

# Triple-Negative Phenotype of Poorly-differentiated Metaplastic Breast Carcinoma in a Male: An Oncological Rarity

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## ABSTRACT

Metaplastic breast carcinoma (MBC) is an extremely rare breast malignancy having highly aggressive clinicopathological behaviour and dismal prognosis. A 75 years old man presented with a painless lump on right side of his chest along with two additional lumps in the ipsilateral axillary and inguinal areas. Microscopic evaluation and immunohistochemistry of tru-cut tissue biopsies of the lumps and that of mastectomy specimen revealed a triple-negative phenotype of poorly-differentiated metaplastic breast carcinoma with metastatic deposits to the axillary and inguinal lymph nodes. Exhaustive internet research has revealed only a few case reports of MBC in the men; thus highlighting its absolute oncological rarity.

**Key words:** Metaplastic carcinoma. Carcinosarcoma. Immunohistochemistry. Tumour markers. Triple-negative phenotype.

## INTRODUCTION

First described by Huvos *et al.* in 1973,<sup>1</sup> metaplastic breast carcinoma (MBC) is a peculiar breast cancer consisting of either pure epithelial metaplastic cells or a mixture of both epithelial and mesenchymal elements. Reportedly, MBC is an aggressive tumour having profound propensity for loco-regional recurrences, widespread systemic dissemination and strikingly dismal prognosis. It represents less than 1% of all breast malignancies.<sup>2</sup> Its extreme rarity can be judged from the fact that although quite a few cases of MBC have been documented in the women, its occurrence in the men is infinitesimal according to the world-wide biomedical literature.<sup>2,3</sup> Its absolute rarity, non-specific symptomatology, diversified imaging morphology, pathological variability, and controversial oncological treatment protocol all can pose perplexing diagnostic and therapeutic dilemmas even to the shrewd surgeons, radiologists and pathologists in its identification, categorization, characterization and therapeutic strategies. The prime rationale of reporting this case scenario is to acquaint the healthcare professionals with biological behaviour, clinical features, diagnostic work-up and treatment modalities of this discrete breast malignancy.

## CASE REPORT

A 75 years old man presented with a painless lump on right side of his chest of 6 months duration with no history of nipple discharge, eczema or distortion. There

were two additional lumps; one in ipsilateral axilla and second in right inguinal area. He gave history of significant weight loss, generalized weakness, easy fatigability, and low-grade fever. There was no history of breast cancer in his siblings. He was a chain-smoker but was non-alcoholic and non-addict. His systemic examination apart from revealing anemia and cachexia was unremarkable. Examination of the chest revealed a solitary, non-tender, partially-mobile, hard lump (6 x 7 x 8 cm) on anterolateral aspect of right side of the chest, about 2.5 cm from right nipple-areolar complex (Figure 1). The overlying skin exhibited oedema, erythema and multiple ulcerated patches. There was considerable basal induration of the lump indicating infiltration into pectoral muscles. Ipsilateral nipple-areolar complex showed no structural or positional abnormality and failed to exude any serous or bloody discharge on compression of the lump. Examination of right axilla disclosed an exquisitely tender and hard lump (8 x 10 cm) of matted axillary lymph nodes; possibly due to malignant infiltration of cords and nerves of the brachial plexus (malignant brachial plexopathy). A second tender and hard lump (3 x 4 x 5 cm) consisting of matted inguinal lymph nodes was present in right inguinal area (Figure 2). Examination of the contralateral breast and axilla revealed no pathology. Chest radiograph showed no osseous, cardiopulmonary, pleural, or pericardial pathology.

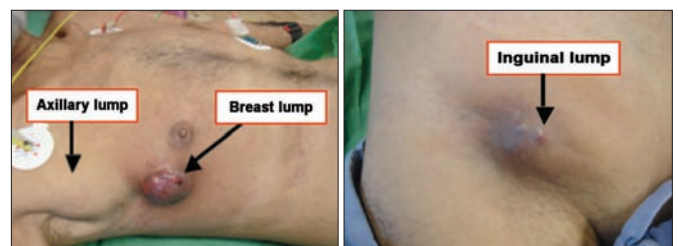


Figure 1: The chest and right axillary lumps.

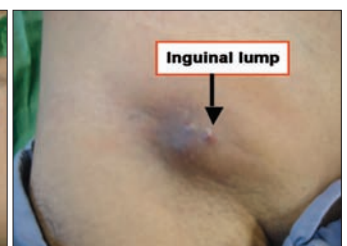


Figure 2: Right inguinal lump.

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Breast sonography and CT scan showed a well-circumscribed solid mass (7 x 8 x 9 cm) on anterolateral aspect of right side of the chest having complex internal echotexture and partially infiltrative deeper margins. CT scan also confirmed the right axillary mass to be made of matted lymph nodes fixed to chest wall and encasing the right axillary vessels. Both lung fields and bony cage were free of secondaries. CT scan of abdomen revealed no ascites or lymphadenopathy. Bone scintigraphy was negative for osseous metastases. FNAC and core-tissue biopsies apart from showing malignant nature of the growth, failed to demonstrate exact histopathology of the lump.

Consequently, palliative right mastectomy was performed with biopsy from the axillary and inguinal masses. Microscopic evaluation of the specimens revealed poorly-differentiated metaplastic breast carcinoma with sarcomatous differentiation (carcinosarcoma) and malignant deposits in axillary and inguinal lymph nodes. Immunohistochemistry showed biphasic nature of the lumps; carcinomatous areas were positive for epithelial membrane antigen (EMA) and cytokeratins while sarcomatous areas were positive for smooth muscle antigen (SMA) and vimentin; thus confirming diagnosis of MBC. Nuclear receptor analysis showed absolute negativity for estrogen, progesterone and HER2/neu receptors (triple-negative phenotype). According to AJCC, the patient was categorized as T4c, N3, M1 (stage 1V). He died of widespread metastases within 6 months of surgery despite completion of adjuvant chemoradiotherapy.

## DISCUSSION

Metaplastic breast carcinoma (MBC) is an exceedingly rare breast malignancy accounting for less than 1% of all variants of breast cancer.<sup>2</sup> It predominantly affects the women in their 5th and 6th decades of lives but its occurrence in the men is limited only to a few case reports thus verifying its absolute rarity.<sup>2,3</sup>

The exact aetiopathogenesis of MBC is still obscured. MBC is a quintessential example of the tumours arising from metaplastic transformation of poorly-differentiated adenocarcinomas into non-glandular stromal tumours. The term metaplastic carcinoma encompasses a heterogeneous group of the tumours having diversified internal morphologies. Structurally, MBC has two variants; pure epithelial and mixed variants. Pure epithelial variants include pure squamous cell and adenosquamous carcinomas while mixed variants are either monophasic (e.g. spindle cell carcinoma) or diphasic (e.g. carcinosarcomas). Carcinosarcomas (matrix-producing carcinomas) are poorly-differentiated adenocarcinomas admixed either with dominant areas of mesenchymal metaplasia (osteoid, chondroid, mucoid, myxoid, rhabdoid, fibroid, or transitional cell) or

frankly sarcomatous malignant tissue like osteosarcoma, chondrosarcoma, fibrosarcoma, liposarcoma, leiomyosarcoma, rhabdomyosarcoma, or malignant histiocytoma. MBC has strong tendency to metastasize by lymphogenous and haematogenous routes to the axillary lymph nodes, lungs, liver, bones, brain, thyroid and adrenals. As MBC arises from poorly-differentiated adenocarcinoma, it rarely expresses estrogen, progesterone and HER2/neu receptors (triple-negative disease). However, epidermal growth factor receptor (HER-1/EGFR) is frequently over-expressed by these tumours which may serve as a therapeutic target for EGFR inhibitors in future.<sup>1,4-8</sup>

The clinical diagnosis of MBC is hardly possible because of its non-specific presentations. It presents as hard breast lump with or without axillary lymphadenopathy and metastatic symptoms. Even sophisticated radiological imagings like breast sonography, mammography and MRI prove inconclusive in diagnosing MBC.<sup>9</sup> FNAC also yields indeterminate results. The exact diagnosis of MBC can only be established after painstaking efforts at histologic evaluation of core-tissue biopsies and mastectomy specimens and immunohistochemistry for tumour markers variously expressed by its indigenous components; the epithelial components express epithelial membrane antigens (EMA) and cytokeratins while stromal components express smooth muscle antigen (SMA) and vimentin.<sup>10</sup>

Surgery (modified radical mastectomy with axillary clearance), of course, is the mainstay of treatment of MBC. Despite being largely chemo- and radio-resistant, post-excision, adjuvant chemoradiotherapy is essentially given to all patients to minimize chances of locoregional and distant recurrences. A wide-spectrum of chemotherapy regimens have been advocated with contradictory results. Triple-negative variant of MBC (70%) responds to FAC (5-fluorouracil, adriamycin and cyclophosphamide) followed by taxanes.<sup>2</sup> While MBC expressing HER2/neu oncogene (30%) shows reasonable response to biological agents (trastuzumab, bivalacizumab, cetuximab, and lapatinib) which are humanized monoclonal antibodies selectively binding to the extracellular domain of HER2/neu receptors and blocking actions of various growth factors on tumour proliferation.<sup>8,9,10</sup>

Keeping in view its extreme rarity and diminutive long-term statistical data, it is hardly possible to draw definite conclusions regarding prognosis of MBC at the moment. A large tumour, high-nuclear grade, triple negative disease, lymphovascular invasion, positive nodal status and distant spread are aggressive tumour factors associated with its gloomy outcome.<sup>4,5,8,10</sup> The diagnosis of MBC can only be contemplated after its impeccable microscopic evaluation of tissue biopsies and irrefutable immunohistochemical staining for tumour markers.

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