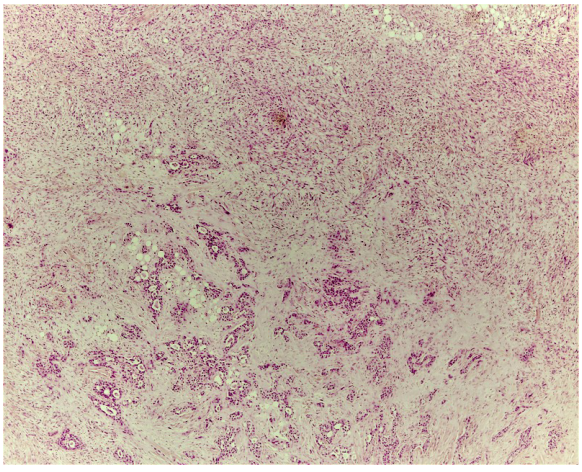


Figure 1: On low power examination the tumor shows a biphasic pattern consisting of epithelial and sarcomatoid elements (Fig. 1, H&E x 4).

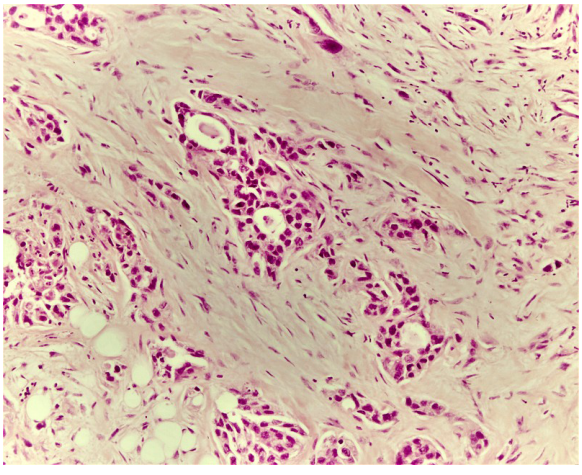


Figure 2: On higher power examination the epithelial component displays high-grade atypia (Fig. 2, H&E x 20).

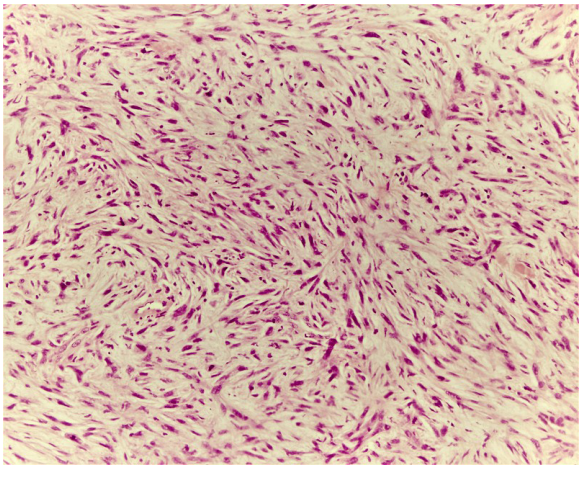


Figure 3: On higher power examination the sarcomatoid component consists of a proliferation of high-grade pleomorphic spindle cells (Fig. 3, H&E x 20).

3. Discussion

MBC is a rare malignancy, representing 0.25–1% of all annually diagnosed breast cancers[8]. WHO classifies this heterogeneous group of neoplasms into several different subtypes[9]. Histologically, MBC diagnosis requires the presence of an epithelial element (usually invasive breast carcinoma NST) admixed with epithelial (squamous), or sarcomatoid (spindle cell or heterologous mesenchymal) elements. In rare cases, even after extensive sampling, an epithelial element is not found. Breast carcinosarcoma is a rare, aggressive neoplasm that has been reported to account for 0.08-0.2% of all breast malignancies[2-4]. These may also be encountered in various organs, including mostly the female genital tract, but also the lungs, prostate, and urinary bladder[10].

The origin of these tumours is still being debated; one controversial idea is that a proliferation of myoepithelial cells develop into this tumour[11]. The histologic and cytologic features of the stromal component are compatible with sarcoma, while the immunohistochemical

staining suggests a cell type possessing both epithelial and mesenchymal characteristics. Therefore, the possibility of the tumour being derived from a cell with potential biphasic differentiation, such as myoepithelial cells, was considered. On the other hand, several reported cases of carcinosarcoma were suggested to arise from pre-existing fibroadenomas or phyllodes tumours[7, 11]. In fact, neither fibroadenoma nor phyllodes tumour was detected in the post-operative material.

The clinical features of breast carcinosarcoma are similar to those of patients with invasive carcinoma NST[12]. SC often presents as a large, rapidly growing lump in the breast that is possibly painful and shows no preference for any particular age group[13]. It shows complex echogenicity during ultrasonography, which may be related to necrosis and cystic degeneration[14]. Regarding the metastasizing routes, carcinosarcoma of the breast metastasizes via lymphatics and the bloodstream. Some of them metastasize as mixed epithelial and mesenchymal tumours, while in others, only the epithelial or the sarcomatous component may metastasize[9]. Pleural and pulmonary metastases are more common than skeletal, liver or brain ones[15]. Aside from distant metastases, local recurrence can also occur, even extremely rapidly, as the primary tumour is very aggressive[12].

Microscopically, these tumours appear to be mostly poorly differentiated, displaying areas of epithelial and spindle cells with high cellularity, high-grade atypia, and several mitotic figures[12]. Thus, the differential diagnosis of breast SCC includes other pathologically similar uncommon breast neoplasms such as metaplastic matrix-producing carcinoma[16], primary breast sarcoma (mainly undifferentiated pleomorphic sarcoma), sarcoma metastasis to the breast, phyllodes tumour, and adenomyoepithelioma[17]. By definition, metaplastic matrix-producing carcinoma lacks a spindle cell element[16]. Primary breast sarcoma should lack either morphological or immunohistochemical evidence of epithelial differentiation[18]. Sarcoma metastasis to the breast can be suspected in cases with history of sarcoma in another anatomical location. Phyllodes show characteristic histological findings (cellular stroma, leaf-like growth pattern and benign epithelial elements) and immunohistochemical findings (lack of reactivity to cytokeratins). Adenomyoepithelioma shows a biphasic pattern with bland epithelial and stromal elements[19]. In difficult cases, immunohistochemistry seems to be the gold standard analysis in the investigation of carcinosarcoma[14]. Regarding the sarcomatoid component, in 55% of cases it is immunoreactive for cytokeratins, and in 98% it is immunoreactive for vimentin[6]. Moreover, carcinosarcomas such as all MBCs show negativity in expressing the estrogen and progesterone receptors[8]. They also do not over-express the HER-2/neu oncogene[20]. Due to this 'triple-negative' phenotype, such tumours tend to be more aggressive[12, 14]. By contrast, the epidermal growth factor receptor HER-1/EGFR protein is usually expressed and may serve as a potential target for EGFR inhibitors.

Regarding survival, breast SCC has the lowest overall survival and disease-free survival rates among all the other types of MBC[2], with its cumulative survival rate accounting to 49%, while the survival rates of SCC and matrix-producing carcinoma are 64% and 68% respectively. The prognostic factors defined in the literature are age at diagnosis (more commonly seen in postmenopausal women, mean age around 58.5 years), tumour size (worst in women with masses bigger than 4 cm), tumour grade, TNM stage, axillary nodal status, hormone receptor status, type of primary surgery, and use of RT[20, 21]. Therefore, the importance of early diagnosis and proper treatment is obvious.

In general, the treatment strategy follows the established guidelines for treatment of patients with invasive breast cancer, although there is no specific established treatment modality[6]. In the majority of the cases reported, mastectomy with or without axillary dissection was performed, accompanied by post-operative chemotherapy and radiation therapy[6, 7, 15]. Neoadjuant chemotherapy is not a well-established option because it is less effective compared to the the conventional adenocarcinoma[22]. It seems that conventional chemotherapy is generally not beneficial (although most patients receive it), due to complex genetic and non-genetic mechanisms producing phenotype-diverse subclones and intratumoural heterogeneity, leading to chemoresistance[23-26]. On the other hand, hormonal therapy also seems ineffective, since breast carcinosarcoma does not express hormone receptors and shows lower HER2/neu overexpression[27]. For the local recurrences, surgical excision is the better therapeutic choice. In the future, tailored therapy options, such as tyrosine kinase inhibitors or anti-epidermal growth factor receptor monoclonal antibodies (i.e. gefitinib and cetuximab), may also be available[28]. Even after surgical resection and radiation therapy, careful follow-up is needed because recurrence can be rapid.

4. Conclusion

In conclusion, we report a rare case of breast carcinosarcoma. This is a malignant tumour with poor prognosis even if treated properly. Obtaining an early and accurate diagnosis of breast carcinosarcoma is

necessary to optimally tailor adjuvant therapy towards this aggressive cancer subtype. Of course, further research is required, because by improving our understanding of this tumour, we may provide patients with novel, effective treatment options that will ultimately be translated into improved overall outcomes.

Author contributions

All authors equally contributed to this paper with conception and design of the study, literature review and analysis, drafting and critical revision and editing, and final approval of the final version.

Conflict-of-interest statement

No potential conflicts of interest. No financial support.

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