

# Metaplastic Breast Carcinoma with Unusual Presentation: Review of Three Cases

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## Established Facts

- Metaplastic breast carcinoma is an uncommon type of breast cancer that usually appears as a large, fast growing breast lump.

## Novel Insights

- Metaplastic breast carcinoma may present unusually as a non-palpable lump.

## Keywords

Breast cancer · Metaplastic carcinoma ·  
Clinical presentation

## Summary

**Background:** Metaplastic breast carcinoma is an uncommon type of breast cancer that usually appears as a large, fast growing breast lump. **Case Report:** We report 3 cases of metaplastic breast carcinoma presented at our clinic in 2014. The mean age at diagnosis was 67.3 years. 1 patient presented with a fast growing, large mass detected by herself. However, in the other 2 patients, the nodule was approximately 1.5 cm in size, not fast growing, and was detected on mammography. All 3 patients were treated surgically (2 lumpectomies and 1 mastectomy), with the final pathology of metaplastic carcinoma with chondroid mesenchymal differentiation in 2 cases and metaplastic carcinoma with myoepithelial differentiation in the 3rd case. The patients are still under adjuvant therapy. **Conclusions:** Metaplastic breast carcinoma may present unusually as a non-palpable lump. This entity must be considered in any breast lump.

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## Introduction

The metaplastic breast carcinoma is a rare malignancy with an incidence of 5% of all breast tumors [1, 2]. It originates from a change in the differentiation of epithelial metaplastic breast tissue cells to squamous cell, spindle cell and/or mesenchymal appearance [3].

The metaplastic component can be benign or malignant. The differentiation degree and proportion of the elements shown in these tumors are highly variable and are visualized using immunohistochemistry and structural analysis [4].

From the pathological point of view, the latest World Health Organization (WHO) classification [3] included the following carcinomas within this group of neoplasms: adenosquamous carcinoma of low-grade fibromatosis type; metaplastic carcinoma; squamous cell carcinoma; and spindle cell carcinoma with chondroid mesenchymal, bone, or other mesenchymal tissue differentiation. In this latest ranking, the myoepithelial carcinoma was newly included within the metaplastic carcinomas [3].

The clinical, pathologic, and imaging diagnosis is complex. It is important to make a proper differential diagnosis since this determines the type of treatment to apply and the prognosis of the patient [4, 5].

Due to limited cases in the literature, there is no general consensus on the diagnosis and treatment, and it is difficult to draw definitive conclusions [4, 5], especially when making decisions about treatment [6, 7]. Most often, complete removal of the lesion is indicated and the definitive diagnosis is deferred to after histological study [8].

We present a comparison of the 3 cases that have occurred in our hospital in 2014, describing the most representative differences.

## Case Report

In 2014, at the University Hospital of Burgos, 3 cases of metaplastic breast carcinoma were diagnosed and treated.

A detailed medical history with personal and family history was taken, and examination of both breasts reflecting the clinical classification was performed in all 3 patients. As complementary tests, mammography and ultrasound-guided breast biopsy (UGB), magnetic resonance imaging (MRI), blood count, biochemistry including liver function, tumor markers (carcinoembryonic antigen (CEA), cancer antigen (CA) 15.3), bone scan, abdominal ultrasound, and thorax radiography were performed in each case. All women were treated surgically. All these data are summarized in table 1.

The histological diagnosis in 2 of the patients was metaplastic carcinoma with chondroid mesenchymal differentiation, and in the 3rd case, it was metaplastic carcinoma with myoepithelial differentiation.

Institutional review board (IRB) approval was obtained and the patients provided their oral consent.

## Discussion

Metaplastic breast carcinoma is a rare tumor (5% malignancies) [6, 7], and when considering only the mesenchymal metaplastic carcinomas with differentiation, they represent 1% of the incidence of invasive breast carcinoma [3]. The true incidence is unknown because sometimes solitary loci were found that were not reflected in the pathology reports [8, 9].

Its nomenclature is also problematic because it has received different names throughout history and different authors have referred to this group of neoplasms using different terms, including carcinosarcoma, sarcomatoid carcinoma, carcinoma with pseudosarcomatous metaplasia, carcinoma with pseudosarcomatous stroma, carcinoma producer matrix, fusiform carcinoma, myoepithelial carcinoma, etc. [3, 5].

Metaplastic breast carcinoma most often affects women over 50 years of age, with an average age between 55 and 60 years [10–12].

The most common form of presentation is a palpable mass with rapid growth, which may begin in any quadrant and is usually well circumscribed. Involvement sometimes can reach a size that may lead to ulceration and fixing of the mass to the skin or chest wall [13]. Most often, the mass is detected by the patient herself and not in a screening program. There are reports of occurrence during pregnancy and of presentation as inflammatory carcinoma [14].

Neither mammograms nor breast ultrasound have provided specific images, but have demonstrated that the tumors are usually well circumscribed, generally without associated microcalcifications, but sometimes some portion of irregular contour appears upon mammography [1, 10].

Most breast tumors, both benign and malignant, have their origin in the mammary epithelium, which in the case of metaplastic carcinoma differentiates in other tissues (metaplasia). This differentiation is corroborated with the help of immunohistochemistry [7, 15]. In the literature, the presence of squamous metaplasia is documented in 3.7% of invasive breast carcinomas, and heterologous metaplasia (usually bone or cartilage) at 0.2%, although the latter is most frequently described when present [16, 17].

The metaplastic carcinomas according to the latest edition of the WHO classification (2012) can be distinguished as: purely epithelial carcinomas (adenosquamous carcinoma of low-grade fibromatosis type, metaplastic carcinoma, squamous cell carcinoma, spindle cell carcinoma), carcinomas in epithelial and mesenchymal elements (carcinoma with chondroid mesenchymal differentiation, marrow, or other mesenchymal differentiation), and myoepithelial carcinomas (which are included within the novel metaplastic carcinomas in the last WHO classification) [3].

Among the differential diagnoses, angiosarcoma, fibromatosis and mesenchymal spindle cell tumors, pleomorphic adenoma and pleomorphic carcinoma must be considered, which is useful for immunohistochemical studies allowing the demonstration that this group of neoplasms is of epithelial origin (cytokeratin 5/6 positive) [3]. A proper diagnosis is important to establish the treatment and prognosis of the patient [16].

In a recent publication, metaplastic breast carcinoma has been associated with radial scars or complex sclerosing lesions, which are low-grade adenosquamous carcinomas. The precise nature of this association is unclear [18].

As for hormone receptors and prognostic markers, metaplastic carcinomas are triple negative in 90% of cases (estrogen receptor-, progesterone receptor-, and human epidermal growth factor receptor 2 (HER2)-negative cases) [3, 11]. This is because they are often associated with poorly differentiated carcinomatous elements [13].

Axillary lymph node involvement is usually not given. These metastases have an incidence ranging from 6 to 25% [12, 13, 17]. In non-metaplastic carcinomas, the frequency is higher (up to 47%) but still lower than in sarcomas [19].

Although we do not have a long record of these cases to know the prognosis, we can determine that survival depends on the tumor size (factor of greatest risk, because in tumors above 5 cm, the prognosis worsens), histology, the degree of tumor differentiation, the type and degree of the mesenchymal component, and the existence of axillary lymph node metastases and distant metastases.

Although there is no axillary involvement, there is a tendency to pulmonary metastases; so the tumor/node/metastasis (TNM) staging system is of little use as a prognostic factor. Most distant metastases occur through the blood, most frequently affecting the pleura, lungs, liver, and abdominal viscera [2, 8, 12].

Survival at 5 years may vary from 38 to 65% [8, 13, 17], and over 50% of the local and/or distant recurrences appear before that time.

The treatment is surgical initially, with lymphadenectomy plus sentinel lymph node biopsy (SLNB) or radical mastectomy being the most common treatments, although as mentioned above the frequency of lymph node involvement is low but higher than in sarcomas.

**Table 1.** Patient characteristics

Patient	1	2	3
Age, years	48	98	56
Reason for consultation	painful nodule in the contralateral breast during follow-up of a benign lump in the affected breast	fast-growing nodule in breast, enlargement accompanied by skin changes	derived from the screening program due to a BI-RADS 3b1 by nodule or mass
Clinical examination	palpable nodule of 1.5 cm, regular, medium consistency, located in the upper external quadrant (already known); no tangible lymphadenopathy	increased breast size, tension; a nodule of soft consistency is palpable and occupies the entire breast, with signs of inflammation in the skin, which is thin and fragile and has increased vascularity	palpable nodule is hard, mobile, with well-defined consistency; greater than 1 cm
Mammography	dense pattern, patchy, pseudonodular; nodules in both breasts, 1 in the upper external quadrant, retroareolar in affected breast; multiple bilateral scattered microcalcifications with benign characteristics	not made	mixed radiological pattern; predominance of glandular tissue of medium density with benign nodules; characteristics affect breast where there is also a faint increase in density in the upper external quadrant
Ultrasound	solid and polylobed nodule of 22 × 13 mm, located in the upper external quadrant, probably benign (BI-RADS 3); UGB was performed because not described in previous studies; bilateral simple cysts	very heterogeneous pattern with destruction of normal ultrasound breast pattern; mainly consisting of cystic areas having multiple echoes inside low impedance with anfractuous walls and increased peripheral vasculature, affecting all quadrants of the breast both in depth and surface	solid or mixed node of 15 × 13 mm in affected breast in the upper external quadrant, very indefinite contours, with peripheral vasculature, shadow interface and irregular subsequent reinforcement; subcentimeter simple bilateral cysts
MRI	cancerous nodule in union of upper quadrants of 23 mm; no involvement of skin, nipple or chest wall; ipsilateral axilla and normal mammary chains; 6 MRI BI-RADS unifocal	MRI not indicated by the advanced age of the patient and the indication of total mastectomy simple	single cancerous nodule of 15 mm in union of upper quadrants; nipple, skin, chest wall and ipsilateral axilla are normal; normal mammary chain; 6 MRI BI-RADS unifocal
Hormonal factors (estrogen and progesterone)	negative	negative	estrogen: weakly positive (3%); progesterone: negative
Prognostic factors	p53: positive 60%; HER2: negative; Ki-67: positive 40%; CK-19: positive	p53: positive 10%; HER2: negative; Ki-67: positive 40%; CK19: negative	p53: positive 30%; HER2: unknown ++; Ki-67: positive 50%; CK19: negative
Surgical treatment	lumpectomy + SLNB	total mastectomy simple	lumpectomy + SLNB
Histopathology	SLN: negative; lumpectomy: metaplastic carcinoma with chondroid mesenchymal differentiation; unifocal; poorly differentiated, grade III; resection margins respected; immunohistochemical study of hormone receptors and prognostic factors identical to the core needle biopsy	metaplastic carcinoma with myoepithelial differentiation with infiltration of all breast quadrants; infiltration of skin and nipple areola complex with neoplastic cells; perineural infiltration without apparent vascular invasion; extensive necrosis	sentinel node (× 2): negative; lumpectomy: poorly differentiated infiltrating ductal carcinoma, grade III, with focal component of metaplastic carcinoma with chondroid differentiation; preserved surgical margins; immunohistochemical study of hormone receptors and prognostic factors identical to the core needle biopsy; no amplification of the HER2/neu gene studied by SISH
Stage	pT1c N0 (0/2 sn) M0	pT3NxMx	pT1c pN0 (0/2 sn) M0
Adjuvant therapy	adriamycin-adjuvant cyclophosphamide every 3 weeks for 4 cycles followed by taxol weekly for 8 weeks; after chemotherapy 3D external radiotherapy is performed at 50 Gy + 16 Gy	no adjuvant therapy is given due to the advanced age of the patient	adriamycin-adjuvant cyclophosphamide every 3 weeks for 4 cycles followed by taxol weekly for 8 weeks; after chemotherapy 3D external radiotherapy is performed at 39.9 + 13.3 Gy

BI-RADS = Breast Imaging Report and Data System, UGB = ultrasound-guided breast biopsy, MRI = magnetic resonance imaging, HER2 = human epidermal growth factor receptor 2, CK = cytokeratin, SLNB = sentinel lymph node biopsy, SISH = silver in situ hybridization, 3D = 3-dimensional.

Due to the scarcity of case series, the utility of chemotherapy and radiotherapy could not be demonstrated, but the tendency is to treat these tumors as high-risk carcinomas, regardless of whether or not they present with axillary involvement [20].

### Disclosure Statement

There are no conflicts of interest for all authors.

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