Triple-Negative Metaplastic Breast Carcinoma with Extensive Squamous Differentiation in a 55-year-old Woman: A Rare entity

Abstract

The World Health Organization in 2003 classified the metaplastic breast carcinomas into, pure epithelial metaplastic carcinomas and mixed epithelial/mesenchymal metaplastic carcinomas, which comprises of squamous cell carcinoma, adenocarcinoma with spindle cell metaplasia, adenosquamous carcinoma, and mucoepidermoid carcinoma in the former and only mixed types in the latter. Metaplastic carcinoma is a rare form of cancer which accounts for <1% of invasive breast cancer and is characterized by areas of metaplasia typically with squamous, spindle, osseous, or chondroid differentiation in the background of adenocarcinoma. We are presenting a case of a 55-year-old female with a fungating, ulceroproliferative mass involving her whole breast including the nipple areola complex which turns out to be a rare form metaplastic breast carcinoma with extensive squamous differentiation.

Keywords: *Breast carcinoma, squamous cell carcinoma, squamous differentiation*

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Introduction

Breast cancer is a heterogeneous entity with ductal type the most common, followed by lobular carcinoma which together account for over 70% of carcinomas. Metaplastic carcinoma is a rare form of cancer which accounts for <1% of invasive breast cancer and is characterized by areas of metaplasia typically with squamous, spindle, osseous, or chondroid differentiation in the background of adenocarcinoma. Etiopathogenesis of this type of lesion in the breast is still fully unknown. It is thought to arises either directly from the epithelium of the mammary ducts or from a foci of squamous metaplasia within a preexisting breast adenocarcinoma.[1,2] The World Health Organization (WHO) in 2003 classified the metaplastic breast carcinomas into, pure epithelial metaplastic carcinomas and mixed epithelial/mesenchymal metaplastic carcinomas, which comprises of squamous cell carcinoma (SCC), adenocarcinoma with spindle cell metaplasia, adenosquamous carcinoma, and mucoepidermoid carcinoma in the former and only mixed types in the latter.[3] Clinical and radiographic characteristics of these tumors are not very specific and these tumors are usually hormone receptor negative (triple negative). In general, these are very aggressive, treatment-refractory tumors, with a poor prognosis. The objective of our case report is to present a very rare, aggressive, and triple-negative breast carcinoma classified as metaplastic carcinoma, squamous subtype.

Case Report

A 55-year-old female patient presented with a large fungating mass involving the whole right breast. Physical examination revealed a large ulceroproliferative growth (fungating mass lesion) involving almost the whole breast. It was immobile with irregular margins. The lesion has involved the whole nipple-areola complex and the same was not appreciable [Figure 1]. Axillary palpation did not reveal any palpable lymph node on either side. Left breast was normal with no palpable lump. The patient denies having any systemic diseases or any family history of breast or ovarian cancer. Ultrasonography of the lesion revealed a large heterogeneous hyperechoic lesion with multiple cystic foci, focal calcifications, and increased internal vascularity involving entire breast. All the other laboratory investigations were with in normal limits except that the patient was having anemia (Hb 8 gm%). Fine-needle aspiration biopsy revealed the presence of malignant cells, suspicious of squamous cell differentiation [Figure 2]. Modified

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radical mastectomy (MRM) along with axillary dissection was done and the specimen was sent for histopathology. Specimen was measuring 20 cm × 15 cm × 8 cm. Growth measured 9 cm × 8 cm × 8 cm and was involving the skin as well as the nipple areolar complex [Figure 3]. All the surgical cut margins were grossly free from tumor except base which was grossly involved by the tumor. Thirteen lymph nodes were dissected out from the specimen and put to histopathology examination. Histopathology examination revealed bizarre tumor cells arranged in sheets and nests infiltrating into the stroma with <10% tubule formation. The individual tumor cells were hyperchromatic, pleomorphic and had eosinophilic granular cytoplasm and prominent nucleoli. Areas with extensive squamous differentiation and necrosis were also seen. Sections also show moderately increased mitotic figures [Figure 4]. Special stains such as mucicarmine and periodic acid–Schiff showed focal areas of mucin positivity [Figure 5]. Immunohistochemistry was positive for cytokeratin (CK)-PAN, focal positive for CK-7, and diffuse positivity for CK-20 [Figure 6].

Figure 1: An ulceroproliferative growth involving almost the whole breast including the nipple areola complex

Figure 3: Gross specimen of the lesion showing the growth involving the entire breast

Immunohistochemistry for hormone status showed negativity for estrogen-receptor (ER), progesterone receptor (PR) as well as human epidermal growth factor receptor 2 (HER2)/neu (triple negative). The final diagnosis was triple negative metaplastic breast carcinoma with extensive squamous differentiation.

Discussion

The histological origin of this entity still remains unclear. Different theories explaining this phenomenon is; malignant growth of intrinsic epidermal elements or metaplasia from breast parenchyma (e.g., cystosarcoma phyllodes, fibroadenomas, or breast malignancies, e.g., intraductal carcinoma) or from chronic abscess.[4] The WHO categorizes these tumors as metaplastic carcinomas.[3,5] Metaplastic carcinoma usually presents with a larger tumor size, advanced stage, less frequent lymph node metastasis as compared to other invasive breast cancers.[6-9] The case in discussion has exactly the same features to qualify for a metaplastic carcinoma. Metaplastic tumors have varying degrees of homogeneity. A tumor is considered to be pure SCC if it meets the criteria of Macia *et al*.,[10] i.e., no other neoplastic component is present, such as ductal or mesenchymal element, the tumor is independent of adjacent cutaneous structures and no other primary epidermoid tumors are present in the patient (oral cavity bronchus, esophagus, renal pelvis, bladder, ovary, and cervix).[10]

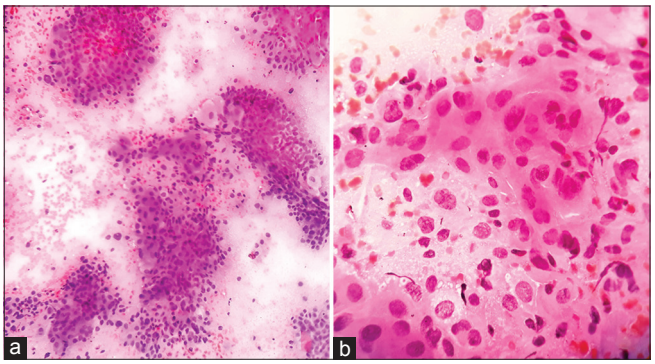

Figure 2: Fine-needle aspiration cytology of the lesion revealed the presence of malignant cells, suspicious of malignant squamous cell (a) H and E ×20, (b) H and E ×40

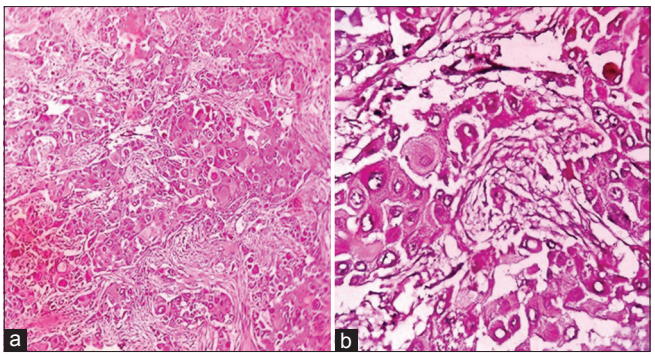

Figure 4: Photomicrograph showing malignant cells with squamous differentiation (a) H and E ×40, (b) H and E ×100

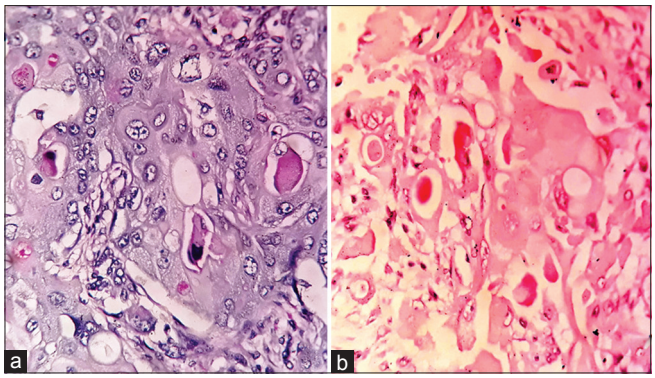

Figure 5: Photomicrograph showing eosinophilic globules (mucin positive) in "5a" (PAS, ×100) and also positivity for mucin in "5b" (mucicarmine, ×100)

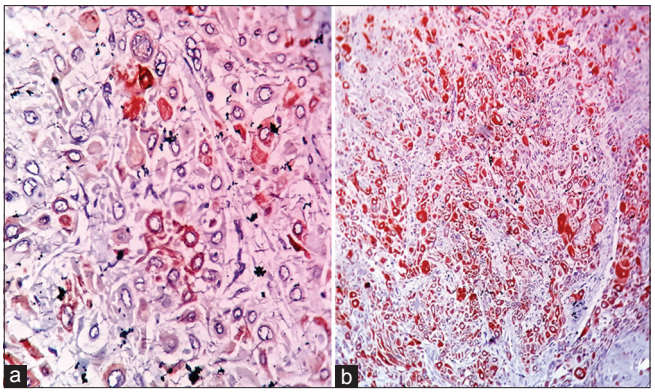

Figure 6: Photomicrograph showing focal positivity for cytokeratin 7 in (a) and diffuse positivity for cytokeratin 20 (b)

SCC/metaplastic carcinoma breast has been diagnosed in adult women of ages ranging from 29 to 90 years, with a median age of 52 years. Primary tumors tend to be relatively large. Approximately, two-thirds of these tumors are cystic or have a cystic component with central necrosis and they very rarely metastasize to the lymph nodes. In the case under discussion, all these features were seen [Figure 3]. Hormone receptors (ER, PR, HER2/Neu) are negative in more than 90% of the cases.[11] Our case also showed negativity for all the hormone receptors (triple negative). The most consistent feature of SCC/metaplastic carcinoma on mammogram is the lack of microcalcifications, same as in our case. Prognosis appears to be dependent on several factors, most importantly tumor size and tumor stage and this tumor has about 64% 5 year survival rate. The definitive management of metaplastic/SCC is MRM with adjuvant radiotherapy and or chemotherapy. Breast conservation therapy is not usually possible because of huge size of the lesion. Adjuvant and neoadjuvant chemotherapy regimens used include, 5-flourouracil alone or 5-flourouracil/cisplatin, 5-flourouracil/taxane, 5-flourouracil/cisplatin followed by pacitaxel, and cyclophosphamide plus methotrexate plus fluorouracil.[12]

Conclusion

MBC is a rare subtype of invasive breast cancer that accounts for <1% of all diagnoses. It is usually seen as a larger tumor at presentation. Clinical and radiological characteristics are not very specific. It usually has lower rates of axillary nodal involvement, higher rates of ER, PR, and HER2 negativity as well as less response to systemic as well as hormonal therapies when compared to other types of invasive breast cancers.

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Conflicts of interest

There are no conflicts of interest.

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