Case Report

Metaplastic breast carcinoma with chondroid differentiation in a patient with prior ovarian carcinoma: A diagnostic dilemma

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ABSTRACT

Metaplastic breast carcinoma is a rare and aggressive subtype of invasive breast carcinoma accounting for <1% of all breast malignancies. Among its variants, chondroid differentiation is particularly uncommon. A 36-year-old female with a known history of ovarian carcinoma, post total abdominal hysterectomy with bilateral salpingo-oophorectomy, and multiple cycles of chemotherapy including bevacizumab, presented with a gradually increasing lump in the right breast upper outer quadrant of 2 months' duration. Fine-needle aspiration cytology confirmed malignancy. Sonomammography demonstrated a hypoechoic lesion (BIRADS IVA). Serial fluorodeoxyglucose-positron emission tomography (PET/CT) scans documented complete metabolic resolution of previously noted outer quadrant lesions, followed by a new low-grade metabolically active lesion, raising the possibility of a metachronous primary. As PET-CT alone cannot reliably distinguish metastatic disease from a metachronous primary malignancy, definitive diagnosis was established through histopathological examination and clinicopathological correlation. Wide local excision with right axillary clearance was performed. Histopathology revealed invasive carcinoma with a distinctive chondromyxoid stromal component and transition zones, consistent with metaplastic carcinoma with chondroid differentiation. All 15 axillary lymph nodes were free of tumor. This case highlights the diagnostic complexity of a rare breast tumor subtype in the setting of a prior gynecological malignancy.

Key words: Chondroid differentiation, Metaplastic breast carcinoma, Ovarian carcinoma, Thyroid swelling, Thyroiditis

Breast carcinoma is the most common malignancy among women globally. In India, the incidence rises sharply after the age of 30 years [1]. Among the histological subtypes, metaplastic breast carcinoma (MBC) is a rare and biologically aggressive variant, constituting <1% of all invasive breast carcinomas [2]. It is characterized by the transformation of neoplastic epithelium toward squamous or mesenchymal elements, including spindle, chondroid, and osseous differentiation. The chondroid variant specifically demonstrates invasive carcinoma merging with a chondromyxoid matrix, producing a biphasic histological pattern [3]. MBC was formally recognized as a distinct entity by the World Health Organization (WHO) in 2000 and was first described in 1973 [2]. It most commonly affects women over 50 years of age, typically presents as a rapidly growing palpable mass, and frequently exhibits a triple-negative immunophenotype (estrogen receptor [ER]/progesterone receptor [PR]/human epidermal growth factor receptor 2 [HER2]-negative), limiting the utility of targeted hormonal and biological therapies. Nodal involvement is less frequent compared to invasive ductal carcinoma of no special type, though hematogenous spread is characteristic [4]. The diagnostic challenge is considerably amplified when MBC occurs in a patient with a pre-existing gynecological malignancy, where breast metastasis from ovarian carcinoma must be rigorously excluded before a diagnosis of primary breast cancer is established.

We present a case of MBC with chondroid differentiation in a 36-year-old woman with a treated ovarian carcinoma, detailing the serial imaging surveillance, pathological findings, and clinicopathological reasoning that guided management. Most reported cases emphasize the clinical manifestations of salivary gland tumors; however, fewer reports highlight the potential for ultrasonographic findings to simulate thyroid malignancy. The present case demonstrates how early cytological evaluation resolved this diagnostic dilemma, prevented an unnecessary thyroidectomy, and reinforced the importance of integrating clinical, radiological, and cytopathological findings while evaluating painful thyroid swellings.

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CASE REPORT

A 36-year-old female presented to the surgical outpatient department with a 2-month history of a lump in the right breast, upper outer quadrant (UOQ). The lump had gradually increased in size from approximately pea-sized to 3 × 3 cm over this period and had initially been painless but subsequently became tender on touch. There was no history of trauma to the breast or chest wall, no features suggestive of metastatic disease (low backache or bone pain), and no history of fever, breathlessness, jaundice, or loss of consciousness. Specifically, there was no nipple discharge, skin ulceration, nipple retraction, contralateral lump, or axillary swelling. The patient had menarche at 13 years of age, married at 17 years, and was gravida 2, para 2, living 2 (P2L2). She had exclusively breastfed both children for 1 year each. There was no family history of breast carcinoma in first- or second-degree relatives and no history of combined oral contraceptive pill use.

The patient had a significant oncological history. She was diagnosed with ovarian carcinoma in 2022. A diagnostic laparotomy performed on February 27, 2022 resulted in excision of a large pelvic mass measuring 10 × 10 cm, which was adherent to and surrounding the transverse colon. Histopathology of the excised specimen was suggestive of ovarian malignancy. She subsequently received six cycles of chemotherapy from March 2023 to July 2023. Total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH+BSO) was performed on August 10, 2023. Postoperatively, she received a further six cycles of chemotherapy from July 2024 to February 2025, followed by bevacizumab (last administered on July 07, 2025). Cancer antigen 125 (CA-125) was 673 U/mL in October 2024. Ascitic fluid cytology performed in December 2024 was negative for malignant cells.

General examination revealed a pulse rate of 90 beats/min, blood pressure of 140/90 mmHg, SpO_2 99%, and respiratory rate of 20 breaths per minute. Systemic examination of the cardiovascular, respiratory, and central nervous systems was unremarkable. Per-abdominal examination revealed a well-healed laparotomy scar with a soft abdomen. On local examination, a 3 × 3 cm lump was identified in the right breast UOQ. It was hard in consistency, ill-defined, and tender. The overlying skin was normal with no puckering, dimpling, peau d'orange, or nipple changes. The lump was not freely mobile within breast tissue and was not fixed to the underlying pectoral muscle or chest wall. No axillary lymphadenopathy was palpable.

Routine hematological investigations demonstrated hemoglobin of 13.7 g/dL, total leucocyte count 8,500/mm^3, platelet count 2,21,000/mm^3, prothrombin time/international normalized ratio 15/1.1, random blood sugar 84 mg/dL, and normal renal and liver function tests. Serological screening (hepatitis B surface antigen, anti-hepatitis C virus, and human immunodeficiency virus) was negative. Fine-needle aspiration cytology (FNAC) from the right breast lump (C/8336/25) yielded a moderately cellular aspirate. Cells were arranged in tight clusters and irregular aggregates demonstrating high nuclear-to-cytoplasmic ratio, hyperchromatic nuclei, and marked hyperchromasia. Tumor giant cells were identified (Fig. 1). The cytological features were consistent with breast carcinoma.

The right breast demonstrated a well-defined, predominantly hypoechoic lesion measuring 9 × 14 × 16 mm with lobulated and irregular margins at the 9 o'clock position in the UOQ (Fig. 2). The lesion was located 5.7 mm from the skin surface and 3.3 cm from the nipple-areolar complex. A few left axillary lymph nodes were noted, the largest measuring 5 × 6 mm, with benign morphology. The overall radiological impression was BIRADS IVA – low suspicion for malignancy.

Serial FDG-PET/CT evaluation: This imaging played a critical role in characterizing the evolution of breast involvement. The first PET-CT (August 2023), performed following chemotherapy for ovarian carcinoma, revealed no significant finding in the thoracic region. The second PET-CT (October 2024), performed after TAH+BSO, identified metabolically active lesions in the outer quadrant of the breast, reported as likely metastatic deposits from ovarian carcinoma. The third PET-CT (March 2025), performed after further chemotherapy, demonstrated complete metabolic resolution of these outer quadrant lesions. The fourth PET-CT (July 2025) identified a new low-grade metabolically active lesion involving the right breast, distinct from the previously resolved lesions. Although the temporal appearance raised the possibility of a metachronous primary malignancy, PET-CT findings alone were insufficient to reliably differentiate metastatic disease from a new primary breast tumor. This finding, combined with the cytological confirmation of malignancy on FNAC, prompted surgical intervention, and the final diagnosis was established by histopathological examination and clinicopathological correlation.

Based on the integrated clinical, cytological, and radiological findings, the working diagnosis was right breast carcinoma, clinically staged as T2N0M0 (Stage IIA). Breast conservative surgery in the form of wide

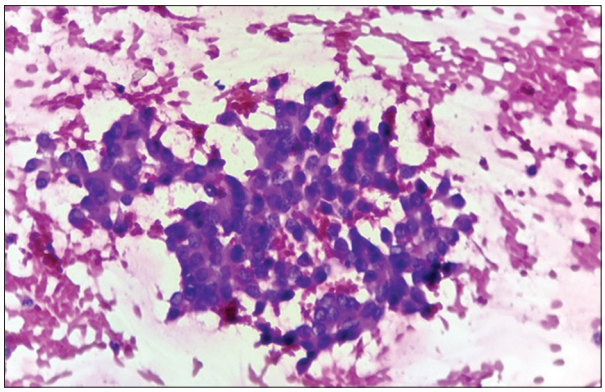


Figure 1: Malignant ductal epithelial cells with high N:C ratio in a hemorrhagic background. Note lack of bare bipolar nuclei in the background (Hematoxylin and eosin, 400)

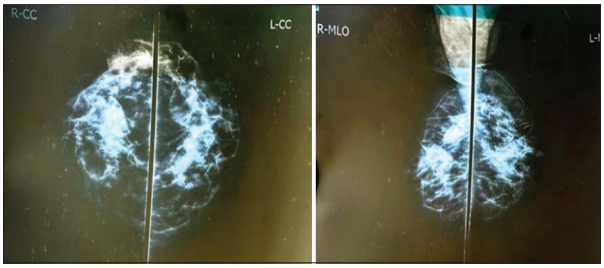


Figure 2: Sonomammography image from right breast mass depicting a circumscribed, hypoechoic lesion with lobulated and irregular margins at the 9 o'clock position in the upper outer quadrant

local excision of the right breast lump with right axillary clearance was performed.

The excised specimen comprised three tissue masses of the breast lump measuring 3.5 × 3.2 × 2.1 cm, 1.8 × 1.8 × 0.8 cm, and 3 × 1.5 × 1 cm, respectively with a combined weight of 28 grams. Cut sections of all masses revealed a gray-white, glistening, firm tumor. Five separately submitted surgical margins were received: superior (0.8 × 0.7 × 0.3 cm), inferior (1.3 × 0.8 × 0.3 cm), lateral (0.6 × 0.4 × 0.3 cm), medial (1.3 × 0.7 × 0.3 cm), and deep (1.4 × 0.7 × 0.8 cm) margins, all gray-white to gray-brown, soft to firm tissue pieces. The right axillary clearance specimen consisted of fibrofatty gray-yellow tissue aggregates measuring 7.5 × 6.1 × 1.8 cm and weighing 70 grams, within which serial sectioning revealed 15 lymph nodes, the largest measuring 0.8 × 0.6 × 0.3 cm.

Histological sections revealed breast tissue infiltrated by a malignant tumor with biphasic architecture (Fig. 3a). Additional findings included ductal carcinoma *in situ* (DCIS) in solid and cribriform patterns within the adjacent breast tissue (Fig. 3b). The malignant tumor cells were arranged in sheets and nests. The tumor was embedded within a chondromyxoid stroma with infiltration of adjacent fibroadipose tissue (Fig. 3c). The malignant cells were pleomorphic ductal epithelial cells exhibiting hyperchromatic nuclei, moderate nuclear pleomorphism, and scant to moderate cytoplasm (Fig. 3d). Crucially, a focal chondromyxoid stromal differentiation was identified, characterized by a pale bluish myxoid matrix in which tumor cells appeared embedded without forming distinct glands, with early cartilage-like matrix formation. Transition zones from the conventional carcinomatous component to the chondroid differentiation were clearly delineated, fulfilling the diagnostic criteria for metaplastic carcinoma. These transition zones demonstrated loss of the glandular pattern with progressive epithelial-to-stromal component transformation.

Regarding margin status, the tumor was found to reach up to the superior, lateral, and medial surgical margins; the DCIS component was identified in the inferior surgical margin; and the deep surgical margin was free of tumor. All 15 lymph nodes from the right axillary clearance were free of tumor metastasis (0/15 nodes positive).

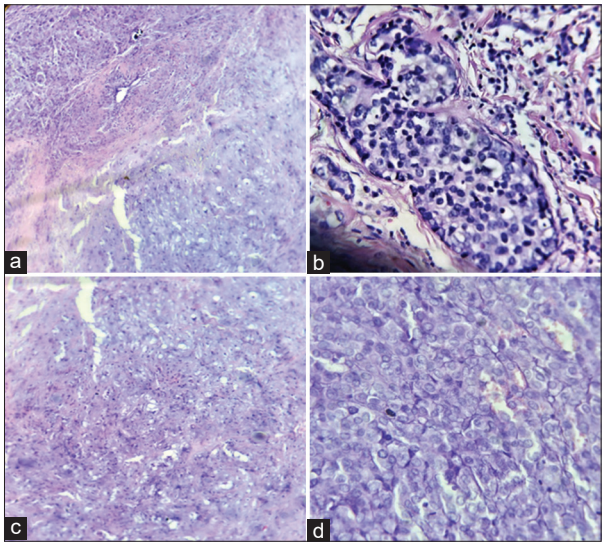


Figure 3: Microphotographs. (a) (Hematoxylin and Eosin [H&E], ×100): Tumor with biphasic architecture of cartilaginous (right) component with infiltrative malignant ductal carcinomatous component (left), (b) (H&E, ×400): Solid type of ductal carcinoma *in situ* component. (c) (H&E, ×400): Cartilaginous differentiation of tumor cells. (d) (H&E, ×400): Ductal carcinomatous cells in sheets

As described in the slides and consistent with the established immunohistochemistry (IHC) profile of metaplastic carcinoma with chondroid differentiation, the epithelial component was expected to demonstrate cytokeratin (CK/AE1-AE3) positivity, confirming the epithelial origin of the neoplastic cells. S100 protein positivity is characteristic of the chondroid areas in MBC. However, these IHC markers were not done due to patient's cost restraints. Nevertheless, on a routinely done breast IHC marker study, the patient's tumor lesion demonstrated a triple-negative immunophenotype (ER-negative, PR-negative, and HER2-negative).

DISCUSSION

MBC is a heterogeneous group of invasive breast tumors characterized by the differentiation of neoplastic epithelium toward squamous cells and/or mesenchymal-looking elements including spindle, chondroid, and osseous cells [2]. It accounts for 0.2–1% of all breast cancers and was formally recognized by the WHO as a distinct entity in 20003. The chondroid variant, as seen in the present case, is particularly rare and represents a diagnostic challenge even for experienced pathologists. The defining histological features – biphasic pattern, chondromyxoid matrix, and well-defined transition zones – were all demonstrated in this case.

The primary diagnostic dilemma in this patient was distinguishing a new primary breast malignancy from a metastatic deposit from her treated ovarian carcinoma. The PET-CT findings provided important temporal information but were not independently diagnostic. The October 2024 scan identified metabolically active lesions in the outer quadrant of the breast that raised the possibility of metastatic involvement from the ovarian primary, and these subsequently showed complete

metabolic resolution on the March 2025 scan following further chemotherapy. The July 2025 scan, however, demonstrated an entirely new low-grade metabolically active lesion in the right breast, a finding that warranted further pathological evaluation. This temporal pattern of complete resolution followed by a *de novo* lesion combined with the overall clinical context, CA-125 trend, negative ascitic fluid cytology, and most importantly the histopathological findings, favored the diagnosis of a metachronous primary breast carcinoma over ovarian metastasis.

Breast metastases from ovarian carcinoma are uncommon, accounting for <1% of breast malignancies, and typically present as multiple bilateral nodules rather than a solitary mass [5]. Histologically, ovarian metastases to the breast tend to show papillary architecture, psammoma bodies, and retain the immunophenotype of the primary (PAX-8 positive, WT1 positive, and CK7 positive), features absent in the present case. The identification of a chondromyxoid stroma with transition zones and a DCIS component in the current specimen are hallmarks of a primary breast neoplasm, as metastatic lesions do not generate DCIS.

Table 1 summarizes the differential diagnosis of metaplastic carcinoma from other biphasic and mesenchymal-appearing breast lesions including phyllodes tumor, primary breast sarcoma, metastatic sarcoma, adenomyoepithelioma, and myoepithelial carcinoma [5-7]. Phyllodes tumor was excluded by the absence of the characteristic leaf-like stromal architecture, and the lesion demonstrated epithelial malignancy on FNAC. Primary breast sarcoma was excluded by the presence of the epithelial carcinomatous component. The absence of a prior sarcoma history and the specific chondromyxoid morphology with transition zones differentiated this case from metastatic sarcoma.

The margin status in this case warrants clinical attention. Tumor involvement of the superior, lateral, and medial surgical margins, along with DCIS in the inferior margin, indicates incomplete excision and necessitates discussion at the multidisciplinary tumor board regarding re-excision or adjuvant radiotherapy. The deep surgical margin being clear is a favorable finding. Nodal negativity (0/15) is consistent with the recognized biology of MBC, which tends to spread hematogenously rather than through the lymphatic route.

MBC with triple-negative immunophenotype carries a poorer prognosis than conventional invasive ductal carcinoma. Hormonal and HER2-targeted therapies are ineffective, and chemotherapy remains the systemic treatment modality of choice. The unique complexity in this patient is the concurrent chronic exposure to bevacizumab for ovarian carcinoma management, which may have implications for wound healing and post-surgical complication rates. Close multidisciplinary coordination between breast surgery, medical oncology, and gynecological oncology is essential for optimizing the treatment plan [5-7].

BRCA1/2 genetic testing was not performed in the present case due to financial constraints. Given the patient's young age and the occurrence of both ovarian and breast carcinomas, referral for genetic counseling and consideration of germline BRCA1/2 testing would be clinically appropriate. Hereditary breast and ovarian cancer (HBOC) syndrome remains a relevant consideration in such patients. Women harboring a BRCA1 mutation carry a cumulative lifetime risk of breast cancer approaching 72% and an ovarian cancer risk of 44%, while BRCA2 mutation carriers face risks of approximately 69% and 17%, respectively [8]. The development of two distinct primary malignancies in a relatively young patient is therefore a strong clinical indicator for HBOC syndrome, and germline genetic evaluation is strongly recommended by current international guidelines including those of the National Comprehensive Cancer Network and the European Society for Medical Oncology.

From a pathobiological standpoint, BRCA1-associated breast carcinomas disproportionately exhibit a triple-negative and basal-like phenotype, and there is emerging evidence suggesting an association between BRCA1 dysfunction and metaplastic differentiation in breast carcinomas [9]. Several case series and molecular studies have reported BRCA1 pathway alterations in MBC, hypothesizing that defective homologous

Table 1: Condensed differential diagnosis of metaplastic carcinoma with chondroid differentiation from other biphasic and mesenchymal breast lesions

Feature	Phyllodes tumor	Primary breast sarcoma	Metastatic sarcoma	Adenomyoepithelioma	Myoepithelial carcinoma
Origin	Fibroepithelial	Mesenchymal malignant	Secondary tumor	Biphasic: Epithelial+ myoepithelial	Malignant myoepithelial proliferation
Age group	33–55 years	Adults (variable)	Depends on primary	Middle-aged women	Wide range
Microscopy	Leaf-like stromal pattern	No epithelial component	Resembles primary sarcoma	Dual cells: Glands+ myoepithelium	Solid, infiltrative growth
Key IHC	CD34+, stromal markers	Vimentin+, subtype-specific	Same as primary	CK+, p63+, SMA+	p63+, S100+, CK+, calponin+
Distinguishing feature versus present case	No leaf-like pattern in present case	Epithelial component present	No prior sarcoma history	No dual-cell population	DCIS present — confirms primary

IHC: Immunohistochemistry, DCIS: Ductal carcinoma *in situ*

recombination repair may contribute to the aberrant epithelial-to-mesenchymal transition that characterizes the metaplastic phenotype. While formal molecular profiling was not available in the present case, the clinical triad of young age at diagnosis, prior high-grade ovarian carcinoma, and triple-negative MBC constitutes a strong pre-test probability for BRCA1 germline mutation.

The clinical implications of BRCA testing in this context are substantial and extend beyond the individual patient. If a germline BRCA1/2 pathogenic variant is identified, it carries direct implications for surgical decision-making (consideration of risk-reducing contralateral mastectomy), systemic therapy selection (sensitivity to platinum-based chemotherapy and PARP inhibitors such as olaparib), and cascade genetic testing for first-degree relatives. The patient's young age further heightens the urgency of genetic counseling, as relatives who test positive can benefit from intensified breast surveillance, risk-reducing surgeries, and chemoprevention. It is strongly recommended that this patient be referred to a clinical genetics or genetic counseling service for germline BRCA1/2 testing at the earliest opportunity, irrespective of family history, given that up to 25% of BRCA mutation carriers report no significant family history of cancer [10].

CONCLUSION

We present a diagnostically challenging case of MBC with chondroid differentiation arising as a metachronous primary in a patient with a treated ovarian carcinoma. The case underscores the critical importance of serial FDG-PET/CT surveillance in patients with prior malignancy, as the temporal evolution of imaging findings was instrumental in distinguishing a new primary breast lesion from suspected ovarian metastasis.

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