Case Report

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Metaplastic breast carcinoma: a rare and aggressive entity

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Introduction: Breast cancer (BC) remains the most prevalent malignancy among women globally, encompassing a variety of tumor subtypes with differing biological behaviors, prognoses, and responses to treatment. Among these, invasive ductal carcinoma (IDC) is the most common, followed by other subtypes such as lobular carcinoma and triple-negative breast cancer. Metaplastic breast carcinoma (MpBC) is a rare and highly aggressive form of BC, representing less than 2% of cases. Characterized by its heterogeneous nature and poorer prognosis compared to other BC subtypes, MpBC often presents significant diagnostic and therapeutic challenges.

Case description: We present the case of a 70-year-old woman who presented to our breast care clinic with right mastodynia following a recent trauma. She reported a palpable retro-areolar mass in the right breast that had increased in size over several years and was associated with calcifications. Imaging studies, including mammography and ultrasound, revealed a 3-cm irregular, heavily calcified mass with indistinct borders. Histological analysis of a biopsy confirmed metaplastic carcinoma with chondrosarcoma and osteosarcoma elements, high histological grade, and lymphovascular involvement. The patient underwent successful tumor excision with sentinel lymph node removal. Adjuvant chemotherapy and radiotherapy were planned based on a multidisciplinary team's recommendations.

Discussion: MpBC typically presents as a palpable, irregular mass that may exhibit rapid growth or changes, often complicating its differentiation from other breast malignancies. Standard imaging techniques like mammography and ultrasound may fail to clearly distinguish MpBC from other tumors, leading to potential misdiagnosis. The heterogeneous nature of MpBC, with both epithelial and mesenchymal components, poses additional challenges in diagnosis and treatment. Although MpBC is generally more aggressive and less responsive to conventional therapies compared to IDC, recent analyses suggest that, when adjusted for confounding factors, survival outcomes for MpBC may align more closely with those of aggressive IDC subtypes. Current treatment strategies include surgery, chemotherapy, and radiotherapy, with emerging targeted therapies offering potential for improved outcomes.

Conclusion: MpBC remains a rare and challenging BC subtype with a typically poor prognosis. Our case highlights the diagnostic difficulties and the aggressive nature of MpBC. Despite its severe clinical features and histological grades, survival outcomes for MpBC may be comparable to those of aggressive IDC subtypes when appropriate treatment adjustments are made. Continued research into targeted therapies and novel treatment approaches is essential to enhance management strategies and improve outcomes for patients with MpBC.

Keywords: breast cancer, breast surgery, case report, diagnostic challenges, metaplastic breast carcinoma

Introduction

Breast cancer (BC) is the most prevalent malignancy among women globally, posing a major public health challenge due to its high incidence and mortality rates[1]. It includes a diverse group of tumors with varying biological behaviors, prognoses, and treatment responses. Among the various types of BC, invasive ductal carcinoma (IDC) is the most common, followed by other subtypes such as lobular carcinoma and triple-negative breast cancer (TNBC)[2].

HIGHLIGHTS

- Metaplastic breast carcinoma (MpBC) is a rare and highly aggressive subtype, making up less than 2% of breast cancer cases.
- MpBC is characterized by its heterogeneous nature and poorer prognosis compared to other breast cancer subtypes, presenting significant diagnostic and therapeutic challenges.
- Treatment strategies include surgery, chemotherapy, and radiotherapy, with emerging targeted therapies offering potential for improved outcomes.
- A multidisciplinary approach is crucial, and further research into targeted therapies and novel treatment modalities is essential to improve management and outcomes for MpBC patients.

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Metaplastic breast carcinoma (MpBC) is a rare and highly aggressive form of BC, accounting for less than 2% of all BC cases[3]. MpBC is distinct from more common types and is considered even more aggressive than TNBC[4]. The World Health Organization classifies MpBC into several subtypes, including squamous cell carcinoma, spindle cell carcinoma, fibromatosis-like metaplastic carcinoma, low-grade adenosquamous carcinoma, and carcinoma with chondroid, mesenchymal, or osseous differentiation[5].

Due to its rarity and heterogeneous nature, MpBC often poses significant diagnostic and therapeutic challenges, and its prognosis is generally poorer compared to other types of BC[6]. This case report presents a patient diagnosed with MpBC, highlighting the clinical presentation, diagnostic challenges, treatment approach, and outcomes, and aims to contribute to the limited body of literature on MpBC by providing insights into a recent case managed at our institution.

Case description

We present the case of a 70-year-old woman who presented to our breast care clinic for right mastodynia after a recent trauma. She reported a clinically palpable retro-areolar mass in the right breast, which she noted had recently increased in size. According to the patient, this calcified mass had been present for several years prior to the trauma. There was no personal or family history of breast or ovary cancer. She has surgical history of hysterectomy for benign lesion without post-menopausal hormonal replacement therapy.

Examination of the right breast revealed the induration of the retro-areolar breast without erythema, associated with a mild tenderness, but not with secretions, nipple retraction, or with palpable axillary lymph nodes. The rest of the physical exam was unremarkable.

Bilateral breast mammography is carried out and has shown an irregular mass of 3 cm in the retro-areolar region of the right breast with indistinct borders, strongly calcified with similarity with cartilaginous calcifications (Fig. 1A and 1B). An ultrasound was also conducted, revealing a well-encapsulated hypoechoic heterogeneous mass due to calcifications in the retro-areolar of the right breast (Fig. 2). Previous exams are not available for comparison.

Ultrasound-guided biopsy revealed a metaplastic carcinoma with heterologous elements of chondrosarcoma/osteosarcoma, Scarff–Bloom–Richardson (SBR) 6, grade II of malignancy according to Nottingham histological score, with Ki67 of 30%. The hormonal receptors were negative.

A breast magnetic resonnance imaging was performed, with T1-weighted imaging post-intravenous contrast administration and subtraction images, revealing a round mass in the retro-areolar region of the right breast. The mass exhibited heterogeneous nodular enhancement with a necrotic center (high signal on T2 weighted image), common but nonspecific feature of MpBC. No other associated lesions or enlarged lymph nodes were observed (Fig. 3). Computed tomography scan of the thorax, abdomen, and pelvis and bone scintigraphy showed no evidence of distant metastatic lesions (Fig. 4A–4C).

The operation has been planned. It went perfectly, by en bloc excision of the tumor, by a peri-areolar incision, with sentinel lymph nodes excision, performed by a board-certified surgeon. The patient expressed relief following the surgery, reassured by the successful removal of the tumor. She was discharged on the second day but had concerns regarding the aesthetic outcome and the potential for breast reconstruction in the future.

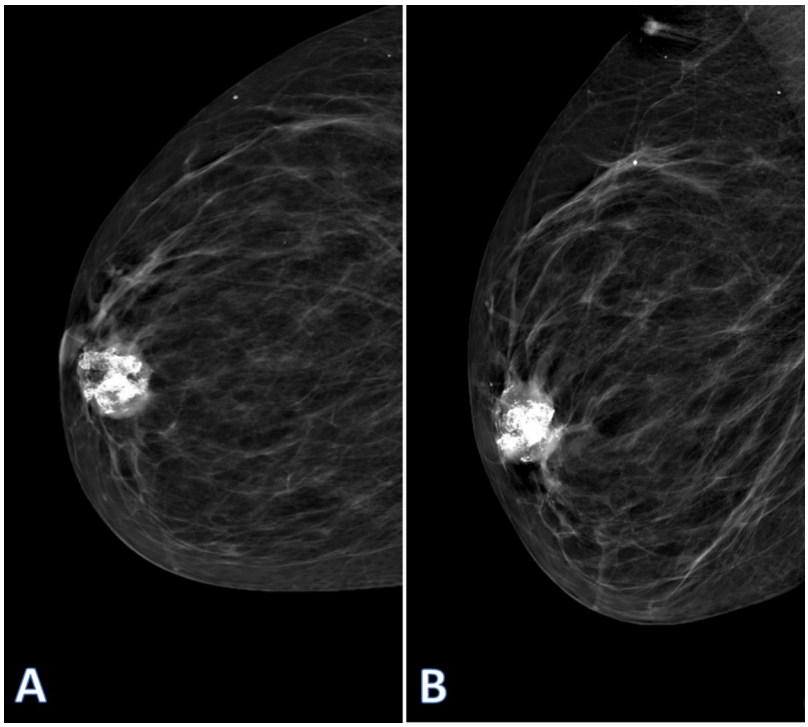

Figure 1. Cranio-caudal (A) and medio-lateral (B) mammographic views, showing an irregular 3-cm irregular heavily calcified mass in the retro-areolar region of the right breast with indistinct borders.

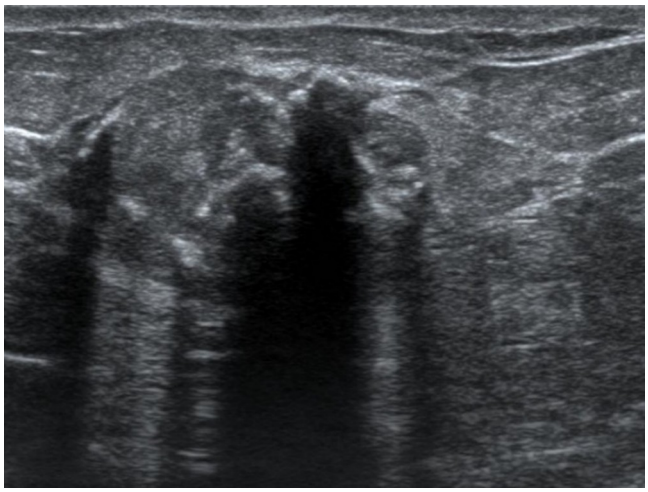

Figure 2. Ultrasound of the right breast showing a well-encapsulated hypoechoic heterogeneous mass due to calcifications in the retro-areolar area.

The final histological report confirmed the diagnosis of 2.5 cm metaplastic carcinoma with heterologous elements of chondrosarcoma and osteosarcoma, SBR 8, grade III of malignancy according to Nottingham histologic score, Ki67 of 50%, negative hormonal receptors, and with lympho-vascular involvement. There was also associated ductal carcinoma *in situ* with high nuclear grade, representing less than 5% of the tumoral volume. One of nine lymph nodes was invaded. The final pathological stage was pT2N1aM0 according to pathologic tumor-nodal-metastasis, American Joint Committee on Cancer 8th edition (Fig. 5).

The case was discussed in multidisciplinary team meeting and was scheduled for adjuvant chemotherapy with 3-fluorouracil, epirubicin, and cyclophosphamide-3 Taxotere and radiotherapy.

This case has been reported in line with the surgical case report guidlines criteria[7].

Discussion

The primary goal of this case report is to highlight the unique presentation and management of MpBC, a rare and aggressive subtype of BC. This report focuses on a patient diagnosed with high-grade MpBC, emphasizing the challenges associated with its diagnosis, histological characteristics, and treatment outcomes. The main findings demonstrate that the patient underwent successful tumor excision with sentinel lymph node removal, confirming lymph node involvement through histological examination. Furthermore, the report underscores the need for awareness regarding MpBC's distinct clinical features and treatment considerations, especially in light of its potentially poor prognosis and the unique treatment approaches required for effective management.

MpBC often presents as a palpable mass, which may be irregular, firm, and associated with rapid growth or changes[8,9]. It presents around the age of 50 in women[9]. It presents unique challenges due to its heterogeneous nature[10]. Standard imaging techniques, such as mammography and ultrasound, often fail to clearly differentiate MpBC from other breast malignancies[11]. On mammography, MpBC often present with more well-defined margins, and on ultrasound, they often appear as round, lobular, or oval masses with well-defined or indistinct margins, exhibiting more benign characteristics than IDCs, and may include posterior enhancement[9], which can lead to a misinterpretation as a benign lesion[9,11]. However, MpBC can also exhibit irregular or spiculated margins[9].

Histologically, MpBC is defined by tumors exhibiting both epithelial and mesenchymal differentiation, often with a combination of these components present within a single tumor. Heterologous histology was observed in 30% of the cases[12], which frequently results in misdiagnosis or delays in diagnosis[10,13]. The World Health Organization classification further divides MpBC into several subtypes, including low-grade adenosquamous, squamous cell, myoepithelial carcinomas, fibromatosis-like metaplastic, metaplastic with mesenchymal differentiation (such as chondroid or osseous

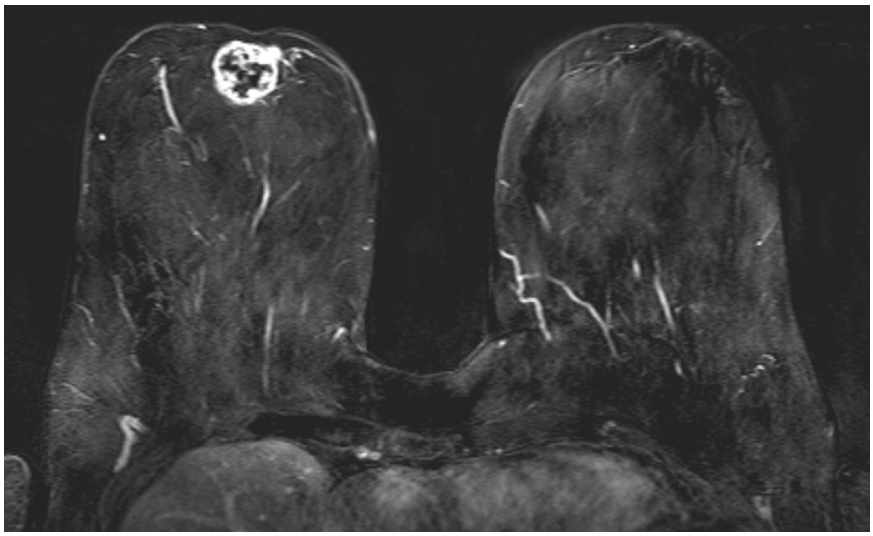

Figure 3. Magnetic resonnance imaging axial view of breasts showing the heterogeneously enhanced mass in the retro-areolar area of the right breast.

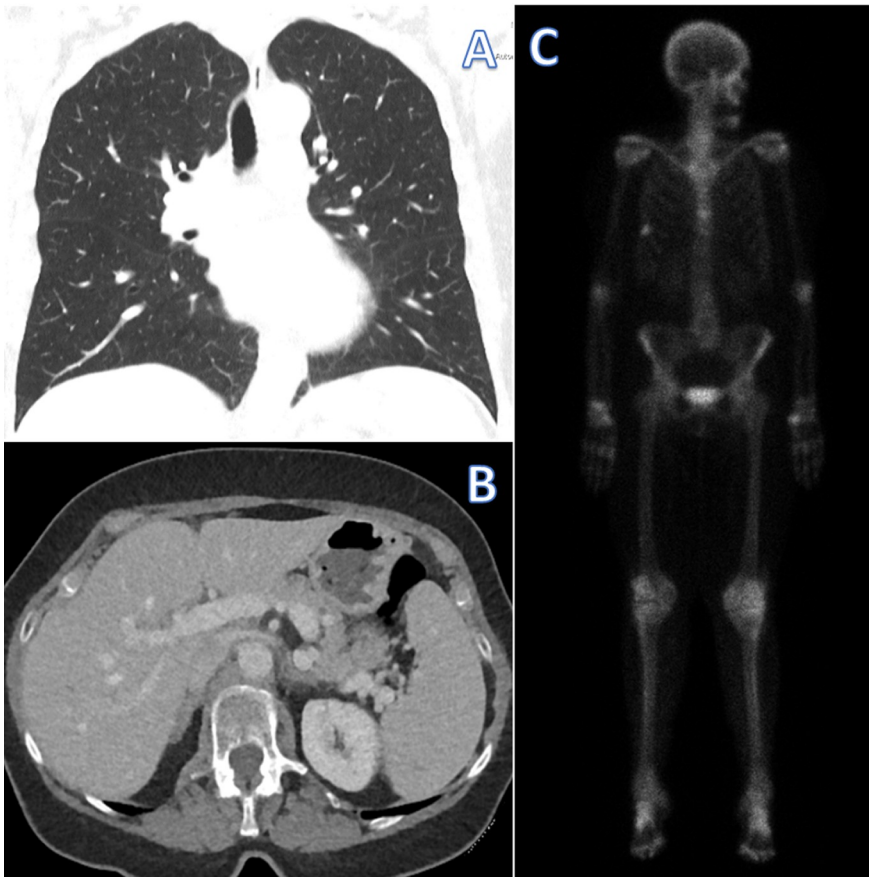

Figure 4. (A) CT scan coronal view of the chest showing no pulmonary metastasis. (B) CT scan axial view of the abdomen with intravenous contrast administration showing no abdominal metastasis. (C) Bone scan showing no bone metastasis, with focal hyperactivity noted in the known right breast lesion. CT, computed tomography.

types), spindle cell, and mixed metaplastic[13]. While aspiration cytology and core needle biopsy can be used for the preoperative diagnosis of MpBC, they are prone to inadequate sampling in the presence of hemorrhage or necrosis; thus, extensive sampling through excisional biopsy is preferred to avoid misleading results and to identify transition foci between IDC and metaplastic elements, which are often observed after excision[9].

The diagnosis of MpBC is generally forthright when associated with conventional invasive or *in situ* carcinoma[12], but in its absence, it relies on demonstrating epithelial differentiation through immunohistochemistry, with over 90% of MpBC showing positive expressions of CK5/6, CK14, and epidermal growth factor receptor, while estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 are negative; immunohistology panels typically reveal at least one keratin-positive profile, and the absence of keratin suggests an alternative diagnosis[12]. Current research has investigated the molecular characteristics of MpBC, uncovering potential genetic mutations and variations in pathways such as TP53, Wnt. and

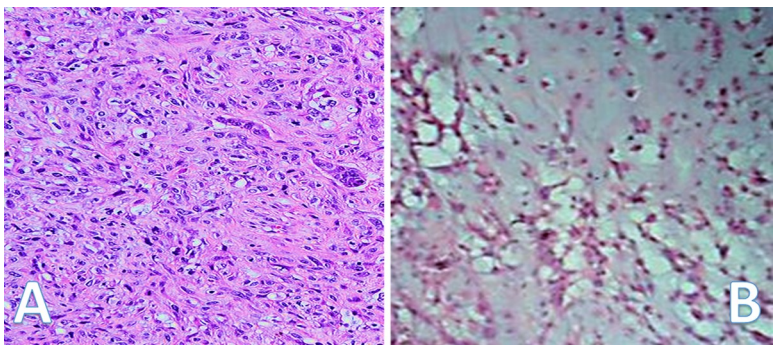

Figure 5. Microscopic photograph of metaplastic breast carcinoma [Hematoxylin & Eosin staining at (A) 20× and (B) 40× magnification].

phosphoinositide 3-kinase (PI3K)/AKT, which could enhance diagnostic accuracy and guide the development of targeted therapies[13].

Treatment for MpBC is not well-defined due to its low incidence[10]. Standard treatments for MpBC include surgery, chemotherapy, and radiotherapy, with Mx being the preferred surgical option due to the typically large tumor size at diagnosis; however, for smaller tumors, conservative surgery combined with radiotherapy may be effective without compromising disease-free or overall survival, as tumor stage is the most crucial prognostic factor[14]. Chemotherapy remains a key element in BC treatment, but there is limited evidence indicating that conventional chemotherapy regimens for IDC are effective for MpBC. MpBC is not responsive to endocrine therapy or targeted molecular therapies due to its distinct biological characteristics. The efficacy of both adjuvant and neoadjuvant chemotherapy for MpBC remains controversial[10]. Targeted therapies for MpBC are emerging as promising options. Given frequent PI3K/AKT/mammalian target of rapamycin (mTOR) pathway alterations, mTOR inhibitors have shown greater efficacy in MpBC than in other TNBCs. MpBC's high programmed death-ligand 1 expression also makes it a candidate for checkpoint inhibitor therapy, such as atezolizumab. Due to poor responses to conventional chemotherapy, exploring targeted therapies and new approaches, including immune modulation, is essential[14].

In our case, the patient underwent successful tumor excision with sentinel lymph node removal and was discharged the following day. Histological findings confirmed a high-grade metaplastic carcinoma with lymph node involvement. The patient was scheduled for adjuvant chemotherapy and radiotherapy based on a multidisciplinary team's recommendations.

MpBC is known for its aggressive nature and poor prognosis compared to other BC subtypes. Despite its typically more severe clinical features and histological grades, recent analyses suggest that, when adjusting for confounding factors, the survival outcomes for MpBC may not significantly differ from those of IDC. This indicates that while MpBC presents unique challenges and tends to be treated more aggressively, its prognosis may align more closely with that of aggressive IDC subtypes when appropriate treatment adjustments are made. Continued research and development of targeted therapies could further refine treatment approaches and potentially improve outcomes for MpBC patients[3].

Conclusion

MpBC represents a rare and highly aggressive form of BC with distinct clinical and histological features that pose significant diagnostic and treatment challenges. Our case highlights the complexities of managing MpBC, including its heterogeneous nature and the difficulties in distinguishing it from other breast malignancies using standard imaging and diagnostic techniques. Despite the aggressive behavior and poorer prognosis associated with MpBC, our findings suggest that with appropriate treatment, including surgery, chemotherapy, and radiotherapy, the survival outcomes for MpBC patients may be comparable to those of aggressive IDC subtypes. The case underscores the importance of a multidisciplinary approach in managing MpBC, given its resistance to conventional therapies and the potential benefit of exploring targeted and immune-based treatments. Further research into the molecular and genetic characteristics of MpBC is crucial for developing more effective treatment strategies and improving patient outcomes. As our understanding of MpBC evolves, tailored therapeutic approaches and novel treatment modalities may offer new hope for better management and prognosis of this challenging cancer subtype.

Ethical approval

The study type is exempt from ethical approval.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

All authors were involved with the design, drafting, revision, and final approval of this case.

Conflict of interest disclosure

This article has no conflict of interest with any parties.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Dr Etienne El-Helou.

Data availability statement

The data that support the findings of this case report are included in the article. Additional data or materials may be available upon reasonable request to the corresponding author, subject to ethical and privacy considerations.

Provenance and peer review

This case report was not commissioned and was externally peer-reviewed.

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Limitation

This case report has several limitations. It is based on a single patient, limiting the generalizability of the findings. Additionally, the subjective nature of clinical observations and the absence of comparative data introduce potential biases.

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