Role of adjuvant radiotherapy in metaplastic matrix producing breast cancer: A case study with review of literature

ABSTRACT
A rare and unique variant of breast cancer - metaplastic matrix producing carcinoma, is presented. Surgery has been the mainstay of treatment. The role of adjuvant postoperative radiotherapy, as has been used in this patient, has been reviewed.

KEY WORDS: Metaplastic, matrix-producing, breast cancer, radiotherapy.

INTRODUCTION
Metaplastic breast carcinomas are regarded as ductal carcinomas, that undergo metaplasia into nonglandular growth patterns and account for less than 1% of all invasive mammary carcinomas.[1] Most patients present with a rapidly enlarging palpable mass, that appears as a well delineated mass, on mammography. Adjuvant treatment in form of either postoperative radiotherapy or chemotherapy, has yet not been defined. The paper reviews the role of adjuvant radiotherapy in these cases.

CASE REPORT
A fifty-year-old, postmenopausal lady, presented with the complaint of swelling in upper outer quadrant of left breast, which had painlessly progressed from pea size to 10 x 12cm², in 6 months. The lump was mobile, nontender and firm, in consistency. The overlying skin was normal and mobile axillary lymph nodes were palpable. She was staged clinically as T3N1M0.

The patient underwent modified radical mastectomy in a private hospital and was referred for further adjuvant therapy. Gross specimen was not available for review. However, sections from the tissue block were reviewed by the pathologist. Microscopically, the tumour was a poorly differentiated carcinoma, displaying sheets and nests of cells with marked nuclear pleomorphism, vesicular chromatin, conspicuous nucleoli and pale eosinophilic cytoplasm. Focal areas of abrupt transition from carcinoma to cartilaginous matrix production, were seen [Figure 1]. Immunohistochemistry revealed diffuse positive staining for cytokeratin, Epithelial Membrane Antigen (EMA) and S100, in the carcinomatous areas. The chondroid areas showed positive immunostaining for S100 and vimentin. No nuclear reactivity for estrogen or progesterone receptors was found. Based on the above features, the histopathology of a metaplastic matrix producing breast cancer, was confirmed.

Haemogram, biochemistry profiles and metastatic workup, were reported to be normal. A dose of 50Gy/5weeks/25 fractions was delivered to the chest and loco-regional area. Presently she is asymptomatic and free of any disease.

DISCUSSION
Of the invasive neoplastic lesions of the breast, matrix-producing carcinoma is reported in less than 1% of all cases.[1] Matrix-producing carcinoma is a variant of heterologous metaplastic carcinoma, composed of overt carcinoma, with direct transition to a cartilaginous and/or osseous stromal matrix, without an intervening spindle cell zone or osteoclastic cells.[2] Age of presentation, clinical features and mammographic appearance, are no different from other invasive mammary carcinomas. Majority of tumours are usually firm to hard, nodular and circumscribed, but some have been reported to have infiltrating borders.[1]

Microscopically, the carcinomatous element comprises moderately to poorly differentiated adenocarcinoma, with infrequent foci of squamous...
or apocrine metaplasia. The most frequently encountered heterologous elements, are bone and cartilage. Most studies support the epithelial or myoepithelial origin of heterologous elements. The mechanism of conversion to the mesenchymal phenotype is unknown. On immunohistochemistry, the cancer cells stain positively for keratin, EMA and S100. The matrix producing areas are S100 reactive and non reactive for cytokeratin.

The incidence of axillary lymph node metastasis, ranges from 6 to 25%. Metastasis derived from metaplastic carcinoma can consist entirely of adenocarcinoma, metaplastic elements, or a mixture of these components. The overall five year survival rates reported in the literature, vary from 38 to 65%. In a study of 32 patients of metaplastic carcinomas with heterologous elements, Chheing et al. reported a more favourable prognosis, compared with patients of infiltrating duct carcinoma, after adjustment for tumour size and nodal status, although the difference was not statistically significant. Treatment advocated usually varies from excision biopsy, to modified radical mastectomy. In a study of 26 patients by Wargotz and Norris, local recurrences or metastasis were observed in nine patients (34.6%). Patients undergoing radical mastectomy showed least incidence of recurrences, with survival advantage compared to other types of mastectomies, or local excision. Cumulative 5-year survival was reported as 68%. Local recurrences or metastases were usually seen within 2½ years, following the initial surgery and 85% of these patients died within four years. Metastasis was seen in lymph nodes, lungs, bones and brain. The role of adjuvant treatment in form of loco-regional radiotherapy or chemotherapy, has not been clearly defined in the literature, due to lack of any long term survival of metaplastic matrix producing cancer breast.

However, as evident from the study of Wargotz and Norris, local recurrences in the chest wall could be present in around 16% of the patients (4/26), in the short span of 2.5 years. Attempts to salvage all these cases with local excision and radiotherapy, appears to be ineffective. Although radical mastectomy may help in reducing the incidence of local recurrence, as this procedure is not commonly practiced, post-operative adjuvant radiotherapy could help.

Postoperative radiotherapy, in a similar fashion as that of invasive cancers of the breast, could help to decrease the incidence of local recurrence, especially in large tumours having a poorly differentiated histology. Thus, such tumours could be benefitted with chest wall radiotherapy. Moreover, since the incidence of lymph node metastasis has been observed in 6-25% of these cases, the lymphatic drainage areas could also be encompassed in the radiation portals. Reduction in loco-regional recurrences could also be anticipated, to prevent a nidus for further dissemination to systemic sites, which have been shown to be associated with poor outcome.

In the present case, in view of the large tumour and aggressive features on histopathology, the patient was considered for postoperative radiotherapy. No adjuvant chemotherapy has been planned for her and presently, she is doing well on follow up.

In view of the rarity of metaplastic carcinomas, it is difficult to identify major prognostic factors to outline the adjuvant therapy. However, as local recurrences are evident in a significant proportion of patients following surgery, these cases should benefit from adjuvant postoperative radiotherapy. In view of the extreme rarity of metaplastic matrix producing breast cancers, these cases should be managed on individual basis, taking into consideration the adverse tumour characteristics – both clinical and histopathological. These could include large tumours, presence of nodal spread and poorly differentiated tumours. The role of adjuvant chemotherapy remains to be established.

REFERENCES