

# Metaplastic carcinoma of the breast: A report of two cases along with review of literature

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## ABSTRACT

Metaplastic carcinomas of breast are uncommon, representing 0.3% of invasive carcinomas of breast. We are reporting two cases of metaplastic carcinoma breast, one revealing rhabdomyoblastic and spindle cell differentiation and other revealing osteoclast like giant cells. Both were estrogen receptor, progesterone receptor and Her2u negative on immunohistochemistry. Early diagnosis of metaplastic carcinomas is essential as these tumors are usually triple negative and hence, do not respond to trastuzumab. Metaplastic carcinomas typically express HER1/epidermal growth factor receptor (EGFR), thus majority of metaplastic carcinomas are treated with EGFR inhibitors such as gefitinib and cetuximab. Also, metaplastic carcinomas are associated with a worse prognosis with a disease free survival rate being 78.1% in metaplastic breast carcinomas compared with 91% in infiltrating duct carcinomas.

**Key words:** Aggressive, metaplastic carcinomas, triple-negative

## INTRODUCTION

Metaplastic carcinomas of breast are uncommon tumors representing 0.3% of invasive carcinomas of breast.<sup>[1]</sup> These tumors represent a heterogeneous group of malignant tumors in which part or all of the carcinomatous epithelium is transformed into a non-glandular (metaplastic) growth process.<sup>[2]</sup> Various types of metaplastic carcinomas have been reported like sarcomatoid carcinoma, spindle cell carcinoma, carcinoma with osteoclast like giant cells and squamous cell carcinoma. It is important to identify these tumors as they are triple-negative, have an aggressive behavior and are requires a change in the patient management. Thus, we are reporting two cases of metaplastic carcinoma of breast one revealing rhabdomyoblastic differentiation and other revealing osteoclast like giant cells.

## CASE REPORTS

### Case 1

The first case is about a 47-year-old female patient who presented with a 4 × 2 cm sized well defined freely mobile lump in the upper outer quadrant of right breast. The patient underwent modified radical mastectomy. The mastectomy specimen revealed a well-circumscribed grey white growth measuring 4 cm × 2 cm × 2 cm. Microscopic examination revealed tumor comprised of epithelial and mesenchymal component. Epithelial component comprised of tumor epithelial cells forming nests, sheets and glands separated by desmoplastic stroma showing focal myxoid change. Mesenchymal component comprised of large tumor cells with eccentrically placed nuclei, prominent nucleoli and abundant deep eosinophilic cytoplasm [Figure 1]. There were areas of bizarre spindle cells with pleomorphic vesicular nuclei, prominent nucleoli and eosinophilic cytoplasm and scattered multinucleate tumor giant cells. There were numerous typical and atypical mitotic figures and marked lymphocytic infiltrate in and around the tumor nests. 1 out of the 12 lymph nodes dissected out of the specimen revealed metastatic tumor deposits. A diagnosis of infiltrating duct carcinoma breast with areas of spindle and rhabdomyoblastic differentiation was rendered.

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## Case 2

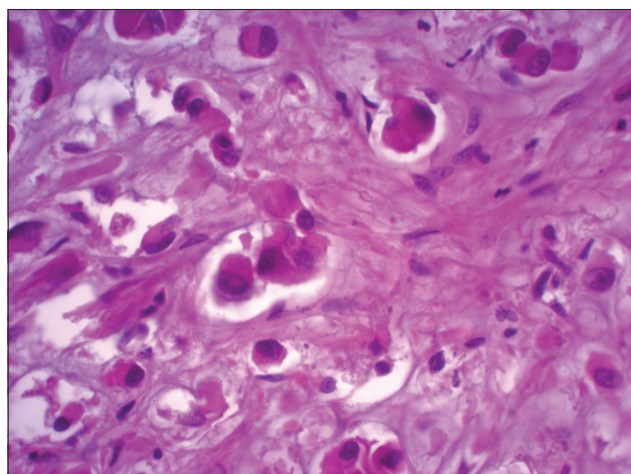
We received a modified radical mastectomy specimen of a 50-year-old female patient. On serial sectioning, 5.5 cm × 5 cm × 2.5 cm sized growth was identified in upper outer quadrant. Microscopic examination revealed tubules, nests, cribriform pattern of tumor cells separated by hyalinized collagenous stroma. Tumor cells were moderately pleomorphic, round to oval with prominent nucleoli and moderate amount of eosinophilic cytoplasm. Numerous osteoclast like giant cells formed a predominant component of the tumor [Figure 2]. Four lymph nodes dissected out of the specimen revealed metastatic tumor deposits. A diagnosis of metaplastic carcinoma with osteoclast like giant cells was made. Both the cases were estrogen receptor/progesterone receptor (ER/PR) and CerbB2 negative.

## DISCUSSION

Metaplastic carcinomas are rare forms of invasive carcinomas of breast. Metaplastic carcinoma is a generic term for breast carcinoma of ductal type in which the predominant component of the neoplasm has an appearance other than glandular and epithelial and more in keeping with other cell type. It includes various categories:

- Sarcomatoid carcinoma, carcinosarcomas and matrix producing carcinomas
- Spindle cell carcinomas
- Carcinomas with osteoclast like giant cells
- Squamous cell carcinoma
- Melanocytic differentiation
- Choriocarcinomatous features
- Pleomorphic carcinomas.<sup>[3]</sup>

The mean patient age for metaplastic carcinomas of breast is 47.6 years.<sup>[4]</sup> Grossly, these tumors form large, firm, nodules



**Figure 1:** Mesenchymal component comprising of large tumor cells with eccentrically placed nuclei, prominent nucleoli and abundant deep eosinophilic cytoplasm (H and E, × 40)

having a median size of 5 cm. Fixity to skin or deep fascia is not uncommon.<sup>[1]</sup>

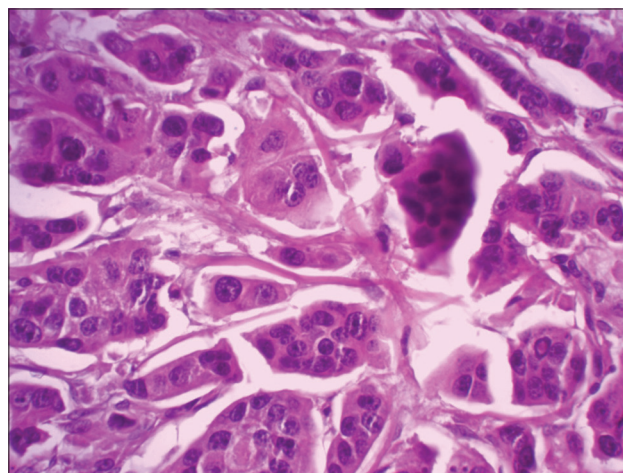
The differential diagnosis of metaplastic carcinomas depends on the degree of atypia observed in the tumor and includes exuberant scars, fibromatosis, nodular fasciitis, myofibroblastomas, pseudoangiomatous stromal hyperplasia, acute and chronic abscess with fat necrosis, malignant phyllodes tumor and primary or metastatic sarcoma.<sup>[2]</sup>

Lymph node involvement is uncommon but was seen in both our cases. Hematogenous spread is common explained by sarcomatous element, leading to metastasis to lung, liver, brain and bone.

These tumors commonly reveal activation of the Wnt signaling pathway, epidermal growth factor receptor (EGFR) gene amplification and over-expression.<sup>[2]</sup> Metaplastic carcinoma of the breast are characterized by ER/PR and Her2u negativity. When compared to triple-negative carcinomas, metaplastic carcinomas significantly more frequently expressed basal markers, such as CK14, CK17 and EGFR and over-express EGFR, vascular endothelial growth factor and caveolin-1, which can be used as therapeutic targets.<sup>[4]</sup>

A study by Lim *et al.* compared the clinical features and prognosis of triple negative metaplastic carcinomas and non-triple negative metaplastic carcinomas and concluded that non-triple negative metaplastic carcinomas had a poorer prognosis compared to triple negative patients.<sup>[5]</sup>

Similarly Bae *et al.* reviewed 47 metaplastic breast carcinoma and 1346 infiltrating duct carcinomas. They concluded that metaplastic carcinomas are associated with a larger tumor size, lower lymph node involvement, higher histological and nuclear grade, high triple negativity, higher p53, CK 5/6



**Figure 2:** Numerous osteoclast like giant cells (H and E, ×40)

and EGFR expression, worse prognosis with a disease free survival rate being 78.1% in metaplastic breast carcinomas compared to 91% in infiltrating duct carcinomas.<sup>[6]</sup>

In general metaplastic carcinomas are triple negative and do not respond to trastuzumab. These tumors classically express HER1/EGFR, thus majority of metaplastic carcinomas are treated with EGFR inhibitors such as gefitinib and cetuximab.<sup>[7]</sup>

## CONCLUSION

Metaplastic carcinomas of the breast are rare but aggressive tumors. Early diagnosis is essential because they are triple negative, but over-express EGFR requiring a change in the therapeutic regime.

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