

Carcinoma or Sarcoma of the Breast

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ABSTRACT

Carcinosarcomas comprise less than 1% of invasive carcinomas of the breast. They are a heterogeneous group of malignant tumors in which part or all of the carcinomatous epithelium is transformed into a nonglandular component by metaplastic growth process. We report a case of carcinosarcoma of breast. She was a 62-year-old female who presented with complaint of pain and lump in left breast of 6 months duration. There was a discharging ulcer measuring 4 × 6 cm over the nipple of 1-month duration. Computed tomography of chest and positron emission tomography report was suggestive of carcinoma of left breast with left axillary lymphadenopathy and lung metastasis. Histopathology of the tumor was reported as infiltrating duct cell carcinoma (IDC) with angiosarcoma. The IDC was estrogen and progesterone receptor negative and Human Epidermal Growth Factor -2 receptor positive. The angiosarcoma was positive for vimentin, vascular endothelial growth factor, CD34, and CD31. The Ki-67 labeling index was 60% and the epidermal growth factor receptor was positive. This is a case of carcinosarcoma of breast adding to the existing literature.

KEY WORDS: Breast, carcinosarcoma, metaplastic carcinoma

INTRODUCTION

Carcinosarcomas of the breast are otherwise known as metaplastic carcinoma. Its synonyms include biphasic metaplastic, metaplastic sarcomatoid carcinoma, and sarcomatoid carcinoma.^[1] Metaplastic breast carcinomas (MBC) are rare primary breast malignancies.^[2-6] They comprise less than 1% of invasive carcinomas of the breast.^[2,6] They are characterized by the co-existence of carcinoma with sarcomatous elements.

They can be classified as monophasic spindle cell (sarcomatoid) carcinoma, biphasic carcinosarcoma, adenocarcinoma with divergent stromal differentiation (osseous, chondroid, and rarely rhabdoid) as well as adenosquamous and pure squamous cell carcinomas.^[2,5]

These tumors are aggressive in nature as majority of them are triple negative for estrogen, progesterone, and Her-2 neu receptor.^[6,7] There is a paucity of information on

clinically relevant pathologic features and clinical outcomes for these rare tumors.^[5] In Indian literature, there are few case reports of this unusual tumor.^[8]

Hereby, we report a case of carcinosarcoma of breast comprising duct cell carcinoma and angiosarcoma.

CASE REPORT

A 62-year-old female presented with complaint of pain and lump in left breast of 6 months duration. There was an ulcer present over nipple with discharge since 1 month. She had been operated for left breast swelling 3 years back, but no details were available. She had no history of abdominal pain or jaundice. There was no history of altered bowel and bladder habits. She is diabetic since last 4 years. She had no history of pulmonary tuberculosis. Her general examination was within normal limit.

She had a lump of size 10 × 10 cm occupying all the quadrants of left breast. There was destruction of nipple and areolar complex with ulceration of size 4 × 6 cm present at nipple areola area. Active discharge was noted. Her routine

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investigations were within normal limit. She was reactive for HBs Ag.

Mammogram revealed a large hypoechoic lesion in the left breast with multiple enlarged axillary lymph nodes. Computed tomography (CT) chest report was suggestive of carcinoma left breast with left axillary lymphadenopathy and lung metastasis.

Histopathology of the biopsy suggested the possibility of duct cell carcinoma and sarcoma. Immunomarkers favored a tumor of mesenchymal origin.

In bone scan report, there was no evidence of osteoblastically active metastatic bone deposits. Positron emission tomography (PET) report showed a primary malignant lesion in left breast with ipsilateral left axillary node [Figure 1]. There was presence of lung metastasis. The stage of the patient was T4N2M1.

Left simple mastectomy was done for this patient. Intraoperatively, the swelling was of size 10 × 8 cm with ulceration of overlying skin, occupying almost all quadrants of left breast. The gross specimen of the mastectomy showed skin ulceration. Beneath this ulcerated area, there was a blackish lesion measuring 8 × 6 cms, also seen was a whitish lesion measuring 2 × 1 cms [Figure 2].

Histopathologically, there was an ulcerated area. Beneath the ulcerated area were granulation tissue and the tumor components. The tumor components were admixed with each other. One was infiltrating duct cell carcinoma (not otherwise specified) and the other was a mesenchymal component. [Figures 3 and 4] The duct cell carcinoma was of low-grade type. The sarcomatous component comprised many poorly formed vascular channels and presence of bizarre hyperchromatic tumor giant cells (angiosarcoma). The basal resected margin of the specimen was free of tumor. According to World Health Organization classification of breast tumors, it was diagnosed as metaplastic carcinoma of breast (carcinosarcoma).^[9] The adenocarcinomatous component was negative for estrogen and progesterone receptors. However, it showed positivity for Her-2 receptor. [Figure 5] The sarcomatous areas showed diffuse positivity for vimentin and vascular endothelial growth factor (VEGF). The giant cells in the sarcomatous area also showed positivity for CD34 and CD31. [Figure 6] Based on the morphologic and immunohistochemical findings, the tumor was diagnosed as metaplastic carcinoma of breast. The Ki-67 labeling index was 60% and the tumor showed intense epidermal growth factor receptor (EGFR) positivity.

Currently the patient is under follow-up.

DISCUSSION

Carcinosarcoma of breast is a rare malignancy. It is characterized by co-existence of two distinct cell lines described as a breast carcinoma of ductal type with a sarcoma-like component.^[1] These tumors pose a diagnostic and therapeutic challenge owing to their rarity.^[10]

The present case histopathologically showed a combination of IDC and angiosarcoma.

Carcinosarcoma breast usually presents as painful large lump in breast. There is no preference for any particular age-group. Their clinical features are usually similar to that of patients with IDC.^[6]

The present case was an elderly female who presented with a large, ulcerated breast lump.

The exact cell of origin of these tumors is not known. According to several theories, these tumors are of myoepithelial origin with presence of both carcinomatous and sarcomatous features on histopathology.^[6,11]

Yamaguchi R *et al.* in their study have opined that the presence of high-grade spindle cells in metaplastic breast carcinoma may indicate aggressive behavior.^[3] One recent study has concluded that the prognosis of metaplastic breast carcinoma is poorer than for both invasive ductal carcinoma and triple negative invasive ductal carcinoma. The poor prognostic factors are tumor size larger than 5.0 cm, lymph node involvement, and Ki-67 ≥ 14%.^[12]

The present tumor showed high Ki-67 labeling index.

Immunohistochemistry plays an important role in the diagnosis of carcinosarcomas. Usually in carcinosarcoma breast, reactivity for both keratin and vimentin is observed.^[6] Majority of metaplastic carcinomas express EGFR and may serve as a potential therapeutic target for EGFR inhibitors.^[11]

The present tumor expressed cytokeratin and vimentin in the carcinomatous and sarcomatous areas, respectively. It was negative for estrogen receptor (ER) and progesterone receptor (PR). However, it showed positivity for Her-2 receptor in the duct cell carcinomatous area. We have not done - Fluorescence in situ hybridization (FISH) for human epidermal growth factor -2 (Her-2). The tumor also showed intense positivity for EGFR.

One study reported 98 patients with carcinosarcoma breast through the surveillance, epidemiology, and end results (SEER) database and concluded that these are aggressive, treatment refractory tumors with shared clinical

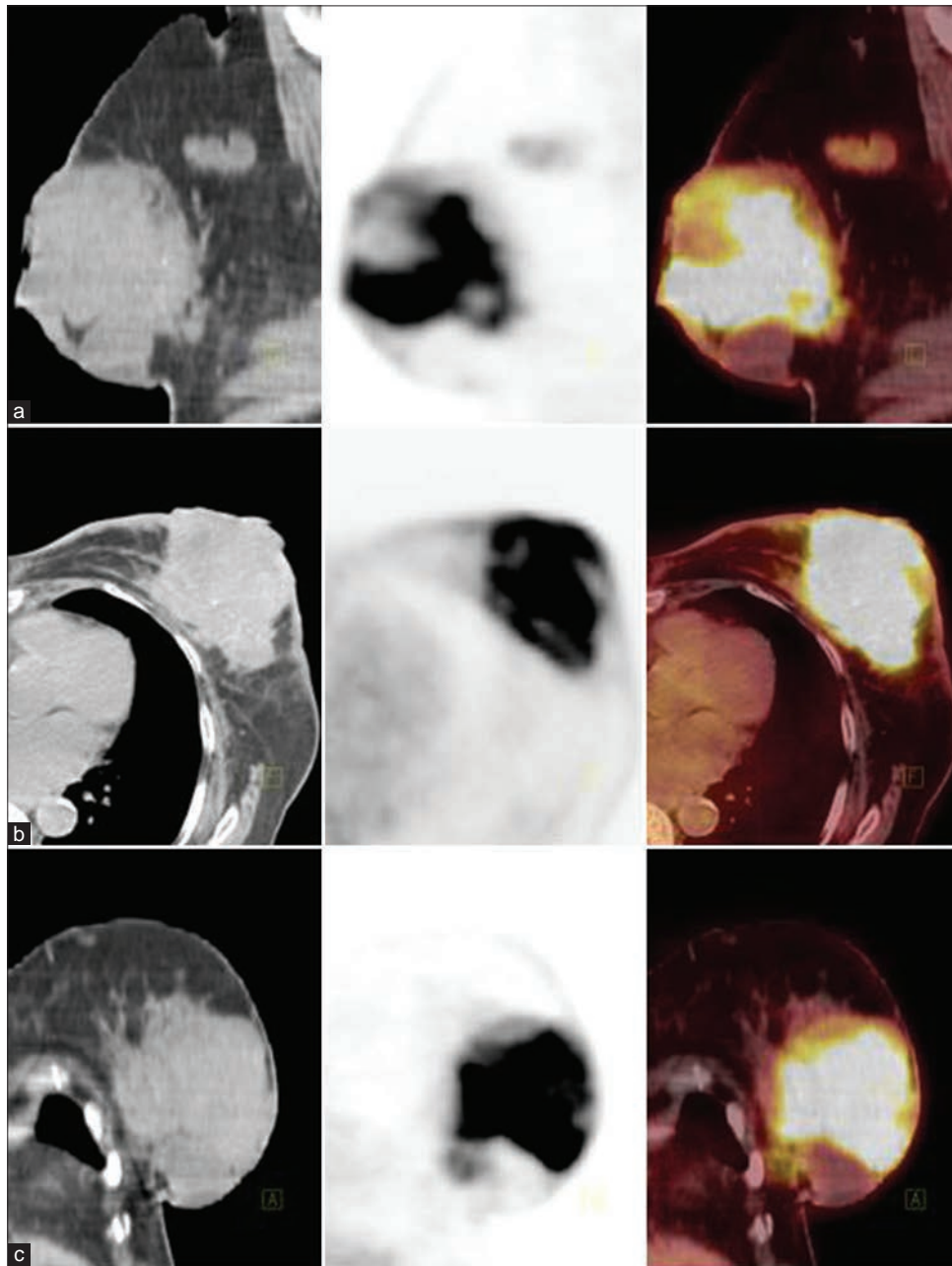


Figure 1: Whole body ^{18}F FDG PET /CT scan (a) Sagittal, (b) Transverse and (c) Coronal sections, showing a heterogeneous soft tissue density mass lesion measuring (9.5 x 8.0 x 10.0 Cms) in size, involving inferior, outer quadrant of left breast, associated with thickening of overlying skin and infiltration of pectoralis major muscle. Intensely increased Fluorodeoxyglucose (FDG) uptake noted in this mass lesion with max standardized uptake value (SUV): 15.8, suggestive of metabolically active primary malignant lesion

features and outcomes similar to poorly differentiated, receptor-negative adenocarcinoma of the breast. They metastasize via lymphatics and bloodstream.^[6,13]

In general, the recommended treatment options are similar to that of treatment of patients with invasive breast cancer. In the majority of the reported cases, mastectomy with or without axillary lymph node dissection was performed, followed by postoperative chemotherapy and radiation therapy.^[6,14] Kim *et al.* have reported that patients who were treated with neoadjuvant or adjuvant anthracycline-based

chemotherapy showed a better clinical outcome compared to those treated with cyclophosphamide, methotrexate, 5-fluorouracil (CMF) and the neoadjuvant chemotherapy for carcinosarcoma breast was less effective than for conventional adenocarcinoma.^[6,15]

Different authors have suggested the 5-year overall survival rate of carcinosarcoma ranging from 49-68%.^[6,16]

The differential diagnosis of metaplastic carcinomas includes both neoplastic and non-neoplastic lesion. Metaplastic

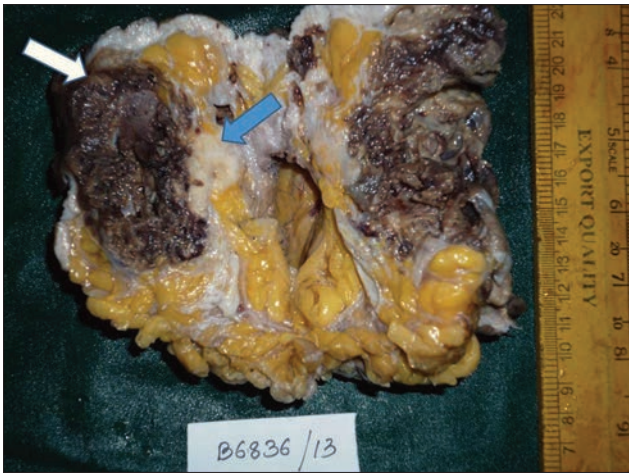


Figure 2: Cut section of the simple mastectomy specimen showing ulceration and the blackish lesion (angiosarcoma, white arrow) and the whitish lesion (duct cell carcinoma, blue arrow)

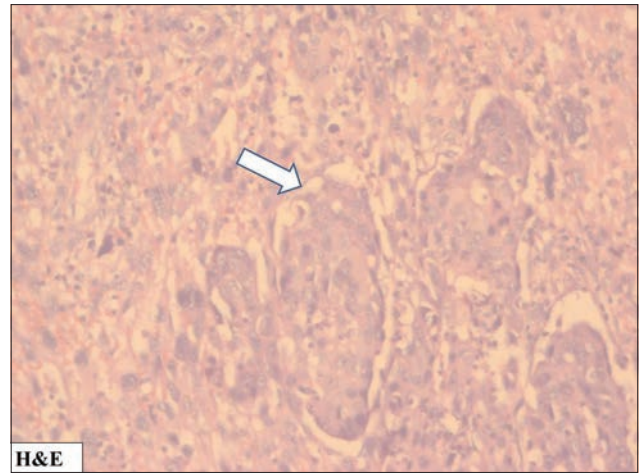


Figure 3: Histopathology of duct cell carcinoma (arrow) and angiosarcoma (hematoxylin and eosin, ×40)

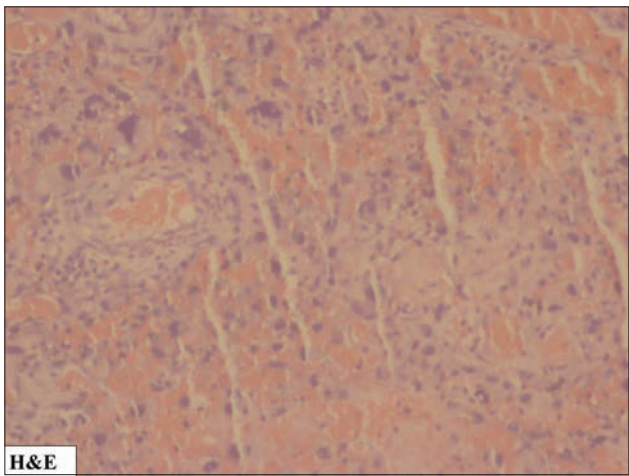


Figure 4: Histopathology of angiosarcoma showing poorly formed vascular channels (hematoxylin and eosin, ×40)

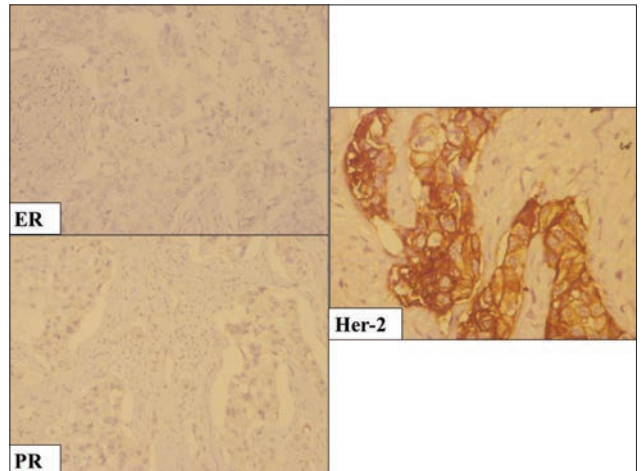


Figure 5: ER, PR negativity, and Her-2 positivity in duct cell carcinomatous area (Immunohistochemistry, ×40)

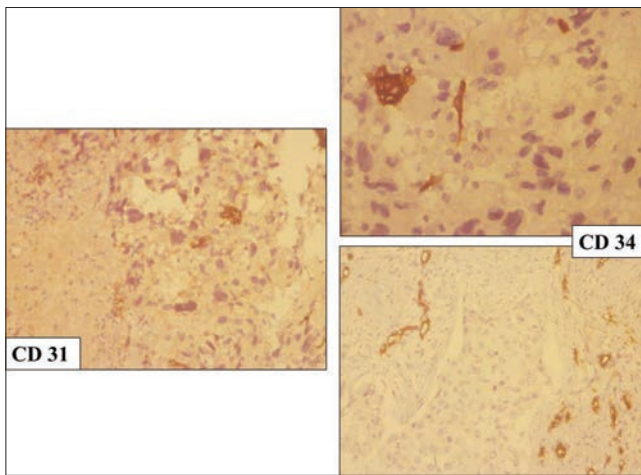


Figure 6: CD 34 and CD31 positivity in the sarcomatous area and negative in the duct cell carcinomatous area (IHC, ×40)

carcinomas with bland spindle cell should be distinguished from exuberant scars, fibromatosis, and nodular fasciitis

and, more infrequently, from myofibroblastomas, pseudoangiomatous stromal hyperplasia, and acute and chronic abscess with fat necrosis. Metaplastic carcinomas with significant atypia must be distinguished from malignant phyllodes tumor and primary or metastatic sarcoma.^[1]

Breast carcinosarcomas are rare and have nonspecific clinical and radiological features. Usually the postoperative pathology helps in the final diagnosis.^[16]

The positive expression of ER/PR and HER-2 in breast carcinosarcoma is low. Since majority of them express EGFR, further study is required for possible new therapeutic target.^[17]

This present case is an additional case of metaplastic carcinoma of the breast to the existing literature, emphasizing study of the histopathological specimen to arrive at a proper diagnosis.

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