Rare disease

Triple negative mixed metaplastic breast carcinoma with squamous and spindle cells in an 84-year-old woman: a rare entity with unclear management strategy and poor prognosis

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Summary

Metaplastic carcinoma of the breast, a rare neoplasm, usually presents at an advanced stage, metastasises to distant sites more frequently, has higher Ki-67 expression and is more often triple negative compared with other invasive breast cancers. Here, the authors discuss a case of an 84-year-old woman with triple negative mixed metaplastic breast carcinoma treated with radical modified mastectomy, axillary lymph node dissection and radiation therapy. Because of the rarity of the disease, the pathogenesis and the management remain controversial, thus contributing to overall poor prognosis.

BACKGROUND

Metaplastic carcinoma, a rare form of cancer accounting for <1% of invasive breast cancer,¹ is characterised by areas of metaplasia typically with squamous, spindle, osseous or chondroid differentiation in the background of adenocarcinoma.² WHO classification of metaplastic breast cancer includes: 1) pure epithelial metaplastic carcinomas which comprise of a) squamous cell carcinoma, b) adenocarcinoma with spindle cell metaplasia, c) adenosquamous carcinoma and d) mucoepidermoid carcinoma; and 2) mixed epithelial/mesenchymal metaplastic carcinomas.³ The rarity of the disease has precluded high-quality research aimed to explore the underlying pathogenesis of the disease and optimal management options, thus leading to poor outcome. Here, we discuss a case of metaplastic breast carcinoma in an older woman and review relevant literature.

CASE PRESENTATION

An 84-year-old Caucasian woman presented to the emergency department with a painless left breast mass progressively increasing in size since last 3 years associated with brown coloured nipple discharge. The patient had not sought any medical care for the condition and denied any screening mammogram in the past. The patient was otherwise healthy and did not have any family history of malignancy. She did not smoke, drink alcohol or use illicit drugs.

Physical examination revealed blood pressure of 120/58 mm Hg, pulse rate of 80/min, respiratory rate of 18/min and temperature of 99.3°F. Left breast examination showed inverted nipple as well as a 9 cm hard mass in the upper outer quadrant fixed to the overlying skin with a 1 cm central ulceration and serosanguinous discharge. There were no palpable axillary or cervical lymph nodes; right breast examination was unremarkable. The rest of the physical examination was normal.

INVESTIGATIONS

Haemogram, glucose, electrolytes, renal and liver function tests were within normal limits. Positron emission tomography (PET)/CT showed pathological uptake within a heterogeneous 7.3×5.1 cm left breast soft tissue mass (maximum SUV of 24.8) and focal uptake within the left axilla (maximum SUV of 3.0); there was no uptake elsewhere (figures 1 and 2). Core biopsy revealed metaplastic carcinoma with squamous and spindle cells with less than 10% of tumour area forming glandular structures. Immunohistochemistry was positive for pancytokeratin, cytokeratin 7, CAM5.2, p63 and vimentin and negative for oestrogen receptor, progesterone receptor and human epidermal growth factor receptor (her2/neu).

Figure 1 CT (axial view) showing 7.3×5.1 cm left breast soft tissue mass.

Figure 2 Positron emission tomography (coronal view) showing pathological uptake within the left breast soft tissue mass.

TREATMENT

The patient refused neoadjuvant chemotherapy and subsequently underwent modified radical mastectomy of the left breast with axillary lymph node dissection; 19 lymph nodes were examined for metastasis. The pathological examination of the mastectomy specimen confirmed the previous findings; resected axillary lymph nodes did not show any metastasis. Thus, the diagnosis of stage III B (T4bN0M0)

triple negative metaplastic breast carcinoma was established. The patient was counselled about different management options and was recommended to get enrolled in a clinical trial. She chose not to receive chemotherapy and subsequently underwent local radiation therapy.

OUTCOME AND FOLLOW-UP

The patient is doing well at 3-month follow-up and is being followed closely.

DISCUSSION

Metaplastic carcinoma of breast usually presents as a palpable breast mass⁴ in the fifth decade of life.⁵ The histological origin of the cancer remains controversial; whether it develops from the epithelial components of mammary tissue or it is the result of the squamous metaplasia in the setting of adenocarcinoma is currently unclear.³ As in our patient, metaplastic carcinoma usually presents with a larger tumour size,^{6,7} advanced stage,⁸ less frequent lymph node metastasis⁹ and more frequent distant metastasis,^{7,10} compared with other invasive breast cancers. Furthermore, metaplastic carcinoma has higher Ki-67 expression⁷ and higher basal-like phenotype^{11,12} and is more often triple negative.^{7,11,12}

Mammography shows high-density mass with variable margins whereas ultrasound may show microlobulated mass with complex echogenicity with solid and cystic components that correspond to necrosis and cystic degeneration seen in pathology.^{13,14} MRI, T2 weighted images show high signal intensity mass with malignant enhancement similar to those of infiltrating breast carcinoma.¹⁵ Although not specific, metaplastic breast cancer should be in the differential diagnosis in the presence of these radiographic findings. As illustrated by this case, it is highly PET avid which can be used for staging and follow-up as for other invasive breast cancer. The diagnosis is made by histopathological examination; however, fine needle aspiration cytology cannot be relied upon because of misdiagnosis in up to half of the cases.¹⁶ Immunohistochemistry, in addition to confirming the diagnosis, also plays important role in subtype categorisation as well as differentiation from other conditions such as phyllodes tumour and pure sarcoma. Detection of p63, for instance, has very high sensitivity (86.7%) and specificity (99.4%) for metaplastic carcinoma and helps in confirmation of the diagnosis.¹⁷ Immunohistochemistry is also positive for vimentin (mesenchymal cells), cytokeratin (epithelial cells) or myoepithelial cell markers (S-100 protein, actin, and high-molecular-weight cytokeratin); the presence of different cell lines establishes the diagnosis of mixed metaplastic carcinoma^{17–20} as in our patient.

Although there is a lack of high-quality data to support, surgery is considered the mainstay of treatment. Metaplastic carcinoma appears to be less responsive to chemotherapy or radiation,¹⁶ although platinum based chemo-regimens (such as 5-fluorouracil (5-FU) and cisplatin or 5-FU, doxorubicin and cisplatin) have shown some benefit in some cases of squamous cell carcinoma of breast.^{21,22} Since most of the cases of metaplastic carcinoma lack hormone receptors, there is no benefit of hormonal therapy. Epidermal growth factor receptor (HER-1) expression, however, is high in these tumours, thus they

might benefit from targeted therapy such as gefitinib^{21 23}; this should be studied. Recently, a phase I clinical trial among five patients with triple negative metaplastic carcinoma have shown promising benefit with liposomal doxorubicin, bevacizumab and temsirolimus,²⁴ which needs to be further confirmed in larger trials before it is routinely recommended.

The biological characteristics are more aggressive and outcomes are generally worse in metaplastic carcinoma.^{7 16 25} A recent study showed that metaplastic carcinoma was poor prognostic factor for disease recurrence and overall survival with significantly higher hazard rates (HR) compared with invasive ductal carcinoma (HR of 3.8 and 5.2 respectively) as well as to triple negative cancer (HR of 3.9 and 3.1 respectively).⁷ As in any other invasive breast cancers, tumour size, nodal involvement and distant metastasis (tumour, node and metastasis) are important prognostic factors for metaplastic carcinoma.⁷ Furthermore among metaplastic carcinoma, age less than 39, presence of skin invasion and presence of squamous cell component in the involved lymph nodes predict poor outcome.²⁵

Learning points

- Metaplastic breast carcinoma presents in an older patient with large tumour size, advanced stage disease and distant metastasis even in the absence of local lymph node involvement.
- The diagnosis can be confirmed by immunohistochemistry, which also plays important role in subtype categorisation as well as differentiation from other conditions such as phyllodes tumour and pure sarcoma. This includes identification of p63, which has very high sensitivity and specificity for the disease.
- Surgery is considered the mainstay of therapy; there is no consensus on adjuvant therapy and given the presence of the triple negative phenotype in most cases, hormonal therapy does not play major role in disease management.

Competing interests None.

Patient consent Obtained.

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