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Case Report General Surgery

Treatment choice in metaplastic breast cancer: A report of 5 cases

Turan Acar,[1] Nihan Acar,[1] Gulten Sezgin,[2] Melek Bekler Gokova,[1]
Betul Bolat Kucukzeybek,[3] Mehmet Haciyanli[1]

[1]Department of General Surgery, Izmir Katip Celebi University Ataturk Training and Research Hospital, Izmir, Turkey
[2]Department of Interventional Radiology, Izmir Katip Celebi University Ataturk Training and Research Hospital, Izmir, Turkey
[3]Department of Pathology, Izmir Katip Celebi University Ataturk Training and Research Hospital, Izmir, Turkey

ABSTRACT

Metaplastic breast carcinoma (MBC) is a general term defining a heterogeneous group that includes biphasic lesions, with both malignant epithelial and mesenchymal tissue components. Although its clinical findings are similar to those present in invasive ductal carcinoma, it rarely presents with the findings of inflammatory breast cancer. It is generally seen in the fifth decade. MBC spreads via lymph and blood circulation. Most common distant metastasis areas include lungs and the bone. Although the treatment generally relies on the same principles applied in invasive ductal carcinoma, a more aggressive treatment should be employed in at-risk groups due to higher rates of local recurrence. In this study, we aimed to discuss clinicopathological features and treatment approach in 5 women with MBC.

Keywords: Breast; cancer; lymph; metaplastic; node; sentinel.

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Metaplastic breast carcinoma (MBC) is a rare lesion, comprising less than 1% of all malignant breast tumors [1, 2]. It is a biphasic tumor, containing both malignant epithelial and mesenchymal tissue components [2]. The World Health Organization classifies metaplastic breast carcinoma into 2 groups: epithelial and mixed type [3]. However, the more popular Wargotz–Norris [4, 5] classification divides MBC into 4 subtypes: spindle cell, squamous cell, carcinosarcoma, and matrix-producing type. This tumor is generally large in size and has a poor prognosis [6]. The lymph node involvement is less common when compared to other breast cancers [7]. The treatment strategy is very important, especially for patients with local recurrence and poor prognosis. Therefore, in this paper, we aim to discuss clinicopathological features and treatment approaches to MBC using records of 5 patients.

CASE REPORT

Table 1 presents the clinical and morphological findings of patients.

One hundred and 10 patients with breast cancer were operated between November 2010 and December 2014. Metaplastic breast carcinoma was diagnosed in 5 of these patients. All relevant patient files were reviewed retrospectively. There were 5 women with the mean age of 52.2 years (36–63 years) in this case series. Four of them were postmenopausal women. A common complaint was a palpable mass, which had been there for a long time, but started growing rapidly in the recent period. Only 1 patient had positive family history (her sibling underwent surgery with the diagnosis of breast cancer) as a risk factor. On physical examination, there was a firm, solid,

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Correspondence: Dr. Turan ACAR. Izmir Katip Celebi Universitesi, Ataturk Egitim ve Arastirma Hastanesi, Genel Cerrahi Klinigi, Izmir, Turkey.
Phone: +90 232 329 35 35 e-mail: drturanacar1982@gmail.com

Table 1. Demographic characteristics and morphological findings

	Case 1	Case 2	Case 3	Case 4	Case 5
Gender	Female	Female	Female	Female	Female
Age	61	63	46	55	36
Family history	–	–	+	–	–
Localization	Left upper-outer quadrant	Right upper-outer quadrant	Left upper-outer quadrant	Right upper-inner quadrant	Right upper-outer quadrant
Mammography findings	BI- RADS 4	BI- RADS 5	BI- RADS 4	BI- RADS 5	BI- RADS 5
Fine-needle aspiration biopsy/ Tru-Cut biopsy	Suspicious cytology	Malignant cytology	Biphasic tumor (fibroadenoma or phyllodes tumor)	Malignant cytology	Malignant cytology (Tru-Cut biopsy)
Treatment	Segmental Mastectomy + *SLNB	**BCS	***MRM	MRM	MRM
Tumor diameter (mm)	20	25	75	10	25
Axilla	0/4	1/19	2/14	0/16	0/21
Metaplastic component	Matrix-producing type	Matrix-producing type	–	–	Squamous cell carcinoma
Stage	T2N0M0	T2N1M0	T3N1M0	T1N0M0	T3N0M0
Estrogen receptor	–	–	+	–	–
Progesterone receptor	–	–	+	–	–
cerbB2	–	–	–	–	–
Systemic treatment	RT**** (Adjuvant)	KT +RT (Adjuvant)	*****KT (Adjuvant)	–	Neo-adjuvant KT + Adjuvant RT
Follow-up (months)	40	40	23	56	11
Local recurrence	–	–	–	–	–
Distant metastasis	–	–	–	+ (bone)	+ (bone)

*SLNB: Sentinel lymph node biopsy; **BSS: Breast sparing surgery; ***MRM: Modified radical mastectomy; ****RT: Radiotherapy; *****CT: Chemotherapy.

fixed, and palpable lump at the upper-outer quadrant in the left breast in 3 patients; at the upper-outer quadrant in the right breast in 1 patient; and at the upper-inner quadrant in the right breast in 1 patient. The Breast Imaging-Reporting and Data System (BI-RADS) Category 4 breast lesions were detected in 2 patients, and the BI-RADS Category 5 breast lesions were detected in 3 patients on the mammogram (Fig. 1). The neo-adjuvant chemotherapy (CT) was planned for 1 patient due to locally advanced disease. The patient was referred to neo-adjuvant CT after confirmation of diagnosis by Tru-Cut biopsy. A fine-needle aspiration biopsy (FNAB) was performed in remaining patients. Malignant cytology was revealed in 2 patients, suspicious cytology in 1 patient, and suspicion regarding biphasic tumor (fibroadenoma or phyllodes tumor) in 1 patient. Neo-adjuvant chemotherapy was offered to patient whose tumor was 75 mm in diameter, but she chose surgery as the primary treatment. No distant metastases were detected by screening tests. Modified radical mastectomy (MRM) was performed in 2 patients, 1 who underwent neo-adjuvant CT and 1 who had diffuse ductal carcinoma in situ (DCIS) areas in the frozen section; while the left-segmental mastectomy and sentinel lymph node biopsy (SLNB) were performed in 1 patient and breast conserving surgery (BCS) in 1 patient. According to a histopathological evaluation, a matrix-producing subtype was detected in 2 patients, and squamous cell carcinoma was detected in 1 patient, while histological subtype was not reported in remaining 2 patients (Fig. 2). Four patients were estrogen-receptor- (ER), progesterone-receptor- (PR), and HER2-negative, while 1 patient was ER and PR positive, but HER2 negative. The mean follow-up duration was 34 months (11–56 months). None of the patients experienced a lo-

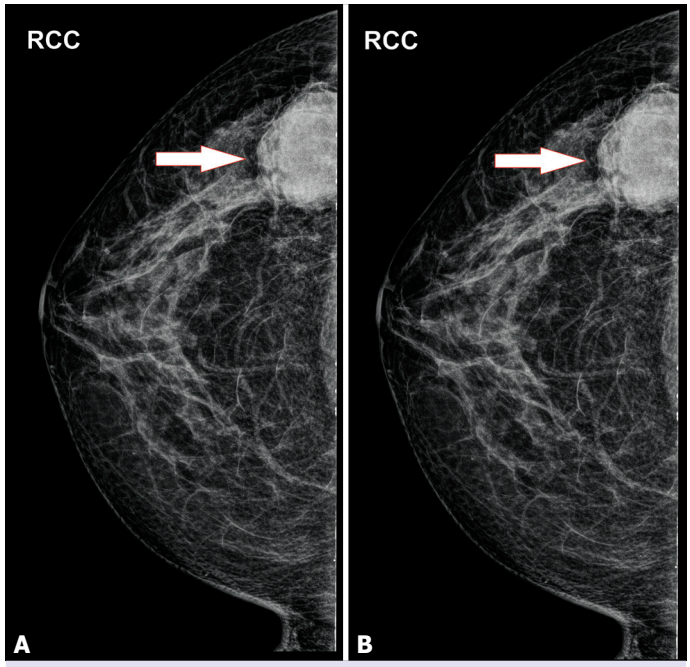

FIGURE 1. (A) On mammography, a high-intensity mass-like opacity (5x4 mm in size) with relatively irregular margins was seen at the upper-outer quadrant next to the axillary tail in the right breast (marked with a circle). (B) On sonography, it was seen that the opacity on the mammography represents a heterogeneous, hypoechoic solid mass lesion (51x32x26 mm in size) with cystic appearance at inferior and malignant features (marked with a circle).

cal recurrence during their follow-up, while further treatment was planned due to bone metastases in 2 patients. Written informed consent was obtained from all patients.

DISCUSSION

MBC is a rare, high-grade, biphasic breast cancer, which contains both malignant epithelial and mesenchymal tissue components. These tumors show no specific appearance on neither mammogram nor sonography. It is mandatory to identify both histological components together for diagnosis. For this reason, it is extremely difficult to diagnose by a FNAB. Most tumors are sporadic, but they also may originate from previous lesions, such as spindle cell carcinoma, papilloma, complex sclerosing lesion, or fibroadenoma [8]. MBC contains sarcoma-like spindle cell areas and areas with squamous, chondroid, osseous differentiation together with adenocarcinoma. MBC is divided into 4 subtypes according to the Wargotz–Norris [4, 5] classification: spindle cell, squamous cell, carcinosarcoma, and matrix-producing type. It is essential to make this classification, because prognosis varies between subtypes, with the squamous subtype having the worst prognosis.

MBC mostly occurs in the fifth decade, just as invasive ductal carcinomas [9]. The patients most commonly present with large tumors varying from 1.4 to 9.5 cm (mean, 3.7 cm) in diameter [10].

As seen in our cases, majority of patients are ER-, PR-, and HER2-negative [9, 11]. Therefore, they are termed "triple negative." It is known that there is a high p53 gene expression, which plays an important role in epithelial proliferation and differentiation. Higher expression of p53 is a poor prognostic factor. In addition, these tumors stain for S100, actin, desmin, vimentin, EMA , and keratin in varying degrees. In our cases, tumors stained positively for S100, vimentin, actin, and keratin in general.

MBC spreads through the lymph and blood circulation. Early hematogenous spreading frequently involves lungs and the bone. The hematogenous spreading route is particularly more common in the subtypes with predominant sarcomatoid spectrum. When compared to adenocarcinomas, the risk of distant metastasis is higher,

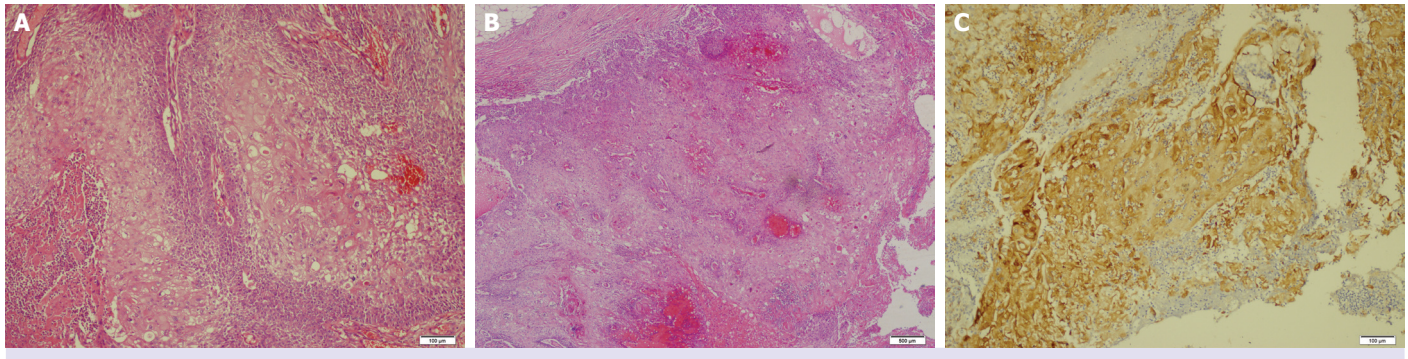

FIGURE 2. (A) Tumor composed of squamous cells showing features (H&Ex10). (B) Tumor composed of squamous cells showing features (H&Ex4). (C) Positive cytokeratin 5/6 staining by immunohistochemically (Cytokeratin 5/6x10).

while the risk of lymph node involvement is lower in MBCs [12, 13]. In a case series, the rate of lymph node metastasis was reported as 8%. Rates of axillary metastasis vary depending on tumor morphology. We performed the axillary dissection in 4 of our patients and detected metastatic lymph node involvement in 2 of these patients. The SLNB was performed in remaining 1 patient. In addition, bone metastases had occurred in 2 patients at an early period during 32 months of the mean follow-up, while remaining 3 patients showed no local recurrence or distant metastasis.

The 3-year disease-free survival (DFS) of MBC patients varies from 15% to 76%, and the 3-year overall survival (OS) varies from 48% to 91% [13, 14]. In another series [15], the 5-year OS rates were reported as 73%, 59%, 4%, and 0% in the order of stages I, II, III, and IV, respectively. These rates reveal that MBC has a poorer prognosis than infiltrative ductal carcinoma.

The tumor size is a more valuable prognostic feature than the axillary lymph node metastasis. Considering the fact that patients with larger tumors have higher recurrence rates and poorer prognosis, mastectomy is recommended rather than BCS [6, 16]. The selection of surgical procedure may affect the 5-year DFS [17]. In the literature [17, 18], it has been suggested that adjuvant hormonotherapy (HT), and CT would be more effective according to the receptor status of primary tumor and prognostic criteria. Radiotherapy has an important role in adjuvant treatment, particularly in those who underwent BCS.

Adjuvant CT is still controversial. There are several studies that support adjuvant CT, especially in Stage 1 and Stage 2 patients. On the contrary, Bae et al. showed that there is no survival benefit of adjuvant CT in metaplastic carcinoma [19]. None of our patients received adjuvant CT or RT. Adjuvant RT is also recommended in patients who underwent breast sparing surgery, just as in patients with invasive ductal carcinoma and those patients with tumors of 4 cm or larger and/or with 4 or more lymph node metastases, according to the study by Tseng et al. [20].

The Tumor–Node–Metastasis Classification of Malignant Tumor (TNM) was used for staging, and they were the following in our patients (in order): IIA, IIB, IIIA, IA, and IIA. All patients were informed comprehensively regarding their diseases. Only 1 patient underwent segmental mastectomy and SLNB due to having an early stage disease, while BCS was performed in 1 patient, and MRM was performed in 3 patients—1 who received neo-adjuvant CT and 2 who had diffuse DCIS areas.

Conclusion

Although the MBC treatment shares similar principles with the infiltrative ductal carcinoma treatment, more aggressive treatments should be applied in groups with risk features due to higher rates of local recurrence and poorer prognosis. However, because of lower axillary metastasis rates, the SLNB will be a more appropriate approach, rather than routine axillary dissection, to reduce postoperative morbidity.

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