



CARCINOSARCOMA OF THE BREAST - A VERY RARE CASE REPORT

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Abstract : Background - Carcinosarcoma of the breast, often referred to as Metaplastic carcinoma of the breast, is a very rare malignancy with two distinct cell lines - ductal with sarcoma-like component. Clinically, Carcinosarcoma is an aggressive breast cancer and its prognosis is less favorable compared to the commoner infiltrating ductal or lobular carcinoma. We report, here, a patient with Carcinosarcoma breast a very rare and often a difficult diagnosis. Case Presentation - A 60 years old post-menopausal woman presented with a 6 month history of left breast swelling a slow-growing mass associated with pain lately. There was no discharge per nipple. Physical examination revealed a huge tender well defined mass in the left breast, with consistency ranging from firm to hard, along with areas of fluctuation. The mass was mobile with the breast tissue but not fixed to the pectorals. The skin over the mass was reddish, not pinchable and had a peau d'orange appearance

. The left axilla and supraclavicular fossa were free. So clinically, the mass was initially thought of as an Inflammatory Carcinoma of the left breast. FNAC yielded only a bloody aspirate, which was followed by an incision biopsy and that clinched the diagnosis of Metaplastic Carcinoma of the breast CarcinoSarcoma. The patient had Left Modified Radical Mastectomy, followed by Adjuvant chemotherapy. Histopathological examination confirmed the diagnosis. The patient is now free from the disease for more than a year post-operatively. Discussion - Carcinosarcoma breast has been reported to account for 0.08-0.2% of all breast malignancies. The true definition of Metaplastic carcinoma of the breast is a tumor of malignant epithelial tissue (carcinoma) mixed with malignant cells of mesenchymal origin (sarcoma) with apparent histologic and cytologic features present on light microscopy and immunohistochemical testing. The origin of these tumours is still being debated and are probably derived of myoepithelial cells. Generally the prognosis of these tumours

is poor, with survival being measured in months. Conclusion - Carcinosarcoma accounts for 0.2 of breast malignancies and should be a differential. Very few cases have been reported in the literature. Treatment involves a multi-disciplinary approach as recommended by the NCCN guidelines.

Keyword :Breast carcinoma, Metaplastic carcinoma, CarcinoSarcoma Breast

Background & Introduction:

Malignant breast neoplasms consisting of mixtures of epithelial and mesenchymal elements are rarity. Pathogenesis of such diverse elements within obviously infiltrating carcinomas has been the subject of much controversy. After the advent of immunohistochemistry, it is now generally accepted that metaplasia of the epithelial elements of a carcinoma gives these lesions their pseudosarcomatous appearance. Hence the name 'metaplastic carcinoma' is given to malignant breast neoplasms which show cytokeratin positivity in both epithelial and mesenchymal elements ⁽¹⁾. Carcinosarcomas, a subset of Metaplastic Carcinoma are still rarer and represent less than 0.2% of symptomatic invasive carcinomas of the breast ⁽²⁾. These uncommon tumors may contain other cellular components besides the glandular component ⁽³⁾. The sarcomatous elements range from cartilage, bone, myxoid changes and spindle cell component ⁽²⁾. These tumors may manifest as well-circumscribed or irregular spiculated masses ⁽⁴⁾. The debate regarding the classification and staging of these tumors still remains unresolved because of the small number of cases reported in the literature. These carcinomas can metastasize to any part of the body. It is difficult to assess the prognosis of carcinosarcomas because of their relative rarity, but some anecdotal evidence has suggested that they behave as highly malignant tumors with early recurrence and poor survival ⁽²⁾.

Study Design: Case Report.

Case presentation: Clinical History:

A 60 year old female patient presented with a swelling in her left breast for the past 6 months. The swelling was initially a small lump and gradually progressed to the present size of approximately 10cm. The patient stated that this swelling was associated with pricking pain for the past 5 months which is not radiating and does not have any aggravating or relieving factors. There was no discharge per nipple. There was also no history of any other swelling in any part of the body, including the other breast and axillae. The patient is a known asthmatic for 8 years and has a history of hysterectomy done for probably a fibroid 25 years back. The patient said that she attained menarche at 12 years old and was married a year later. She gave birth to 4 children by full term normal delivery and breast fed each one of them for an average of 2 years each. Family history was not contributory and the patient takes mixed diet. She never had any oral contraceptive pills or was on hormone replacement therapy or any other drugs.

Fig. 2: Peau d' orange, nipple retraction, Incision biopsy scar

The patient was comfortable and stable, with normal systemic examination – cardiovascular, respiratory, abdominal, nervous systems and the spine & cranium. The other breast (right), right axilla and the right supraclavicular fossa were free. She was examined in broad daylight with a female attender and with adequate exposure in the following positions: sitting; arms by the side, arms raised, arms over hips;

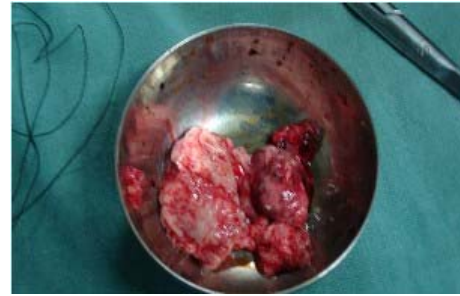
Physical Examination (refer Fig. 1 & 2):



Fig. 1: Peau d' Orange appearance of skin

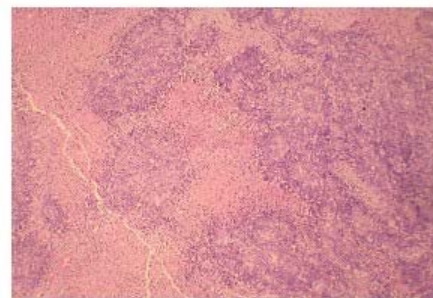


bending forward; recumbent. It was found that a huge globular swelling of size 8X10 cm was occupying predominantly the upper medial and encroaching upon the upper lateral quadrant of the left breast. It was well defined and smooth surfaced and the skin was shiny, reddish with peau d'Orange appearance. The nipple was retracted circumferentially but there was no active discharge. There were no scars or sinuses or dilated veins over the left breast. On the whole, the left breast was bulkier and sagging than the right although the left nipple-areola complex (NAC) was higher than the right. The swelling was not warm but tender. The skin was not pinchable over the swelling and the consistency was firm to hard with areas of fluctuation. The swelling was mobile with the breast tissue and not fixed to the pectorals. The left axilla and supra-clavicular fossa were normal.



A provisional clinical diagnosis of Carcinoma of the Left Breast: probably Inflammatory Carcinoma; T_{4d} N₀ M₀; Stage III_b was made and the patient was evaluated. **Investigations:** Routine investigations were normal. Metastatic workup – skeletal survey, X-ray chest, ultrasound abdomen & pelvis, Ultrasound right breast & bilateral axillae was normal. Since FNAC yielded a hemorrhagic aspirate, a Trucut biopsy was planned which was converted to an Incision biopsy subsequently, due to the following findings: Hemorrhagic fluid with grey-white soft tissue mass (refer Fig. 3).

Fig. 3: Incision biopsy specimen Fig. 4: Spindle cells with Necrosis



So multiple bits of grey-white tissue were obtained by incision biopsy because it is technically difficult to do a Trucut without a solid mass. This was reported as Metaplastic Carcinoma of the Breast: Carcinosarcoma subtype; with the following microscopic findings (refer Fig. 4, 5 & 6):

predominant spindle cells with indistinct cytoplasm and bizarre nuclei, plump polyhedral cells arranged as diffuse sheets, focal clusters & ductules with vesicular nuclei, tumor giant cells, foci of hemorrhage & necrosis, myxoid change, plenty of mitoses (>10 per hpf) with lymphovascular invasion.

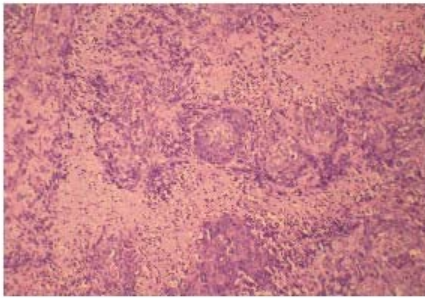


Fig. 5: Epithelial cells in Ductule formation

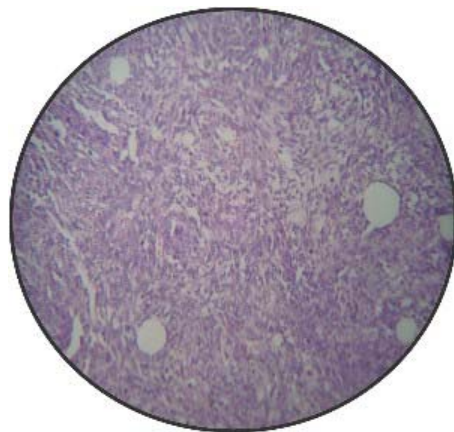
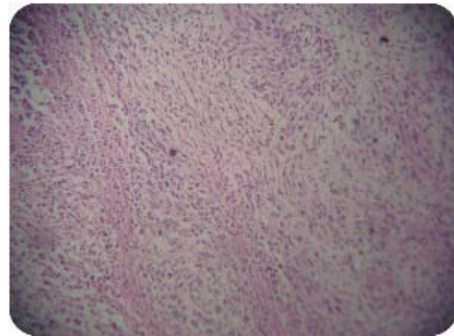
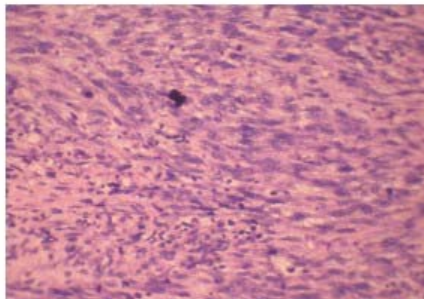


Fig. 7: Spindle cells in HPE
Fig. 8: Ductule formation in HPE



The patient is now free from the disease for more than a year post-operatively.

Treatment:

The final diagnosis is: Metaplastic Carcinoma of the Left Breast: CarcinoSarcoma subtype; T_{4b} pN₀ M₀; Stage III_b. The patient underwent a Left Modified Radical Mastectomy followed by Adjuvant Chemotherapy – 6 cycles of CAF regimen and Adjuvant Radiotherapy. The Histopathological (HPE) report confirmed the diagnosis (*refer Fig. 7 & 8*) with safe margins and the axillary lymph nodes were free from malignant spread. During follow-up, the patient developed flap necrosis in a month which was also revised.

Discussion:

Carcinosarcoma of the breast (metaplastic, biphasic metaplastic, metaplastic sarcomatoid carcinoma, sarcomatoid carcinoma) is an aggressive, rare neoplasm that has been reported to account for 0.08–0.2% of all breast malignancies ⁽⁵⁾⁽⁶⁾⁽⁷⁾. Carcinosarcomas have been observed in various organs throughout the body, including the ovary and uterus. The true definition of metaplastic carcinoma of the breast is a tumor of malignant epithelial tissue carcinoma) mixed with malignant cells of mesenchymal origin (sarcoma) with

(apparent histologic and cytologic features present on light microscopy and immunohistochemical testing⁽⁷⁾⁽⁸⁾⁽⁹⁾⁽¹⁰⁾. Indeed, this tumor type is often referred to as metaplastic breast cancer, characterized as an unusual and uncommon neoplasm that is comprised by an admixture of two or more components⁽¹¹⁾. The term carcinosarcoma was previously reserved for neoplasms where the demarcation between carcinomatous and sarcomatous components was distinct in all microscopic fields. The cells of origin for this neoplasm have yet to be agreed upon, but most research leads us to believe the cells are of myoepithelial origin. The tumor components may be homogeneously adenosquamous, or heterogeneously epithelial (adenocarcinoma) and mesenchymal (matrix, spindle cell and sarcomatous) in origin⁽¹¹⁾⁽¹²⁾. However, it seems more appropriate to term all breast carcinomas with obvious carcinomatous and sarcomatous features as biphasic metaplastic sarcomatoid carcinoma (MSC)⁽¹³⁾. Regardless of the name given to this entity, most metaplastic tumors of the breast are poorly differentiated, high grade, highly cellular, with mitotically active pleomorphic spindle cells. The majority are estrogen and progesterone receptor negative, and HER2-neu negative by immunohistochemistry⁽¹²⁾. The clinical and pathologic features of metaplastic breast carcinomas are important to distinguish from other types of uncommon breast malignancies such as spindle cell carcinoma, matrix producing carcinoma, fibrosarcoma, osteosarcoma, malignant fibrous histiocytoma, phylloides tumor and stromal sarcoma as their behavior, response to treatment and survival rates differ greatly.

Carcinosarcomas usually present as large masses, are often painful and show no preference for any particular age group⁽¹⁴⁾. The macrocyst containing bloody fluid, as seen in our case, has been noted in other reports⁽¹⁵⁾. Carcinosarcomas metastasize via lymphatics and bloodstream. They also tend to recur locally because neoplastic cells often extend within the perivascular tissues beyond the capsule of the tumour. Clinical features of metaplastic breast cancer are similar to those patients with invasive ductal carcinoma⁽¹¹⁾. Recurrence can be rapid as the primary tumor is aggressive, thus mandating close interval follow-up after resection. Axillary node involvement is rare, but reported. Hennessy *et al* reported on 100 patients with biphasic metaplastic sarcomatoid carcinoma (MSC) and 98 patients with carcinosarcoma identified through the SEER database. They compared clinical features and survival parameters for the two cancer types⁽¹³⁾. They conclude that both MSC and carcinosarcoma are aggressive, treatment-refractory tumors with shared clinical features and outcomes similar to poorly differentiated, receptor-negative adenocarcinoma of the breast. In comparing these two entities, they found that the initial T-stage of the tumor had a very strong association with overall outcome. They also identified significant differences in the metastatic spread capacity to regional nodal basins. Pulmonary metastasis is more common than brain, skeletal or hepatic metastasis, and the prognosis for these patients is poor⁽¹⁶⁾. Outcomes for local recurrences are somewhat improved when surgical resection is achievable. In general, the recommended treatment options have followed the established NCCN guidelines for patients with invasive breast cancer. In the majority of the reported cases, mastectomy with or without axillary node dissection was performed, followed by post-operative chemotherapy

and radiation therapy in various combinations. Adjuvant hormonal therapy and chemotherapy is based upon the receptor status of the primary tumor and is an important tool in treatment recommendations. The HER1/EGFR receptor is reported to be over-expressed in the majority of metaplastic sarcomatoid carcinomas of the breast and should be included in the initial evaluation of the various tumors. The most common differential diagnosis to be considered in a case of metaplastic carcinoma with squamous cell differentiation is primary squamous cell carcinoma of the breast, which was ruled out in the present case owing to the presence of areas of invasive ductal carcinoma along with the other metaplastic elements. However, squamous cell carcinoma of breast is in itself considered to be a special type of metaplastic carcinoma⁽⁷⁾. In a case of metaplastic carcinoma with spindle cell differentiation, the possibility of a phylloides tumor has to be ruled out considering the presence of malignant glandular elements. New treatment opportunities may exist with the development of agents targeting the EGFR receptor such as gefitinib and cetuximab. In a study of 20 cases of metaplastic carcinomas of the breast, they found that 14/20 MSC's were positive for EGFR expression, highlighting the potential utility of targeted therapies to the EGFR receptor⁽¹⁷⁾. Monoclonal antibodies and small molecule inhibitors of EGFR are currently being evaluated in clinical trials of patients with lung and colorectal cancer. It has been suggested that the frequent expression of EGFR in the absence of steroid receptors or other receptors of the EGFR family might render metaplastic breast carcinomas even more sensitive to EGFR tyrosine kinase inhibitors⁽¹⁸⁾.

Conclusion:

CarcinoSarcoma is one of the four variants of Metaplastic Carcinoma Breast, as described by Wargotz & Norris⁽⁸⁾⁽⁹⁾. The prognosis depends upon the tumor size, histologic type, grade, lymph node status and the type & grade of the mesenchymal component. The overall 5-year survival rate is 40%. Chemotherapy, if given, should be directed towards the sarcomatous component. A multi-disciplinary approach with good follow-up is highly recommended.

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