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FULL PAPER

Imaging overview of metaplastic carcinomas of the breast: a large study of 71 cases

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Objective: To review the clinical presentation, baseline imaging features, surgical management and final surgical pathology of metaplastic carcinoma of the breast.

Methods: A total of 71 cases were identified over a 10-year period from two major UK breast cancer institutions. Imaging at diagnosis including mammography, ultrasound, MRI and CT scans and histological diagnosis were reviewed. Follow-up data including local and systemic recurrence were retrieved.

Results: Of the 71 cases, 60 (84.5%) cases presented with a palpable lump. 60 (84.5%) cases showed a mass on mammography, of whom 47 (78.3%) cases were ill defined and 17.0% cases showed calcifications associated with a mass lesion. All 71 cases were seen as a mass on ultrasound. The imaging score was R3 or R4 in 26 cases and R5 in 47 cases. 16 patients underwent MRI with most

(93.8%) showing a solid mass with central necrosis. No metastatic disease was seen in the 13 patients who underwent staging CT. Despite having a larger size, 50% of the cases successfully underwent breast conservative surgery. Positive axillary lymph nodes were seen in 11 (15.5%) cases.

Conclusion: In this series, metaplastic cancers were palpable in 85% cases, tended to be large at the time of presentation and imaging showed characteristics of malignancy. Only 11 (15.5%) cases had nodal involvement.

Advances in knowledge: Metaplastic carcinomas are often palpable and of large size at the time of presentation. Metaplastic carcinomas raise the concern for malignancy on mammography and ultrasound, warranting further biopsy. Metaplastic carcinomas tend to be grade 3 and triple receptor negative.

INTRODUCTION

Modern treatment of breast cancer takes into account the heterogeneity of the disease and accordingly, each patient with breast cancer has a patient-specific treatment plan. The individual make-up of the cancer can allow clinicians to predict the likely prognosis and survival for the patient. Metaplastic carcinomas comprise 0.2–5% of all invasive breast carcinomas.¹ They consist of a heterogeneous group of invasive carcinomas characterized by an admixture of adenocarcinoma with dominant areas of spindle cell, squamous and/or mesenchymal differentiation. The metaplastic component, however, may exist in a pure form without any associated adenocarcinoma. Several histological classifications for metaplastic carcinoma exist. Previously described variants include spindle cell carcinoma,² matrix

producing carcinoma,³ squamous cell carcinoma⁴ and carcinoma with bizarre giant cells.⁵

The World Health Organization (WHO) officially recognized metaplastic breast cancer as a distinct pathological entity in 2000.⁶ The updated histological WHO classification¹ has been used to classify the metaplastic morphological subtypes into: squamous cell carcinoma, spindle cell carcinoma, low-grade adenosquamous carcinoma, metaplastic carcinoma with mesenchymal differentiation, fibromatosis-like metaplastic carcinoma, low-grade adenosquamous carcinoma and mixed metaplastic carcinoma. Spindle cell carcinoma in this series encompassed the fibromatosis-like and spindle cell carcinomas in the new WHO classification.¹

Table 1. Patient and tumour characteristics

Patient and tumour characteristics			Total
Age (years)	Median (range)	61 (41–93)	
Referral source	Screening	10	71
	Symptomatic	51	
	Interval	9	
	FHx	1	
P score ^a	1	3	71
	2	6	
	3	18	
	4	14	
	5	24	
	Not recorded	6	
R score ^b	1	0	71
	2	0	
	3	8	
	4	18	
	5	45	
Mammography size (mm)	<20	14	71
	20–50	36	
	>50	7	
	Not recorded	14	
Ultrasound size (mm)	<20	27	71
	20–50	38	
	>50	4	
	Not recorded	2	
MRI performed	Yes	16	71
	No	55	
MRI size (mm)	<20	1	16
	20–50	13	
	>50	2	
CT performed	Yes	12	71
	No	55	
	Not recorded	4	
Surgery	WLE	36	71
	Mastectomy	35	
LN surgery	SLNB	46	71
	ANC	17	
	ANS	4	
	No axilla surgery	4	
Size (mm)	<20	27	71
	20–50	37	
	>50	7	

(Continued)

Table 1. (Continued)

Patient and tumour characteristics			Total
Grade	1	2	71
	2	5	
	3	58	
Hormone receptor status ^c	ER		71
	Positive	6	
	Negative	64	
	Unknown	1	71
	PR		
	Positive	7	
	Negative	56	71
	Unknown	8	
	HER2		
	Positive	4	71
	Negative	60	
	Unknown	7	
LN stage	0	55	71
	1	9	
	2	2	
	Unknown/no LN surgery	5	
NPI	Excellent	1	71
	Good	3	
	Moderate	46	
	Poor	5	
	Post NACT/not recorded	16	
Local recurrence (breast/axilla)	Yes	7	71
	No	64	
Systemic recurrence	Yes	15	71
	No	56	
Survival	Alive	52	71
	Dead	19	
Survival time (months)	Median (IQ range)	53 (33–85)	

ANC, axillary node clearance; ANS, axillary node sample; ER, oestrogen receptor; FHx, family history; HER2, human epidermal growth factor receptor 2; IQ, interquartile; LN, lymph node; NACT, neoadjuvant chemotherapy; NPI, Nottingham prognostic index; PR, progesterone receptor; SLNB, sentinel lymph node biopsy; WLE wide local excision.

^aClinical palpation score.

^bUK radiological score.

^cHormone receptor positivity defined as Allred score 3/8 and above for ER and PR.

In view of the rarity of the lesion, there are limited data correlating the imaging findings with clinical presentation and histopathology.^{7–11} Metaplastic breast carcinomas were reported to display a biological behaviour different from that of invasive ductal carcinomas, were larger at presentation, were hormone and human epidermal growth factor receptor 2 (HER2) receptor negative, had a lower incidence of lymph node involvement¹² and had a poorer prognosis than ductal carcinomas of no special type.^{13,14}

These findings were similar to that of the non-imaging study performed by Pezzi et al,¹⁵ who identified 892 patients with metaplastic breast cancer from their National Cancer Data Base over a 3-year period. They found that compared with invasive ductal cancer, patients with metaplastic breast cancer presented with larger tumours, tended to be node negative and fewer patients were oestrogen receptor (ER) positive. When considering surgical and oncological management, breast-conserving

surgery was performed less and chemotherapy was used more often in the group of patients with metaplastic cancers. The findings by Pezzi *et al* were supported by Nelson *et al*¹⁶ who, using surveillance epidemiology and end results data, reported on the survival outcomes of 1011 metaplastic breast cancers. They showed that controlling for risk factors such as the large tumour size, surgical management and differing oncology treatment regimens through multivariate and matched analyses, lower survival rates in patients with metaplastic breast cancer persisted.

We report the clinical presentation, baseline imaging features, MRI and CT findings, surgical management and final surgical pathology of a large series of metaplastic carcinoma in two major UK centres over the last 10 years.

METHODS AND MATERIALS

This is a retrospective cohort study. We reviewed all cases that met with the WHO histological classification for metaplastic carcinomas.¹ Patients were identified from the pathology database from the Leeds Teaching Hospitals National Health Service

Figure 1. Mammographic abnormalities: (a) left mediolateral oblique (LMLO) view showing asymmetry in the upper half; (b) left craniocaudal (CC) view showing a spiculated mass; (c) left CC view showing a mass in the outer half which is predominantly well defined except anteriorly; and (d) right CC view of an ill-defined mass is seen in the outer half.

Table 2. Mammographic appearances of 69 cases

Mammographic abnormality	Number of cases	Size (mm) (range)
Mass	45	41 (10–76)
Mass with calcifications	10	26 (15–50)
Multifocal	5	41 (30–45)
Asymmetry	4	27 (20–40)
Calcifications	2	13 (11–15)
Asymmetry with calcifications	1	32
Normal	2	

Trust and Nottingham University Hospital over a 10-year period from 2001 to 2011.

A total of 71 cases were identified. There were no exclusions. Comprehensive pathological data including the tumour size, grade, lymph node status, ER, progesterone receptor and HER2 status were documented. The presence of associated ductal carcinoma *in situ* was also recorded.

The imaging and imaging reports, where imaging was not available, were reviewed by an experienced radiologist from each institution.

We collected details of the clinical presentation, clinical score (defined as the score given by the clinician when examining the breast, using the P1–5 scoring: P1 = normal, P2 = benign, P3 = indeterminate probably benign, P4 = suspicious for malignancy and P5 = cancer), imaging findings on mammography, ultrasound and MRI, radiological score (using UK classification of breast imaging Score 1–5),¹⁷ indications for and results of the staging CT scan and details of surgical treatment.

RESULTS

Presentation

In this series, metaplastic cancers were palpable in 87.3% (62/71) cases and tended to be large at the time of presentation, but only 15.5% (11/71) cases had nodal involvement, which is consistent with previous reports.

Of the 71 cases identified, 60 (84.5%) cases presented to the symptomatic breast clinic with a palpable lump. 9 (15%) of these patients had had a normal screening mammogram within 3 years and were therefore classified as interval cancers: defined as females of screening age who had a normal screening

mammogram and then presented with a cancer before their next routine screening mammogram.¹⁸ 10 (14.1%) patients were identified from the National Health Service Breast Screening Programme, of whom 7 patients had a palpable lump at the time of clinical examination. One patient was identified through higher risk surveillance MRI. Patient and tumour characteristics and clinical scores are summarized in [Table 1](#).

Mammography and ultrasound

Mammography was performed in all but two cases. The mammographic abnormalities are illustrated in [Figure 1](#) and are described in [Table 2](#).

The majority [60 (84.5%) cases] showed a mass on mammography with a mean size of 32 mm (range 10–76 mm). Of these, 47 (78.3%) cases were ill defined, 5 (8.3%) cases were well defined and 8 (13.3%) cases were spiculated ([Table 3](#)).

In 5 (8.3%) cases, the masses were recorded as being dense on mammography ([Figure 2](#)) and in 10 (16.7%) cases, the masses contained coarse calcification ([Figure 2](#)).

Ultrasound findings were documented in 69 cases; the mean size was 26 mm (range 3–70 mm). All were seen as masses; predominantly solid and ill defined, acoustic enhancement ([Figure 3](#)) was documented in three cases and shadowing in one case. Five were complex solid/cystic masses ([Figure 3](#)).

Ultrasound of the axilla identified abnormal nodes in five cases and equivocal nodes in nine cases. Malignancy was confirmed on cytology in 5/5 abnormal nodes and 2/9 equivocal nodes. Ultrasound of the axilla is now routine practice in patients presenting with primary breast cancer, but was not routinely

Table 3. Mammographic appearance of the 60 cases presenting as a mass lesion

Lesion	Margin description	Number of cases
Mass	Ill defined	37
Mass with calcifications	Ill defined	10
Mass	Spiculated	8
Mass	Well defined	5

Figure 2. Mammographic appearances: (a) left craniocaudal view showing a well-defined mass with increased density in the outer half of the left breast and (b) left mediolateral oblique view showing an irregular mass with coarse calcification.

performed in all the earlier cases. The final imaging score was R3 in 8 cases, R4 in 18 cases and R5 in 45 cases.¹⁹

MRI

In this study, a total of 16 patients had MRI performed during their routine management pathway. The majority of tumours were seen as a solid mass with some central necrosis on MRI [in 15/16 (93.8%) patients] and only 1 case was seen as an area of nodular enhancement. All masses showed mixed signal on the T_2 and T_1 weighted sequences (Figure 4a) and showed rim enhancement following i.v. contrast (Figure 4b).

MRI was performed in 16 patients either to determine the extent of the lesion prior to neoadjuvant chemotherapy (NACT) or as surveillance for a patient with BRCA mutation.

In the four patients who underwent MRI to determine the extent of the lesion, MRI findings correlated with conventional baseline imaging in two patients. MRI increased the disease extent in the ipsilateral breast in one case and mastectomy was therefore recommended and multifocal disease was confirmed on final histology. In the second patient, who had a previous wide local excision (WLE), MRI was performed to assess the appropriateness of mastectomy and it revealed a contralateral breast cancer (Figure 5). The index tumour measured 35 mm on MRI and the contralateral tumour measured 10 mm. The patient opted for bilateral mastectomy.

11 patients underwent MRI prior to NACT, with the index mass size ranging from 20–50 mm. It was multifocal in four cases. Three patients required a second-look ultrasound after additional

Figure 3. Ultrasound appearances: (a) a focal mass with posterior acoustic enhancement and (b) a well-defined complex mass with solid and cystic components. LT, left; PALP, palpable; RT, right.

Figure 4. MRI appearances: (a) a mass showing mixed signal on the T_2 weighted sequence and (b) a mass showing rim enhancement on the post-contrast subtracted early dynamic sequence. TE, echo time; TR, repetition time.

abnormalities were found on MRI two in the contralateral breast and one in the ipsilateral breast. In all cases, ultrasound confirmed benign lesions. There was a mixed response to NACT seen on MRI with 6/11 cases showing a partial response with concentric reduction in size (Figure 6). In four patients, tumours

Figure 5. MRI appearances in a patient showing contralateral breast cancer: (a) known left breast showing rim enhancement and (b) a contralateral 10-mm mass adjacent to the right pectoralis muscle. Second-look ultrasound with biopsy-confirmed carcinoma. TE, echo time; TR, repetition time.

Figure 6. MRI evidence of partial response to neoadjuvant chemotherapy: (a) the baseline scan showing a 35-mm focal irregular mass and (b) concentric reduction in the focal mass following two cycles of chemotherapy. TE, echo time; TR, repetition time.

were down sized to allow breast conservation while one patient showed disease progression while on NACT (Figure 7). Finally, one patient undergoing MRI for routine surveillance owing to

Figure 7. MRI evidence of disease progression on neoadjuvant chemotherapy: (a) the baseline scan showing a focal large rim-enhancing mass and (b) increase in the size of the mass following four cycles of chemotherapy. TE, echo time; TR, repetition time.

carrying a BRCA mutation showed non-specific nodular enhancement. A 6-month follow-up MRI showed increased bulk and MRI biopsy-confirmed cancer. This patient underwent a bilateral mastectomy.

CT staging

No evidence of metastatic disease was seen in the 12 patients who underwent a staging CT scan.

Surgery

35 patients underwent mastectomy and 36 patients underwent WLE, of whom 2 patients had a further WLE to clear margins. Positive axillary lymph nodes were seen in 11/71 (15.5%) cases, of whom 50% were identified by pre-operative ultrasound axilla with needling and 5 of whom were identified following SLNB or axillary node sample.

Pathology

The majority, 82% of tumours, were of grade 3 differentiation, with only 7 tumours found to be grades 1 and 2 on final histology. The mean size was 27.1 mm (range 5–75 mm). Most tumours, 79%, were triple receptor negative. <10% were ER positive or HER2 positive. Lymphovascular permeation was confirmed in 22% of cases.

The Nottingham prognostic index was documented in 60 cases and ranged from 2.26 to 7.44. It was not calculated in the 11 patients who underwent NACT. All patients who underwent NACT were deemed to have a minimal or partial response on MRI and the final pathological cancer size was smaller than the MRI-estimated size (pre-NACT).

Follow-up

Patients were followed up for a median of 62 months (3–151 months). To date, 7 patients have developed a local recurrence (5 in the breast, 1 in the axilla and 1 in both the breast and later axilla) and 15 patients have developed systemic disease. Disease-free survival was 71 months and overall survival was 61 months (3–151 months). 19 patients have died and 52 patients are alive, 3 of whom have systemic disease.

DISCUSSION

We present a large and comprehensive radiological review of metaplastic breast cancer.

While anecdotally metaplastic cancers were previously commonly mistaken radiologically for benign lesions,^{7–9} over 90% of metaplastic cancers in the present series raised concern for malignancy on imaging. Breast cancers commonly present as

spiculated masses but in our series, the commonest presentation for metaplastic carcinomas was that of an ill-defined mass. This may be because they are often rapidly growing, grade 3 tumours with less desmoplastic reaction. Like Choi et al and Yang et al, we found metaplastic breast cancer to present with slightly larger, grade 3 and triple receptor-negative pathology.^{11,12} However, they conclude that metaplastic carcinomas display more radiological benign features than ductal carcinoma. This is quite different to our radiological findings.

Pathological assessment remains the gold standard for diagnosing metaplastic carcinoma. While there are no specific radiological features for this type of breast cancer, our results show that they can be identified as suspicious for malignancy in the majority of cases.

In our series, standard imaging, mammography combined with ultrasound, was sensitive in picking up all abnormalities (R3–5 in 100%). Ultrasound of the axilla was effective in picking up abnormal lymph nodes, with 100% of abnormal nodes on ultrasound positive on ANC.

Despite presenting with larger tumours, 50% had breast conservation surgery. NACT does have a role to play in patients with metaplastic carcinomas, particularly if they are unifocal and large at the initial presentation as in our series where over half of the patients showed a response to chemotherapy and four patients were then able to undergo breast conservation. The tumours tended to respond by concentric reduction in size. These cases should be discussed within the multidisciplinary team, and in our units patients having NACT are monitored using MRI.

By default, most patients tended to fall into the moderate or poor prognostic group because of their size and grade, but none in our series had distant metastases at the time of presentation.

In conclusion, metaplastic carcinomas are rare tumours that often present as palpable lumps with corresponding signs suggestive of malignancy on mammography and ultrasound and therefore will warrant further investigation to make the diagnosis. They are often grade 3 tumours that are triple negative and therefore require treatment with chemotherapy. MRI outlines the extent of disease well and is useful in monitoring response to NACT. Those tumours respond by showing concentric reduction in size, aiding breast conservation. Although they are histologically poor prognosis tumours,^{20,21} in this series they appear to have a lower incidence of nodal involvement when compared with grade 3 invasive ductal carcinomas.

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