

## Metaplastic breast cancer

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### SUMMARY

Metaplastic breast carcinoma is uncommon and constitutes less than 5% of all breast cancers. The cancerous epithelium becomes non-glandular through metaplastic differentiation. There are various subtypes and the extent to which this process occurs varies. A case of a 52-year-old female patient is reported and the published literature is reviewed.

**Key words:** *breast cancer; breast screening; breast ultrasound; mammography; metaplastic cancer.*

A 52-year-old woman was recalled to BreastScreen Auckland after a routine screening mammogram in November 2001. The lesion for assessment was a discrete mass in the right upper inner breast with associated calcification. She was asymptomatic, had no prior history of breast problems and no family history of breast cancer. She was not on hormone replacement therapy. Her last mammogram was in 1999 and it was clear.

At assessment, clinical examination, additional mammographic views, and ultrasound examination were performed. Clinical examination was normal. The mammogram showed a new 12 × 10 mm mass with associated microcalcifications in the right upper inner breast at 2 o'clock (Fig. 1). The mass appeared well circumscribed although the associated calcification appeared indeterminate in type (Fig. 2). Ultrasound showed a deep, well-marginated hypoechoic lesion (Fig. 3). A 14-gauge core biopsy was performed. The result was infiltrating carcinoma with possible metaplasia.

The patient underwent a right partial mastectomy and sentinel node biopsy. Final histology showed a 10 mm poorly differentiated Grade 3 carcinoma with metaplastic features. Poorly differentiated epithelial cells were seen surrounded by pleomorphic spindle cells (Fig. 4). The margins were clear. The specimen was extensive intraductal component (EIC) negative and oestrogen and progesterone receptor negative. The two

sentinel nodes identified were free of tumour on routine examination and immunohistochemical stains.

Following operation, the patient underwent four cycles of doxorubicin and cyclophosphamide chemotherapy and radiotherapy to the right breast. She is currently being followed up according to routine postoperative protocols.

### DISCUSSION

Metaplastic breast carcinoma is uncommon. It is thought to constitute between 0.2<sup>1</sup> and 5%<sup>2</sup> of all breast cancers. The term describes a range of cancers of mixed epithelial and mesenchymal origin.<sup>2–5</sup> Histologically, the neoplastic epithelial cells show non-glandular differentiation. How this occurs is not well understood. The degree of differentiation varies from small foci to complete glandular replacement.<sup>3,6</sup>

Microscopically, the tumour can show a pure spindle cell pattern or mixed epithelial and mesenchymal pattern. The epithelial component is often of a ductal, non-specific type pattern but may also have squamous features or apocrine, medullary and mucinous patterns. Associated ductal carcinoma *in situ* might be present in 50% of cases.<sup>5</sup> The mesenchymal elements in mixed metaplastic carcinoma are usually fibro-sarcomatous but bone, cartilage, muscle and vascular components can be present.

The differential diagnosis of metaplastic carcinoma includes other common and rare primary breast cancers, lymphoma,

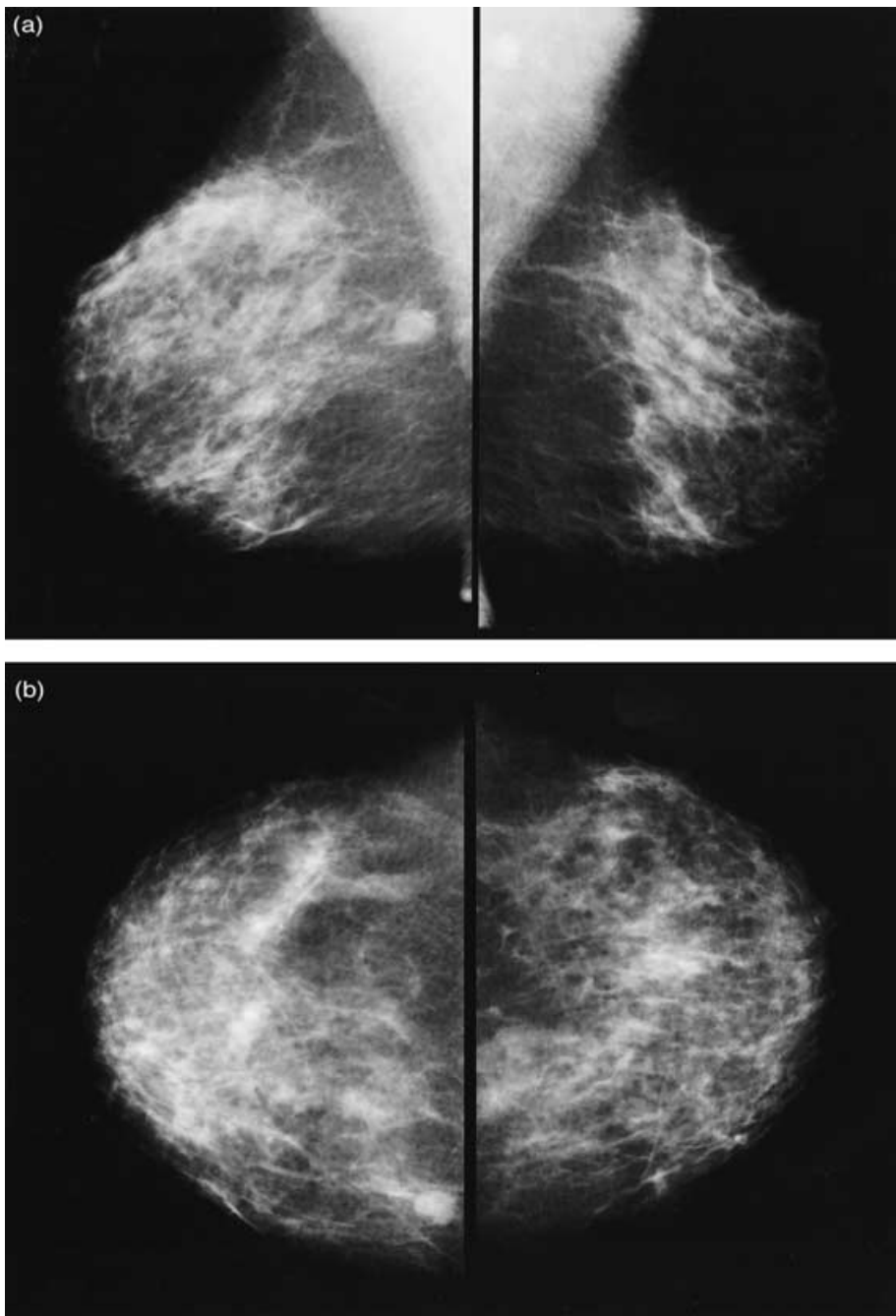
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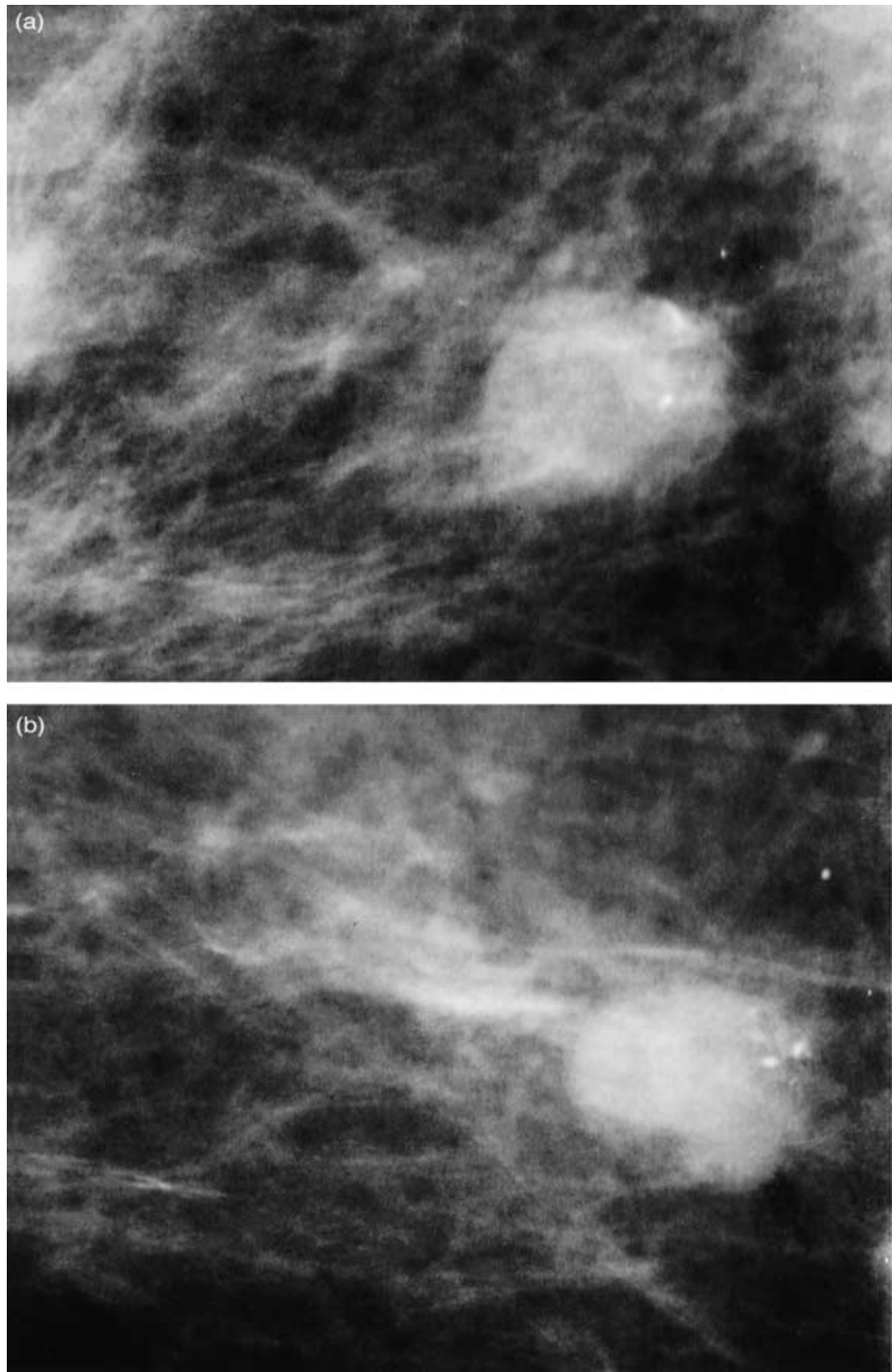
**Fig. 1.** (a) Medial-lateral oblique and (b) cranio-caudal mammography views demonstrating a discrete mass in the right upper inner breast.

malignant phyllodes tumour, metastatic carcinoma and some benign entities. The correct diagnosis relies on immunocytochemistry.<sup>5</sup>

Clinically, the usual presentation is with a mass.<sup>7</sup> The age distribution is as for breast cancer in general. Most articles in the published literature present large palpable masses.<sup>7</sup> A study from Edinburgh cites tumour sizes of 2.2–10 cm,<sup>8</sup> a study from South Korea states that all patients presented with

palpable masses and mean tumour size was 4.2 cm,<sup>9</sup> and a study from Taipei presents patients with metaplastic carcinomas ranging from 2.5 to 18 cm (median 4.8 cm) in size.<sup>10</sup> Data are sparse on smaller tumours, especially those detected by mammographic screening. A study from the Mayo Clinic retrospectively looked at patients diagnosed with metaplastic breast cancer between 1976 and 1997. Median tumour size in this study was only 3.4 cm with a range from 0.5 to 7.0 cm<sup>11</sup> As

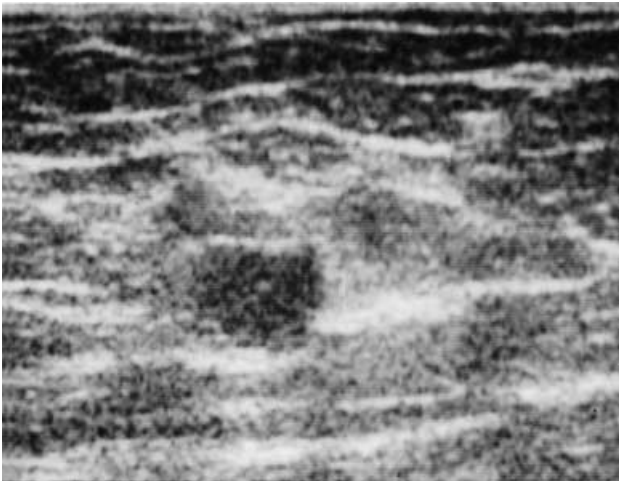
**Fig. 2.** Magnification views in both true (a) lateral and (b) cranio-caudal planes demonstrating the mass with associated calcification and an ill-defined inferior border anteriorly.



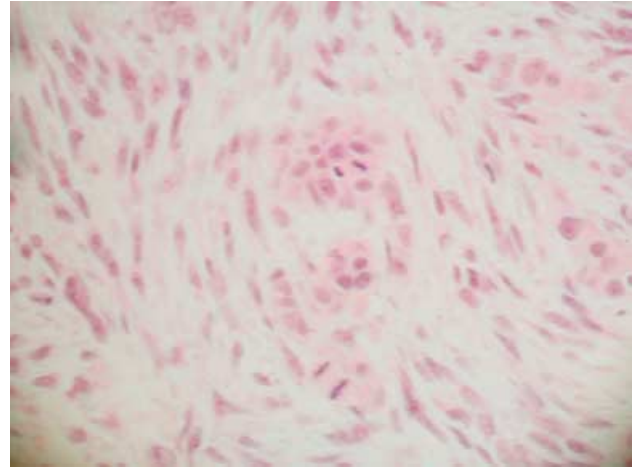
would be expected, a study from Nottingham, England also shows substantially smaller lesions, two of five being detected by routine screening. The mean lesion size in this series is only 1.6 cm with a range from 0.7 to 2.4 cm.<sup>12</sup>

There are no known specific radiological features of metaplastic breast cancer. Most cases have presented with masses on mammography. These vary from relatively well defined to ill defined and spiculated. The study of 16 patients

analyzed retrospectively in South Korea found 15 masses and one clustered calcification without an associated mass.<sup>9</sup> Eleven of the 15 masses were round to ovoid, 13 had ill-defined margins and 10 had associated architectural distortion. On ultrasound, only 11 lesions were seen. Six were round to ovoid, nine were well-defined, and six were of mixed solid/cystic echotexture. A study from Santa Monica reviewed only three patients.<sup>13</sup> The mammographic features ranged



**Fig. 3.** Ultrasound view of a discrete hypoechoic mass. (Standard linear array small parts probe 7–13 MHz). Apart from a small superior lobulation, the mass appears ovoid and mainly well defined.



**Fig. 4.** High power histology slide showing nests of malignant epithelial cells between malignant spindle shaped cells.

from well-defined to spiculated masses. A study from University of Michigan Medical Center concluded that metaplastic carcinomas are usually masses of low suspicion on mammography, and it should be included in the differential diagnosis of predominantly circumscribed, non-calcified masses.<sup>14</sup> The authors offered that a salient feature may be the occurrence of a circumscribed portion with a spiculated portion, which is seen in carcinomas with a significant mixture of metaplastic and invasive components.

The aetiology of this rare type of breast cancer is unknown. The study from Nottingham reported five cases where metaplastic carcinoma was seen to arise in a complex sclerosing lesion.<sup>12</sup>

There are no data on specific treatment for metastatic breast cancer.<sup>3</sup> The determination of prognosis for metaplastic breast carcinoma is limited by the uncommon occurrence of this cancer. In a study of 29 metaplastic breast carcinomas from Michigan, it was suggested that prognosis best correlated with the size of the lesion rather than with the nodal status.<sup>15</sup> The study indicated that patients with tumours less than 4 cm had a better prognosis than those with larger lesions. Nodal metastasis was noted to be relatively rare and thought to be of lesser importance. Microscopic pattern had no correlation with prognosis. Tumour size, nodal status, grade, histological type and treatment are the usual determinants of prognosis. Most data suggest metaplasia confers a poorer prognosis. The Mayo Clinic study reported on 27 patients retrospectively.<sup>11</sup> The study concluded that although metaplastic carcinoma more commonly presents with node-negative disease, disease-free survival and overall survival

are decreased compared with typical adenocarcinomas. They also concluded that systemic therapy appears to be less effective in this group of patients. The degree of differentiation and morphological type might also affect outcome. Previous studies show 5-year survival rates ranging from 38 to 86%.<sup>5</sup> The study from Taipei shows different findings and a different conclusion.<sup>10</sup> Of 14 patients studied retrospectively, seven had nodal metastases at the time of surgery. The study concluded that duration of symptoms, TNM stage, tumour size, and nodal status were significant prognostic factors for survival. The conclusion was that patients with metaplastic carcinomas might have a favourable prognosis (despite the histological type).

## CONCLUSION

The published literature review of the entity of metaplastic carcinoma identifies a number of interesting findings. Most lesions are large at presentation. This appears to be more likely as a result of the retrospective nature of the studies and the absence of mammographic screening programmes in some of the populations studied than because of the nature of the disease. Mammographic findings generally show a circumscribed mass more commonly than a spiculated mass. The common finding of node negativity (despite relatively large lesions) appears to be a valid observation. Prognostic indicators are difficult to assess given slightly conflicting findings and relatively small study series. It appears that current evidence-based medicine indicates that these patients should be treated the same as patients with the more common forms of breast cancer and followed up routinely.

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