Carcinosarcoma of Breast: A Rare tumor with Triple Positive Phenotype

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ABSTRACT

Primary sarcomas of the breast are rare and constitute 0.6% to 1.2% of the total number of malignant tumors of the breast. Clinically, these are aggressive tumors and majority of them do not express the estrogen and progesterone receptors and do not over express the Her2/neu oncogene. A 35 years female presented with a mass in her right breast. Physical examination and radiological findings were consistent with malignancy. Patient underwent surgery and modified radical mastectomy was performed. Histological examination revealed carcinosarcoma of the breast. On immunohistochemistry, tumor cells were positive for hormone receptors Estrogen Receptor (ER), Progesteron Receptor (PR) and Her2/neu gene, which is a rare entity. The patient is on chemotherapy and hormonal therapy and is under follow up. There was no axillary lymph node involvement or distant metastasis. The present case merits presentation because of its rarity.

Key Words: Carcinosarcoma, Estrogen Receptor (ER), Progesteron Receptor (PR), Her2/neu.

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INTRODUCTION: Carcinosarcoma of the breast also known as metaplastic carcinoma, metaplastic sarcomatoid carcinoma or sarcomatoid carcinoma is a rare and aggressive neoplasm,[2] with very few cases reported in the literature.[3] Its incidence is reported as 0.1% of all breast cancers and shows no predilection for any particular age group.[1] Clinically, features are similar to those patients with invasive ductal carcinoma.[2] These tumors usually present with triple negative phenotype that include negativity for estrogen, progesterone receptors and Her2/neu oncogene.[1] Here we report a case of carcinosarcoma of breast in a 35 years old female with triple positivity

for hormone receptors ER,PR and Her2/neu gene, which is very rare.

CASE REPORT: A 35 years old premenopausal female presented with lump in right breast which grew rapidly in 4 months. Physical examination showed a firm mass 7 cm in greatest dimension in upper outer quadrant of right breast with no enlarged lymph nodes in axillary region. Left breast and systemic examination were unremarkable. Ultrasonography revealed solid hypoechoic mass of 6.5 cm in greatest dimension with irregular boundaries. On mammography a dense lesion with irregular boundaries was seen. Patient underwent modified radical mastectomy (MRM) of right breast. On gross examination, MRM specimen measuring 19x15x8 cm showed a well defined mass of size 7x5.5x5cm on serial sectioning. Tumor appeared to be extending up to overlying skin and involving base. Two lymphnodes were identified. Sections from tumour tissue showed a well encapsulated tumour comprising of oval to spindle shaped cells in groups and fascicles with mild to moderate pleomorphism with areas of hemorrhage, necrosis and myxoid degeneration. Few mitotic figures were also seen. Few atypical glandular structures were also seen embedded in between the spindle cells. Compressed normal breast tissue were identified at the periphery. Nipple and areola were unremarkable. Lymph nodes identified were free from tumor involvement. Immunohistochemistry revealed cytokeratin (CK), ER, PR, Her2/neu positivity in glandular structures and Vimentin positivity in spindle cells. Final diagnosis of metaplastic carcinoma or carcinosarcoma was made.

DISCUSSION: Metaplastic carcinomas of the breast are a heterogenous group of neoplasms that includes carcinosarcoma, matrix producing carcinoma, spindle cell carcinoma, squamous cell carcinoma of ductal originand metaplastic carcinoma with osteoclastic giant cells.[6] Carcinosarcoma of the breast is a distinct form of metaplastic carcinoma, being most aggressive of all subtypes.[5] They have been observed in various organs throughout the body, including the ovary and uterus.[2] The unifying feature of these tumors is the presence of an epithelial or mesenchymal cell population admixed with adenocarcinoma.[6] the origin of these tumors is still being debated, and is probably derived from myoepithelial cells. [4] These tumors are poorly differentiated, high grade, highly cellular with mitotically active

pleomorphic spindle cells.[2] they tend to recur locally as neoplastic cells often extend within the perivascular tissues beyond the capsule of the tumor.[4]

Most metaplastic tumors of the breast have clinical features are similar to those patients with invasive ductal carcinoma.[1] Clinical findings often reveal swelling in the breast or a palpable mass. Rarely, nipple discharge, nipple retraction or skin ulceration may also be present.[3] Metaplastic breast carcinomas are usually associated with a lower incidence of axillary node involvement than would be expected for typical breast adenocarcinoma of similar size.[6]

Histopathologically, carcinosarcomas are biphasic neoplasms with at least 50% of tumor composed of a cellular malignant appearing spindle cell component consisting of pleomorphic bipolar cells or a polymorphous cell population, with nuclear atypia and high mitotic activity and an *in situ* or ductal, squamous, or mixed infiltrating carcinoma which is contiguous or admixed with the sarcomatous component.[5] Differential diagnosis may include fibrosarcoma, osteosarcoma, malignant fibrous histiocytoma, and carcinoma arising in cystosarcoma phylloides.[5] Also, carcinosarcoma should be distinguished from other forms of metaplastic carcinoma such as spindle cell carcinoma.[5]

Immunohistochemistry is the gold standard investigation in the diagnosis of carcinosarcomas[1]Epidermal growth factor receptor (EGFR) protein is expressed in most cases and may serve as potential therapeutic target for EGFR inhibitors such as gefitinib and cetuximab.[1] Typically, metaplastic carcinomas of the breast do not express the estrogen and progesterone receptors and donot overexpress the Her2/neu oncogene, however our case showed triple positivity for hormone receptors and Her2/neu, which is very rare. Multidisciplinary approach is required for treatment.[3] In the majority of reported cases, mastectomy with or without axillary lymph node dissection was performed, followed by postoperative chemotherapy and radiation therapy.[1] Prevention of local recurrence is of particular importance and radiotherapy is significant for the same.[3] Increasingly treatments are targeted toward molecular markers. [6] The development of hormonal therapies validates the distinction between estrogen receptor (ER) positive and ER negative cancers.[6] Currently, the evaluation of breast carcinoma includes hormone

receptor analysis of the tumor tissue, with those positive for estrogen or progesterone responding better to both hormonal and chemotherapy.[2] Trastuzumab (Herceptin) is available as an adjunct treatment for tumors which overexpress the Her2/neu gene.[2]

The prognosis for carcinosarcoma of the breast is less favorable compared to more common types such as infiltrating ductal or lobular carcinoma.[2] They metastasize via lymphatics and bloodstream.[1] Pulmonary metastasis is more common than brain, skeletal or hepatic metastasis, and the prognosis of these patients is poor.[2] Tumar size, differentiation rate, high histologic grade, atypia and active pleomorphic spindle cells play a role in prognosis.[3] In metaplastic breast cancer, the non triple negative group has been found with poor prognosis compared with the triple negative group, which is contrary to what has been reported in patients with invasive ductal carcinoma of breast.[6] The different prognosis between the two has been attributed to adverse prognostic impact of Her2 amplification or overexpression in itself, because Her2 positive metaplastic cancers consist of the majority of non triple negative metaplastic cancers.[6]

Carcinosarcoma is a rare tumor, with very few cases published in the literature with majority of cases showing triple positivity for hormone receptors and Her2/neu gene, however our case is a rare entity in this aspect revealing triple positivity for ER, PR and Her2/neu.

Figure 1: H&E sections of tumor showing oval to spindle shaped cells in groups and fascicles with mild to moderate pleomorphism along with few mitotic figures and few atypical glandular structures embedded in between the spindle cells.(1a) 200X (1b) 400X.

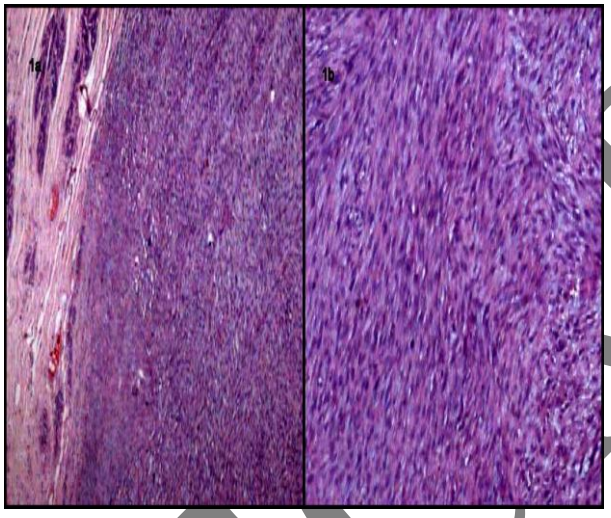
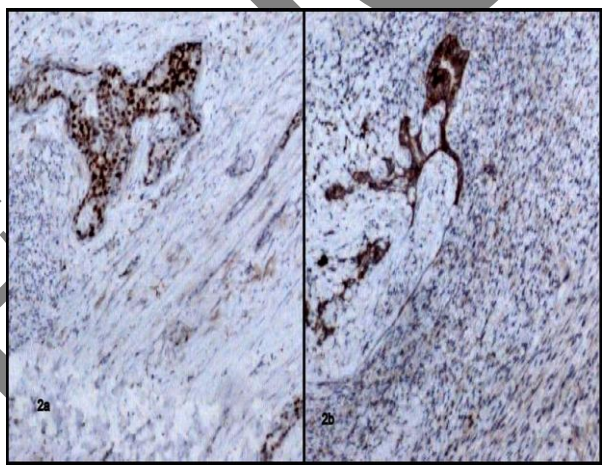


Figure 2: Tumor cells showing (2a) ER positivity and (2b) Her2/neu positivity.



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