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Case Report

Metaplastic carcinoma with osteosarcomatous differentiation in the breast: Case report ☆

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ABSTRACT

Metaplastic breast carcinoma is rare and may present as a highly aggressive subtype of breast cancer. In this case report of metastatic metaplastic breast carcinoma with osteosarcomatous differentiation in a female patient previously treated for invasive ductal carcinoma, we describe the new presentation of a palpable mass with associated calcifications on imaging near the site of prior partial mastectomy. This article will detail the clinical presentation, imaging findings, histopathology, and clinical course following treatment of our case. Knowledge of the clinical and imaging presentation of this rare subtype, which can present with benign features on mammography and ultrasound, can facilitate timely diagnosis as treatment paradigms evolve.

Introduction

Breast cancer has the highest incidence of all cancers affecting women and is the second most common cause of cancer-related death in women in the United States [1] with 5-year relative survival of 90% [2]. Metaplastic breast carcinoma (MBC) is a heterogeneous group of indolent to highly aggressive tumors that consists of epithelial and non-glandular elements such as matrix-production, spindle cell morphology, squamous differentiation, or heterologous differentiation (ie, osseous or chondroid) [3]. Of the breast carcinoma subtypes, MBC accounts for less than 1%-5% of all cases of invasive breast cancer [4,5].

In contrast to low-grade variants like fibromatosis-like metaplastic carcinoma, a subset of these rare tumors is highly aggressive with poor prognosis and high mortality rate [6,7]. MBC is usually triple negative and in general portends a worse prognosis and 5-year survival than triple-negative breast carcinomas without metaplastic features [5,8]. Osseous and sarcomatous differentiation are the rarest mesenchymal subtypes of MBC and are typically poorly differentiated [9] with osteosarcomatous differentiation accounting for between 0.003% and 0.12% of all breast cancer cases [10,11]. We present a case of a 61-year-old female with a history of previously treated left invasive ductal carcinoma with subsequent diagnosis of a triple negative metaplastic left breast

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Table 1 – Timeline of initial and recent breast cancer diagnosis and treatment.

Initial breast cancer diagnosis and treatment		Recent breast cancer diagnosis and treatment	
May 2014	Clinical presentation of left upper outer quadrant breast mass.	July 2021	Patient detected painful palpable mass in the upper outer posterior left breast.
February 2015	Diagnostic mammography and ultrasound guided core needle biopsy of 1.9 cm upper outer quadrant mass with histology of infiltrating ductal carcinoma.	September 2021	Diagnostic mammography, left breast ultrasound, and ultrasound guided core needle biopsy. Pathology demonstrates invasive poorly differentiated carcinoma with heterologous osteosarcomatous differentiation involving skeletal muscle.
April 2015	Left partial mastectomy and sentinel lymph node biopsy. Surgical pathology confirmed metastasis to one axillary lymph node.	November 2021	Radical chest wall resection, left simple mastectomy, latissimus dorsi flap reconstruction. Surgical pathology demonstrates 7.4 cm mass with osteosarcomatous differentiation.
May 2015	Left partial mastectomy re-excision of anterior and superior margins.		
June 2015-July 2015	Adriamycin & cyclophosphamide weekly therapy.	March 2022	Presentation for evaluation of left axillary pain and swelling. 6.2 cm left axillary soft tissue mass identified by ultrasound. Multiple bilateral pulmonary nodules (increased in size and number) and large soft tissue mass involving the left upper outer breast and axillary region on CTA chest.
August 2015-Novermber 2015	Weekly Paclitaxel chemotherapy.		
January 2016- February 2016	Radiation therapy.		
March 2016-September 2021	Anastrozole endocrine therapy.		

carcinoma with osteosarcomatous differentiation approximately 7 years after an initial breast cancer diagnosis.

Case report

Patient history

Our patient is a 61-year-old female patient with a history of treated left breast carcinoma diagnosed in 2015 who presented for diagnostic mammography and ultrasound in September 2021 for evaluation of a new palpable mass in the left breast upper outer quadrant at posterior depth at the site of prior partial mastectomy in 2015. Initial diagnosis of T2N1 left breast invasive ductal carcinoma (ER+, PR+, high Ki67 at 35%, HER2 equivocal but not amplified by FISH) in 2015 was treated with partial mastectomy and sentinel lymph node biopsy with one positive lymph node and positive surgical margins, re-excision of margins with final margins negative, adjuvant chemotherapy, and radiation therapy. Reproductive history includes menarche at age 13, 5 pregnancies, and 4 live births with the first live birth at age 21, and menopause at age 52 years. The patient never had germline genetic testing. Table 1 summarizes the timelines of initial and recent breast cancer diagnosis and treatment.

Diagnostic assessment

In September 2021, mammography of the left breast demonstrated a high-density irregular mass with microlobulated and spiculated margins with associated areas of coarse, heterogeneous, and dystrophic appearing calcifications in the upper outer quadrant in the posterior third of the breast 11 cm from the nipple at the site of the clinically palpable mass (Figs. 1 and 2). This mass was new when compared with the most recent prior mammogram from 2 years and 10 months previously. Focused left breast ultrasound revealed a 5 cm x 3.8 cm x 2.5 cm irregular mixed echogenicity mass with angular margins and posterior acoustic shadowing at the site of cutaneous lumpectomy scar and area of palpable mass at 2:00 11 cm from the nipple (Fig. 3). Left axillary ultrasound demonstrated a normal axillary lymph node. Ultrasound-guided core needle biopsy demonstrated an invasive high-grade malignant neoplasm consisting of spindled epithelioid cells with invasion into skeletal muscle (Fig. 4). Rare clusters of glandular elements were identified, as well as areas of eosinophilic osteoid with areas of mineralizing osteoid, consistent with osteosarcoma. A cytokeratin AE1/AE3 immunostain demonstrated the glandular elements were positive, while the high-grade undifferentiated malignant cells, as well as the osteosarcomatous elements, were negative. Breast prognostic markers revealed that the neoplastic cells were ER-, PR-, HER2-, with high Ki67 at 70%. These features were reported as consistent with high-grade metaplastic transformation of the patient's prior breast carcinoma in 2015.

Breast MRI with contrast was ordered but not obtained. A whole body F18-FDG PET/CT without contrast was performed for staging in October 2021 and demonstrated a multilobulated intensely FDG avid mass in the left upper outer breast with invasion of the left pectoralis major muscle and abutment of the left pectoralis minor muscle (Figs. 5A and B). The mass measured approximately 6.6 cm x 5.7 cm with coarse calcifications and biopsy clip (SUV max 8.8). Few sub-6 mm nodes in the left axilla were noted adjacent to the mass with minimal FDG uptake (SUV max up to 0.9), as well as an indeterminate 1.5 cm non-FDG avid right apical ground glass nodule, interpreted as inflammatory although adenocarcinoma in situ was a consideration. A few additional sub-6 mm pulmonary nodules/micronodules were also seen (Figs. 6A and B). Correlation with prior outside imaging was recommended if available versus attention to short-term follow-up imaging. Next gene sequencing was ordered in-house for the pathological specimen to identify a possible molecular target for therapy.

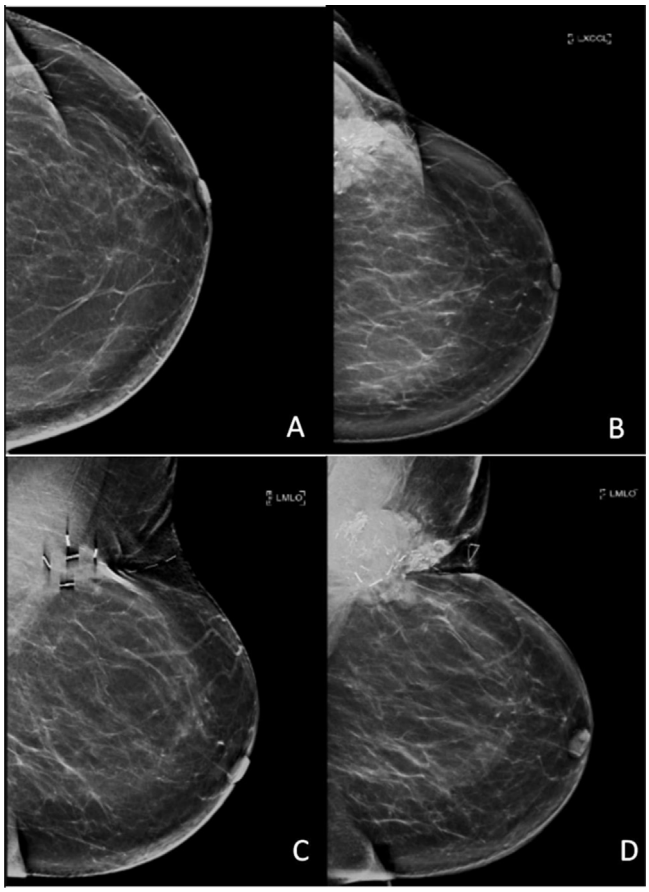

Fig. 1 – Left mammogram with most recent prior comparison. Prior craniocaudal view (A), current craniocaudal view (B), prior mediolateral oblique view (C), and current mediolateral oblique view (D) demonstrate interval development of an irregular high-density mass in the upper outer breast at posterior depth at the site of prior partial mastectomy with associated calcifications.

Therapeutic intervention

Multidisciplinary oncology team discussed various treatment options including radiation, chemotherapy, surgery, and tumor testing for somatic mutations. The patient was treated with left simple mastectomy with latissimus flap reconstruction and en bloc resection of the chest wall including skin, soft tissue breast, and the entire portion of the invaded pectoralis muscle. No additional axillary lymph nodes were removed. Surgical pathology revealed a 7.4 cm mass with osteosarcomatous differentiation, lymphovascular invasion, and skeletal muscle invasion of the chest wall.

Follow-up and outcomes

The patient had satisfactory wound healing following surgery with residual postoperative pain. During postoperative follow-up at 4 months, the patient was found to have a new palpable left axillary mass with associated left arm pain at rest. Duplex ultrasound at the time of evaluation demonstrated a heterogeneous soft tissue mass with internal vascularity measuring 6.2 cm (Fig. 7), with an adjacent 3.0 cm soft tissue mass. Findings were highly concerning for tumor recurrence. The patient was subsequently evaluated with chest CT which demonstrated a new large soft tissue mass in the left axilla (Figs. 5C and D) and increased size and number of multiple pulmonary nodules, some of which were partially calcified (Figs. 6C and D). There were no plans for a biopsy at the time.

Discussion

This case report highlights the importance of understanding the clinical presentation and imaging features of metaplastic breast carcinoma given its aggressive nature and treatment implications. It also adds to the available data on recurrent metaplastic breast carcinoma with osteosarcomatous differentiation in the initial presentation, imaging features, and features of disease progression.

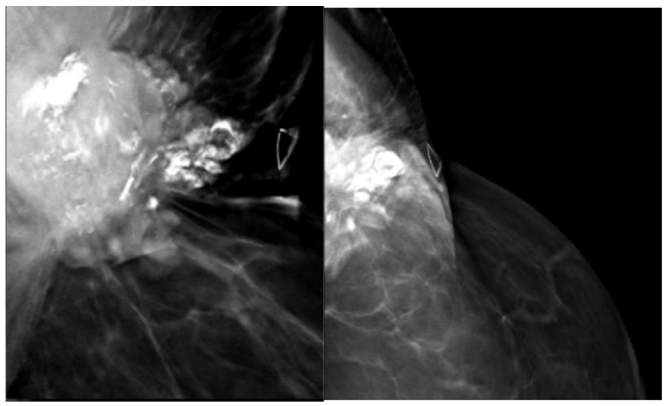

Fig. 2 – Mass with calcifications on tomosynthesis. Mediolateral oblique (left) and craniocaudal (right) digital breast tomosynthesis images demonstrate the interval upper outer left breast mass with irregular shape, spiculated margins, and associated coarse and coarse heterogeneous calcifications.

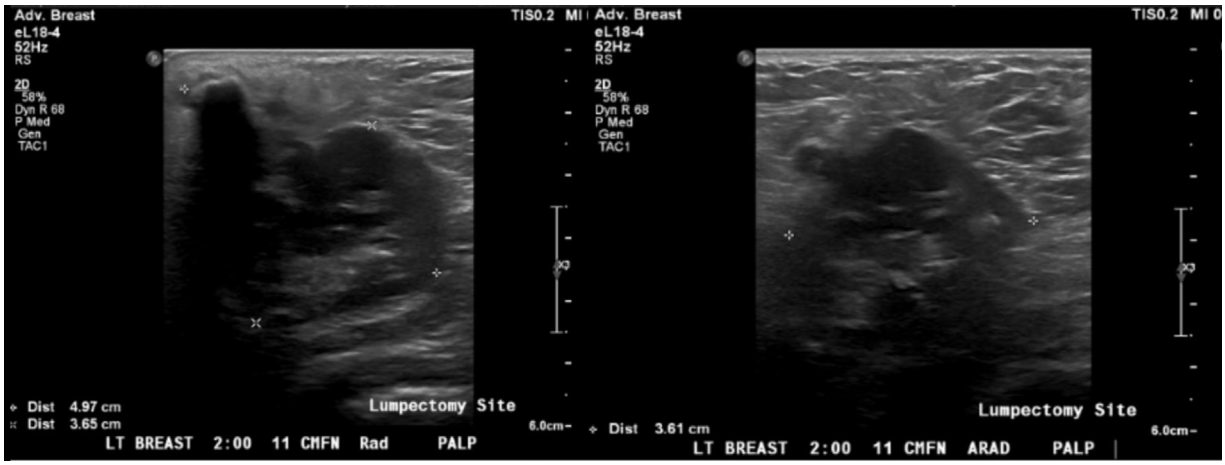

Fig. 3 – Diagnostic ultrasound of the left breast mass at the site of prior partial mastectomy. Grayscale ultrasound images in the radial (left) and antiradial (right) planes demonstrate the irregular mass with heterogeneous internal echotexture and posterior acoustic shadowing that correlate with mammography findings of the new irregular high density mass with calcifications.

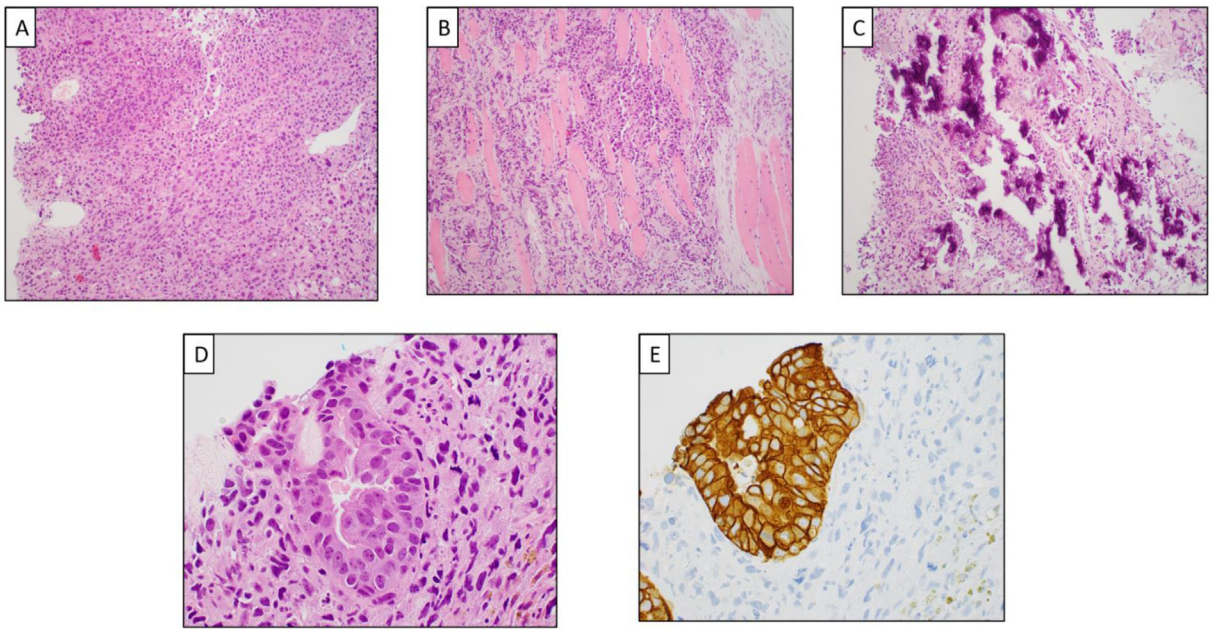

Fig. 4 – Pathology of biopsied mass. Invasive high-grade malignant neoplasm consisting of predominantly spindled to epithelioid cells (A) with extensive invasion into associated skeletal muscle (B). Eosinophilic osteoid with areas of mineralization, consistent with osteosarcoma, were present (C). Rare clusters of glandular elements were identified (D) which were positive for cytokeratin AE1/AE3, while the high-grade undifferentiated malignant cells as well as the osteosarcomatous elements were negative (E).

Clinical and imaging presentation

Metaplastic breast carcinoma often clinically presents as a large palpable mass ranging from 1 to 21 cm, [3]. which was observed in this case. The maximum dimension of the mass was 7.2 cm by surgical pathology. Other reports of MBC describe mass measurements at initial presentation as greater than 2 cm [10–18]. Many cases of MBC also present clinically as a rapidly growing mass [16,19]. MBC can also present with pain [10] as in this case.

The imaging appearance of MBC is variable on mammography and ultrasound. Both benign and malignant imaging features are described in the literature. A retrospective analysis comparing imaging features of 43 patients with MBC matched by tumor stage with 43 patients with ductal carcinoma of the breast found that MBC on mammography was less frequently irregular in shape and less often

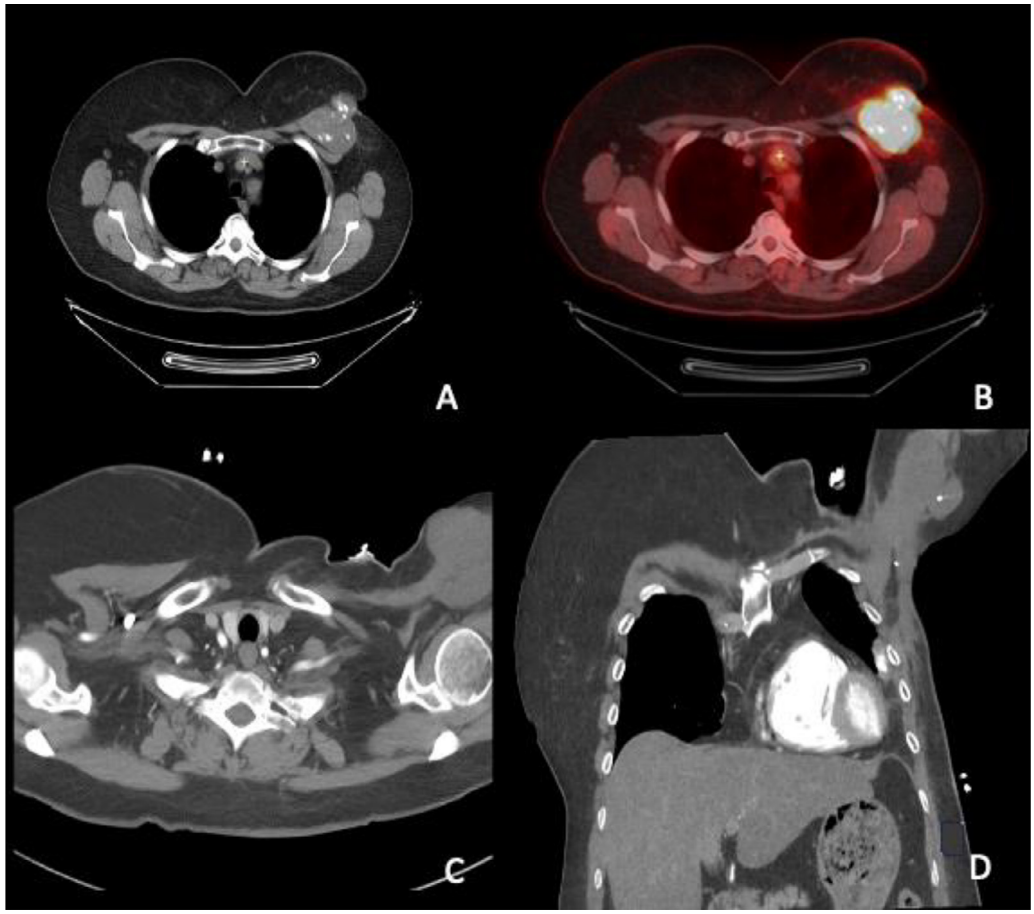

Fig. 5 – Initial staging PET/CT with upper outer MBC and subsequent CT chest with recurrent left axillary MBC after mastectomy. Initial staging PET/CT in the axial plane demonstrates avid FDG uptake of the upper outer left breast mass with tissue diagnosis of MBC (A, B). Five months after left mastectomy, CT chest with contrast in the axial (C) and coronal (D) planes demonstrates a new large soft tissue mass in the left axilla suspicious for recurrent MBC.

showed microlobulated or spiculated margins or calcifications than ductal carcinoma [20]. MBCs can also present with circumscribed margins and posterior acoustic enhancement on ultrasound [19].

In a retrospective single-institution review of 72 cases of MBC by Yoon et al [12], MBC was more often an oval or round mass with noncircumscribed margins without calcifications on mammography. Similarly, in a retrospective review of 65 cases of MBC by Aydin et al [5] MBC was most commonly presented as a microlobulated, round, high-density mass on mammography without calcifications. In a smaller retrospective review, Jia et al [13] reported that on mammography, MBC usually demonstrated an oval shape, indistinct mass margin, and high density without associated calcifications.

Like the majority of cases of MBC reviewed in Yoon et al [12], Aydin et al [5], and Jia et al [13] mass margin on mammography and ultrasound in our case was not circumscribed. Similar to Aydin et al [5] and Jia et al [13] the mass was high density. Unlike Yoon et al, [12] Aydin et al [5], and Jia et al [13] the mass in our case was irregular with associated calcifications on mammography. Mass shape and margin, as well as associated features on mammography such as calcifications, could be partially confounded in our case by the mass location at a site of prior breast conservation therapy.

On ultrasound, Yoon et al [12] described most often a complex or hypoechoic appearance for MBC while Aydin et al [5] and Donato et al [18] reported predominantly a hypoechoic or heterogeneous internal echotexture. The internal echotexture of the mass in our case was heterogeneous. The nonhomogeneous internal echotexture on ultrasound likely reflects the intertumoral heterogeneity seen in pathology due to internal hemorrhage and necrosis [16,18].

Regarding posterior features on ultrasound, Yoon et al [12] and Donato et al [18] report posterior acoustic enhancement in the majority of their cases while approximately 70% of cases in Aydin et al [5] showed no posterior features. In a smaller retrospective review, Lai et al [19] also described posterior acoustic enhancement as a common sonographic feature in MBC positing tumor hypercellularity as the etiology. Although posterior acoustic enhancement is a more commonly observed ultrasound feature in MBC, [7] both the calcifications within the mass or the IDC component could have contributed to the posterior acoustic shadowing in our case. Furthermore, differences in ultrasound equipment or software algorithms

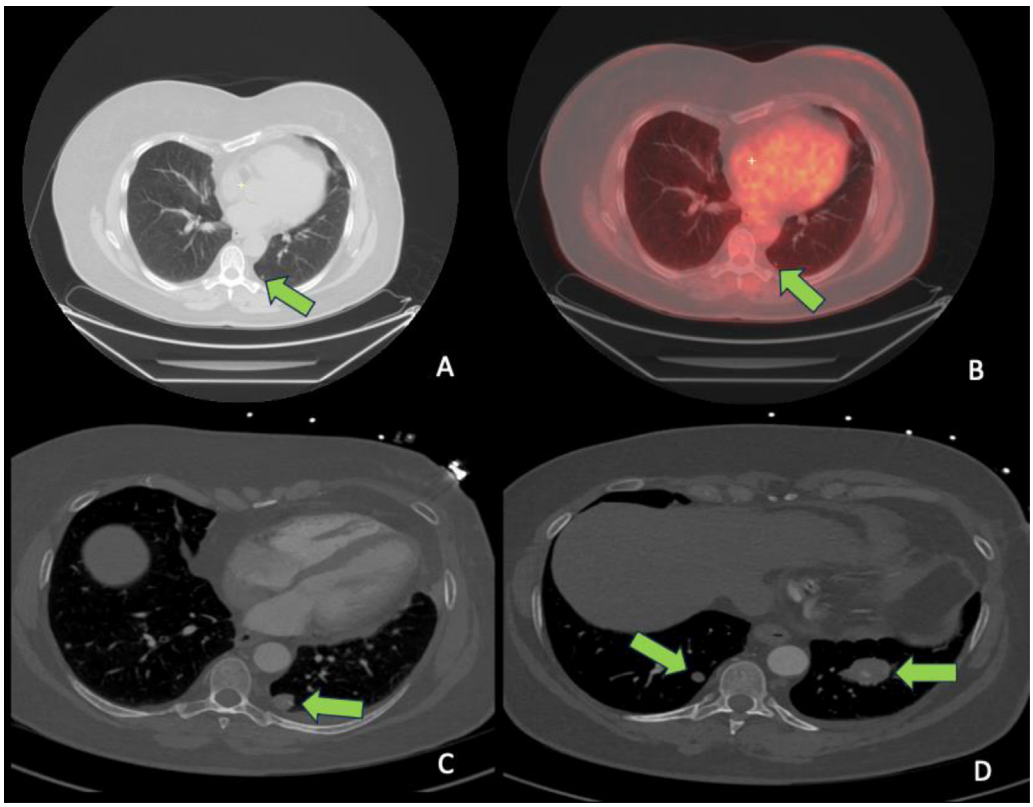

Fig. 6 – Pulmonary findings on initial staging PET/CT and subsequent CT chest after mastectomy. Axial images from initial staging PET/CT (A, B) demonstrating a subcentimeter pulmonary nodule (arrow). Axial images from subsequent CT chest with contrast 5 months after mastectomy (C, D) demonstrating multiple large pulmonary nodules (arrows) with central and peripheral foci of calcification.

at various institutions could impact the appearance of posterior features.

Calcifications

Calcifications associated with the MBC in this case appeared coarse, coarse heterogeneous, and dystrophic. Although coarse and dystrophic calcifications are usually considered benign descriptors for calcifications on mammography [21], their association with a new mass, as in this case, would typically warrant further diagnostic evaluation including ultrasound.

In Yoon et al [12], less than one-third of the masses (31.3%) demonstrated calcifications on imaging with calcification morphology not specified. Similarly, Aydin et al [5] demonstrated associated calcifications by mammography in 33% of cases of MBC, with predominantly amorphous calcifications, fine pleomorphic, fine linear, and lastly coarse heterogeneous in descending order of frequency. Jia et al [13] reported MBC in association with calcifications on mammography in only 3 of 13 cases and described calcifications as pleomorphic, coarse heterogeneous, and fine linear branching. In another case series, calcifications were present on mammography in 3 of 22 cases and described as pleomorphic [14]. Coarse calcifications were reported in a case of MBC with osseous differentiation, [17]. pleomorphic calcifications were described in a case of MBC with osteoblastic differentiation, [10] and “osseous matrix” was described in a case of malignant phyllodes with osteosarcomatous differentiation with subsequent diagnosis of invasive ductal carcinoma [11] Lai et al [19] also described calcifications in MBC as typically larger than those seen in DCIS, which was seen in our case report.

Pathology findings

Metaplastic breast carcinoma is a heterogeneous group of malignant neoplasms of the breast comprised of malignant invasive breast carcinoma and an admixed non-gland-forming component [3]. Less than 5% of breast carcinomas demonstrate metaplastic pathology, with subtype differentiation including squamous, spindle, matrix-producing, and those demonstrating frank heterologous sarcomatous differentiation [3,9]. Heterologous sarcomatous differentiation is the least common subtype of metaplastic breast carcinoma, in which case the sarcomatous component is typically high-grade and aggressive [9]. Frequently, the tumors will not demonstrate KIT activating mutations, but upregulation of EGFR copies [3]. Typically, this group is triple-negative for ER/PR/HER2 [8].

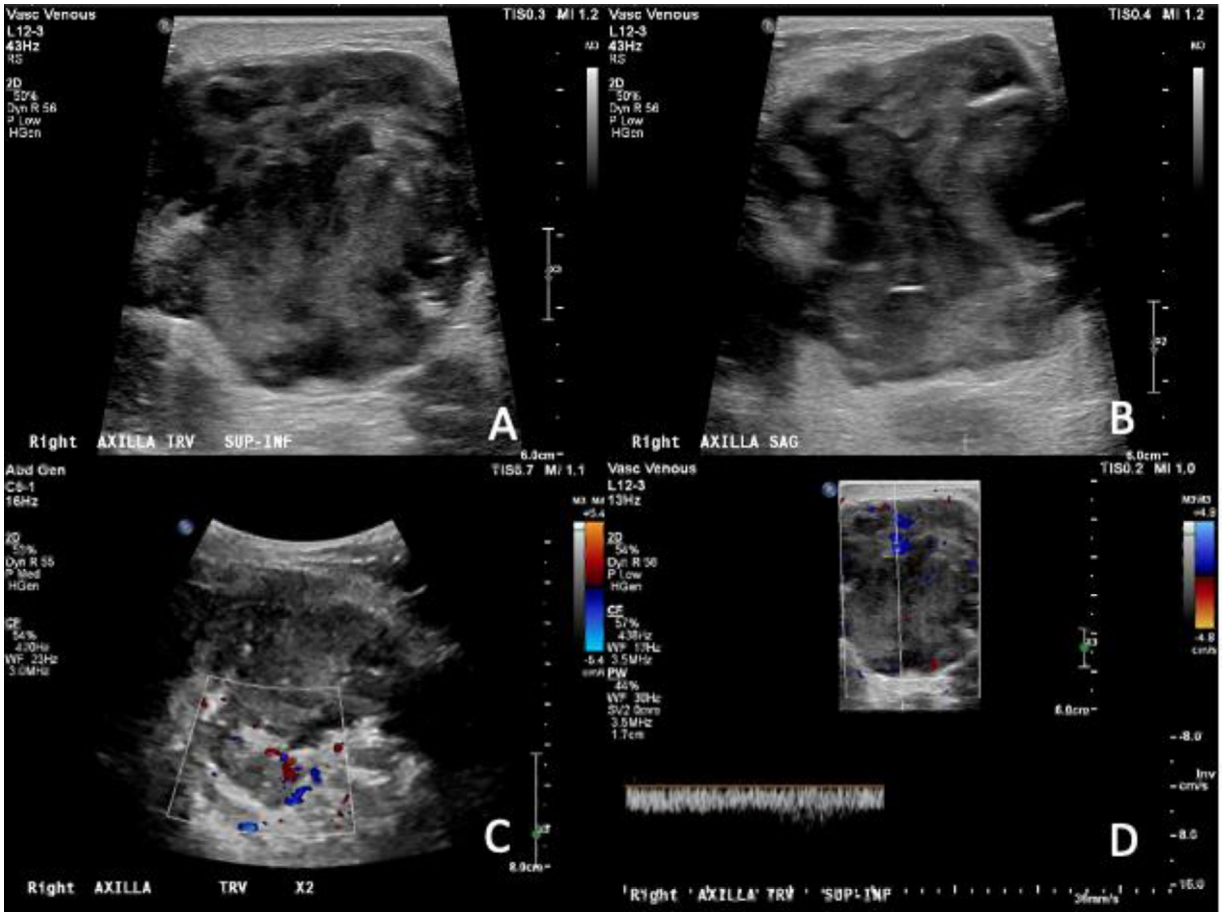

Fig. 7 – Ultrasound of the left axilla performed for pain and swelling after mastectomy. Duplex ultrasound of the left axilla in the transverse (A) and sagittal (B) planes demonstrates a complex cystic and solid mass with irregular margins with areas of internal vascularity (C, D).

Clinical course

Given the low rate at which metaplastic cancers of the breast are diagnosed, there is little evidence available to guide the most appropriate and effective management for patients with this diagnosis. Overall survival and disease-free survival in patients with MBC are significantly less when compared to the more common adenocarcinomas of the breast [6] including triple-negative invasive ductal carcinoma [8]. Recurrence rate is typically influenced by stage at diagnosis, estrogen receptor (ER) status, and adjuvant therapy [22]. With MBC, there is high risk for recurrence after initial treatment, with little evidence to support the use of selective estrogen receptor modulators or aromatase inhibitors after initial treatment [6]. The patient in this case not only developed MBC after an initial diagnosis of invasive breast carcinoma, but also experienced recurrence after surgical management of MBC while maintaining therapy with an aromatase inhibitor.

Moreover, it is possible that each subtype of metaplastic carcinoma of the breast responds uniquely to the treatments currently available. Recently, a small case series demonstrated the use of antiprogrammed death ligand 1 immunomodulation in metaplastic breast carcinoma, with limited response to treatment in 3 out of the 5 patients evaluated, 2 of which were triple negative on immunohistochemistry [23]. This demonstrates a need to further understand this disease process to improve overall prognosis by identifying effective treatment options.

Considering the rarity and highly aggressive nature of metaplastic breast carcinoma with osteosarcomatous differentiation, contributing additional case reports to the literature facilitates diagnostic acumen. A recent study comparing clinical and pathological features between MBC and nonspecific invasive breast carcinoma (NSIBC) demonstrated a significantly greater risk of higher clinical stage of disease at diagnosis of MBC when compared to NSIBC [24]. In that study, MBC was significantly more often triple negative on immunohistochemistry, an important factor that limits treatment options for patients with MBC. Moreover, in that analysis, skin and chest wall invasion was more often typically seen in MBC than in NSIBC, as was observed in this case, which can contribute to a more advanced stage at clinical presentation for MBC.

Aggregating cases to describe the clinicopathological features of MBC could also further support investigations into various treatment options for a rare but often lethal

disease. A large case series with less than 3% of patients with histopathology results of rare invasive breast cancer types determined that for limited disease (breast carcinoma with tumors less than 4 cm greatest dimension) and extensive disease (breast carcinoma with tumors greater than 4 cm), cumulative disease specific survival at 5 years was above 90% and between 80% and 90%, respectively [25]. This exceeds the 5-year survival rate with MBC estimated at 57.7% in one retrospective review [24].

Conclusion

Breast cancer has the highest incidence and the second largest mortality rate of all cancers affecting women. Metaplastic breast carcinoma, although a rare subtype, includes highly aggressive tumors with poor prognosis when compared to the more common invasive breast carcinomas of no special type and invasive lobular carcinoma. When evaluating a new, large, or rapidly growing breast mass with or without benign appearing calcifications, especially at a site of prior lumpectomy, rare but aggressive histopathologies like MBC should be considered and prompt core needle biopsy performed with careful radiology-pathology correlation. There is little evidence regarding the most effective treatment of MBC. Understanding the clinical and histopathological presentations, diagnosis, and management of this subtype facilitates timely diagnosis and may ultimately support efforts to further reduce breast cancer mortality.

Patient consent

Verbal and written informed consent were obtained from the patient.

REFERENCES

[1] Cronin KA, Scott S, Firth AU, Sung H, Henley SJ, Sherman RL, et al. Annual report to the nation on the status of cancer, part 1: National cancer statistics. Cancer 2022;128(24):4251–84. doi:10.1002/cncr.34479.

[2] Cancer stat facts: female breast cancer. National Institutes of Health. [accessed December 12.01.22]. https://seer.cancer.gov/statfacts/html/breast.html

[3] Ingle SB, Katkade P, Chavan K, Girji D. Pathological diagnosis of breast cancer. Hauppauge, United States: Nova Science Publishers, Inc; 2016.

[4] Salih AM, Kakamad FH, Saeed YA, Muhialdeen AS. Metaplastic breast carcinoma with osseous differentiation: A rare case report. Int J Surg Case Rep 2017;34:100–2. doi:10.1016/j.ijscr.2017.03.022.

[5] Aydin H, Guner B, Bostanci IE, Ciledag N, Bulut MB, Bozgul M, et al. Radiologic findings of a rare subtype of invasive breast cancer with poor prognosis: metaplastic carcinoma of the breast. Curr Med Imaging Rev 2019;15(3):338–48. doi:10.2174/1573405614666180813120227.

[6] Rayson D, Adjei AA, Suman VJ, Wold LE, Ingle JN. Metaplastic breast cancer: prognosis and response to systemic therapy. Ann Oncol 1999;10(4):413–19. doi:10.1023/a:1008329910362.

[7] Schwartz TL, Mogal H, Papageorgiou C, Veerapong J, Hsueh EC. Metaplastic breast cancer: histologic characteristics, prognostic factors and systemic treatment strategies. Exp Hematol Oncol 2013;2(1):31. doi:10.1186/2162-3619-2-31.

[8] Song Y, Liu X, Zhang G, et al. Unique clinicopathological features of metaplastic breast carcinoma compared with invasive ductal carcinoma and poor prognostic indicators. World J Surg Oncol 2013;11:129. doi:10.1186/1477-7819-11-129.

[9] Yang X, Chen L, Shen Y. Breast metaplastic carcinoma with osteosarcomatous differentiation: a case report and literature review. Clin Pathol 2022;15:2632010X221118056. doi:10.1177/2632010X221118056.

[10] Twadell S, Schilling K, Gleckman A, McDonald KA. Imaging characteristics of metaplastic breast cancer with osteoblastic differentiation. BMJ Case Rep 2020;13(8):e235050. doi:10.1136/bcr-2020-235050.

[11] Tsukuda K, Tsuji H, Kunitomo T, Aokage K, Miyake T, Nakahara S, et al. Breast cancer with cartilaginous and/or osseous metaplasia diagnosed by lymph nodal metastasis: a case report. Acta Med Okayama 2009;63(6):367–71. doi:10.18926/AMO/31828.

[12] Yoon GY, Cha JH, Kim HH, Shin HJ, Chae EY, Choi WJ, et al. Clinicopathological and imaging features predictive of clinical outcome in metaplastic breast cancer. Curr Med Imaging 2020;16(6):729–38. doi:10.2174/1573405615666190219105810.

[13] Jia Y, He C, Liu L, Sun L, Chen Y, Luo Y, et al. A retrospective study of the imaging and pathological features of metaplastic breast carcinoma and review of the literature. Med Sci Monit 2019;25:248–58. doi:10.12659/MSM.912107.

[14] Puri G, Lohani KR, Khadka S, Kataria K, Ranjan P, Hari S, et al. Clinicopathological and radiological features with long term follow up of metaplastic carcinoma breast in India. Asian Pac J Cancer Prev 2021;22(11):3483–92. doi:10.31557/APJCP.2021.22.11.3483.

[15] Smitt MC. Metaplastic breast cancer. Clin Breast Cancer 2003;4(3):210–11. doi:10.3816/cbc.2003.n.027.

[16] Andreou S, Soule E, Long D, Jasra B, Sharma S. When something seems amiss: radiology-pathology correlation of metaplastic breast cancer. Cureus 2020;12(5):e8239. doi:10.7759/cureus.8239.

[17] Luo K, Wang X. Bone in the breast: a case report of a metaplastic breast cancer with osseous differentiation. Radiol Case Rep 2021;16(1):136–9. doi:10.1016/j.radcr.2020.11.001.

[18] Donato H, Candelaria I, Oliveira P, Goncalo M, Caseiro-Alves F. Imaging findings of metaplastic carcinoma of the breast with pathologic correlation. J Belg Soc Radiol 2018;102(1):46. doi:10.5334/jbsr.1386.

[19] Lai YC, Hsu CY, Chou YH, Tiu CM, Tseng LM, Wang HK, et al. Sonographic presentations of metaplastic breast cancers. J Chin Med Assoc 2012;75(11):589–94. doi:10.1016/j.jcma.2012.08.005.

[20] Yang WT, Hennessy B, Broglio K, Mills C, Sneige N, Davis WG, et al. Imaging differences in metaplastic and invasive ductal carcinomas of the breast. AJR Am J Roentgenol 2007;189(6):1288–93. doi:10.2214/AJR.07.2056.

[21] Sickles EA, D'Orsi CJ, Bassett LW, Appleton CM, Berg WA, Burnside ES, et al. ACR BI-RADS mammography. In:ACR BI-RADS Atlas, Breast Imaging Reporting and Data System. 5th ed. Reston, VA: American College of Radiology; 2013.

[22] Colleoni M, Sun Z, Price KN, Karisson P, Forbes JF, Thurlimann B, et al. Annual hazard rates of recurrence for

breast cancer during 24 years of follow-up: results from the International Breast Cancer Study Group Trials I to V. J Clin Oncol 2016;34(9):927–35. doi:10.1200/JCO.2015.62.3504.
[23] Kim I, Rajamanickam V, Bernard B, Chun B, Wu Y, Martel M, et al. A case series of metastatic metaplastic breast carcinoma treated with anti-PD-1 therapy. Front Oncol 2021;11:635237. doi:10.3389/fonc.2021.635237.
[24] Qiu Y, Chen Y, Zhu L, Chen H, Dai Y, Bao B, et al. Differences of clinicopathological features between metaplastic breast carcinoma and nonspecific invasive breast carcinoma and prognostic profile of metaplastic breast carcinoma. Breast J 2022;2022:2500594. doi:10.1155/2022/2500594.
[25] Tot T, Gere M, Pekar G, Tarjan M, Hofmeyer S, Hellberg D, et al. Breast cancer multifocality, disease extent, and survival. Hum Pathol 2011;42(11):1761–9. doi:10.1016/j.humpath.2011.02.002.