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A RARE CASE FOR AWARENESS: METAPLASTIC CARCINOMA OF BREAST

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ABSTRACT

Aims: Metaplastic breast carcinoma is an infrequent kind of breast carcinoma, more aggressive and has poorer prognosis than other breast carcinomas. With this case report, we aim to reveal pathologic and clinical features of the metaplastic breast carcinoma and its similarities to ductal invasive carcinoma. However its differentation is possible and should not be skipped in diagnosis.

Case Report: A BIRADS category of 4c mass that measured 38x31 mm in the ultrasonography was detected in a 71-year-old female patient who applied with a complaint of a palpable mass under the right areola. The result of biopsy was interpreted morphologically as spindle cell proliferation containing necrosis. Thereafter, the mass was excised with simple mastectomy. The results of the immunohistochemical examination of the tumor with the diameter of 6 cm revealed progesterone receptor, estrogen receptor and HER2 to be negative, p63 staining to be positive. The mass was histopathologically diagnosed as metaplastic carcinoma with well differentiated squamous cell and malignant mesenchymal component (osteosarcomatous area).

Conclusion: Metaplastic breast carcinoma which resembles invasive ductal carcinoma with general characteristics is differentiated from invasive ductal carcinoma with larger tumor size, less lymph node involvement, less hormone receptor positivity. In order to prevent the delay of diagnosis, invasive ductal carcinoma should be considered in the definitive diagnosis in the elderly patients. Treatment should be started immediately and followed closely because of the high risk of local recurrence.

Keywords: Carcinoma, breast cancer, simple mastectomy

INTRODUCTION

Metaplastic breast carcinoma (MBC) which makes up all less than 1% of malignant breast lesion formings, is a rare high grade lesion (1-4). Huvos et al. (1) first introduced the term metaplastic carcinoma in 1974. The incidence of MBC which includes both of epithelial and mesenchymal components is increasing gradually. The late inclusion of MBC in pathological assortment is effective in this increasing.

Although it has the same clinical findings of invasive ductal carcinoma (IDC), it might give the similar sign of inflammatory breast cancer. MBC is observed in the 5th decade like IDC (5). The youngest case is 16 years old (2, 3). The foundation of approaching patients diagnosed with malignant breast carcinoma should be based on the individual and type of carcinoma.

CASE REPORT

A 71-year-old female patient with palpable mass under the right areola, applied to an external center. During ultrasonography (USG), cystic degenerated hypoechoic lesion with the size of 38x31 mm, with lobulated contour featured was identified on the right upper outer dial retroareolar field of the breast. The lesion is classified as category 4c according to Breast Imaging Reporting and Data Systems (BIRADS) and tru-cut biopsy was applied to that lesion. During biopsy, lying ductal structures and

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squamous looking small islets were detected inside the fibromyxoid-looking stroma. The human epidermal growth factor receptor 2 (HER2), progesterone receptor (PR), estrogen receptor (ER) were evaluated as a negative (triple negative) carcinoma on histopathological examination. Positive staining was observed in ductal structures with E-cadherin and p63 staining and also in the epithelial field with CK 5-6 staining. Furthermore, a slight increase was found with Ki-67 staining. Consultation had been asked from Trakya University Faculty of Medicine, Department of Pathology Laboratory.
According to immunohistochemical examination of Trakya University Faculty of Medicine, Department of Pathology Laboratory, P63 scrapper chain and actin were detected as negative and Ki-67 index was detected as low (Figure 1).

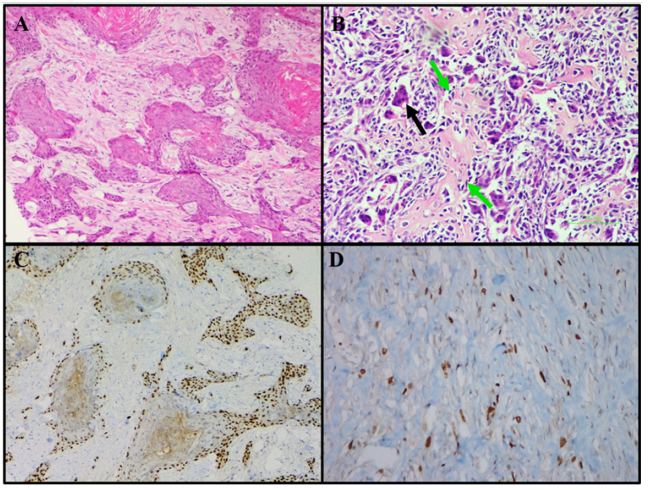

Figure 1: A. Squamous-looking islets in fibromyxoid stroma (H+EX40) B. Supporting the diagnosis of malign mesenchymal component, osteoclast-like giant cells (black arrow), osteoid matrix and osteoblast cells (green arrow) containing osteosarcomatous component (H+EX100) C. Positive staining pattern with p63 at basal level of squamous islands (p63X100) D. Ki67 immunoreactivity in 20% of the mesenchymal component (Ki67X200)

Morphological identification was interpreted as "the spindle cell proliferation that contains necrosis". Metaplastic carcinomas and the lesions such as cellular stromal fibroadenoma, phyllodes tumor, primary mesenchymal tumors of the breast and fibromatosis were considered for definitive diagnosis. Excision of the lesion was recommended because accurate description cannot be possible on the tru-cut biopsy.

As a result of thorax computed tomography (CT) and positron emission tomography (PET) (Figure 2), multiple lymphadenopathies were detected in the right paratracheal region and also a few lymphadenopathies which have 10 mm diameter were detected in left para-aortic area and 5 mm diameter in right hilar region. All lymphadenopathies were evaluated as having metastatic character. Increased fluorodeoxyglucose (FDG) involvement on the 1 cm, subplevral nodule which is located on left upper anterior lobe of lung, was evaluated as a malign lesion. The mass which was identified as BIRADS category 4c according to the USG results of the external center was identified as BIRADS category 5 according to USG and mammography at Trakya University Faculty of Medicine.

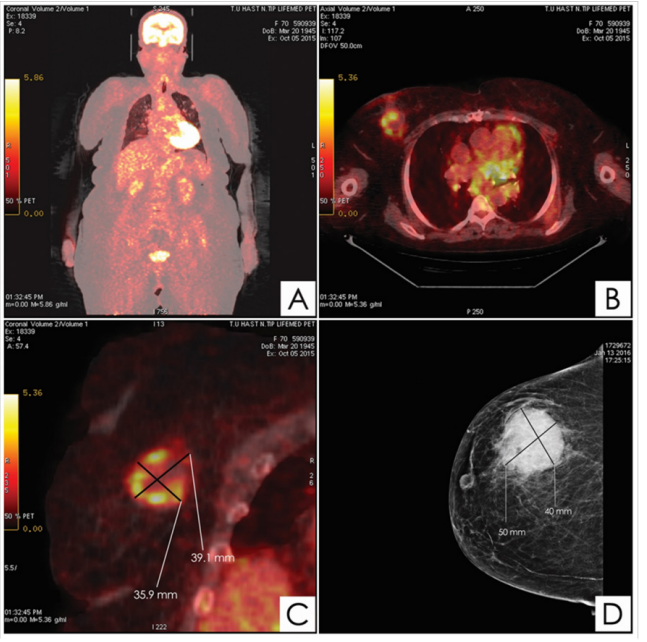

Figure 2: PET and mammography images of the patient A. Increased FDG uptake (involvement) assessed as lymph node metastasis B. and C. Increased FDG uptake (involvement) in the breast D. Mass appearance in mammography

After all examinations, simple mastectomy was applied to patient. Tumor was not detected in the right axillary lymph node biopsy which was taken by frozen. Therefore, sentinel modified radical mastectomy (MRM) were excluded from the process. On histopathological examination of the mastectomy; the tumor with a maximum diameter of 6 cm was consisted of well differentiated squamous cell carcinoma and malignant mesen-

chymal component (osteosarcomatous area). Therefore, histologic diagnosis was metaplastic carcinoma. In addition, in TNM stage it was identified as pT3, pN0, pMx because the largest size of the tumor was higher than 5 cm and there were no remote organ metastasis and lymph node involvement.

DISCUSSION

Since MBC was not recognized as a specific pathologic diagnosis until 2000, doctors had limited information about patients' demographic information, presentation, tumor characteristics and treatment modalities. Up to the present, the factors that differ MBC from more prevalent malignant breast histologic features, have been attempted to be familiarized only with small series and case reports.

Metaplastic carcinoma of the breast, which includes malignant mesenchymal and malignant epithelial tissue components with biphasic lesions, is a general term that describes the heterogeneous group (Table 1). Heterogeneity is increasing in malignant breast lesions and this condition depends on many factors such as hormone receptor expression, changing gene expression and histologic appearance.

Table 1: MBC classification according to the components it contains

World Health Organization (WHO) 2003 Metaplastic Breast Carcinoma Classification	
Pure epithelial metaplastic carcinoma	Mixed epithelial/mesenchymal metaplastic carcinoma
• Squamous cell carcinoma • Cord cell metaplasia adenocarcinoma • Adenosquamous carcinoma • Mucoepidermoid carcinoma	• Chondroid metaplasia carcinoma • Osseous metaplasia carcinoma • Matrix-producing carcinoma

Most of the metaplastic carcinomas are occasional, but there may be a trace of tendency to metaplastic spindle cell carcinoma developed from pre-existing lesions, including papillomas, complicated sclerosing lesions and nipple adenomas (6).

The most important prognostic factor is the tumor size and phase. Tumor size can change between 0.8-12 cm (av. 3 cm) (2). Size being less than 4 cm is a good prognosis sign (3). Spread of the MBC to other parts of the body often occurs by blood circulation or rarely through the lymphatic circulation. The most common regions of metastasis are lung and bone (2, 3). There is no specific finding in mammography and ultrasound imaging (5).

Table 2: At the table below Pezzi et al. (6) used National Cancer Data Base of 892 MBC and 255.164 IDC cases. According to this ratio, ER, PR values are negative in the vast majority of MBC patients while IDC patients' values are positive. Nodal involvement is high in both of cancer types. The tumor size is less than 2 cm in more than half of IDC patients. Tumor size is between 2 to 5 cm in nearly half of MBC patients.

	Metaplastic Breast Carcinoma	Infiltrative Ductal Carcinoma
Mean age	61,1	59,7
Tumor size <2 cm 2-5 cm >5 cm	 29.5% 49.6% 20.4%	 65.2% 29.5% 5.2%
Estrogen receptor status Positive Negative	 11.3% 88.7%	 74.1% 25.9%
Progesterone receptor status Positive Negative	 10.4% 89.6%	 62.4% 37.6%
Nodal status Positive Negative	 78.1% 21.9%	 65.7 34.3

Metaplastic breast carcinoma which has similar clinical features with IDC, is usually considered to be a high grade carcinoma (Table 2). Despite this, it may rarely give similar evidence of inflammatory carcinoma (2, 3, 6).

A difference was seen in MBC patients in comparison with IDC patients due to race/ethnicity. MBC patients are mostly Afro-American or Hispanic. The reason for these variations is unknown, however these ethnic groups represent low but increased risk for MBC (7).

Invasive ductal carcinomas are diagnosed earlier than MBC. Since MBC has a faster and more aggressive growth, it is relatively rarely seen. Therefore, its diagnosis can be skipped easily and it can be confused with be-

nign lesions during imaging.

Lim et al. (8) have been classified 51 MBC patients whether they have ER, PR and HER2 expiration. Being negative for all three receptors have been interpreted as worse prognosis.

By comparison with IDC; ER, PR and HER2 oncogene expressions are lower and Ki-67 and p53 oncogene expressions are higher in MBC. Literature-based studies identify the ratios as 35% for HER2 positivity and is 0% for MBC in high grade (grade 3) breast carcinoma. ER and PR positivity have been reported as a percentage between 0% and 25% in the literature (2, 7) . After performed studies, low hormone receptor positivity has generally been characterized for MBC therefore, the treatment approaches have changed. Thereby, hormones or anti-HER2 treatment are less successful on these patients. In MBC, extreme expression of p63 gene is also known (8).

Although some studies have reported that breast-conserving therapy and modified radical mastectomy conclude with the same results, having large size of tumor and the risk of local reoccurrence for the first 2-5 years being between 35% and 62% increase the propensity to MRM (3, 5). Respectively MRM, Radiotheraphy (RT) and systemic chemotherapy (CT) are applied in usual treatment protocol. After evaluating 27 patients with results of different chemotherapy studies from Clinic of Mayo for 30 years, Rayson et al. (9) have been reported that systemic CT has low effect. Low incidence of MBC's lymphatic spread can explain its resistance to traditional CT agents and sensitivity of RT.

In our case, squamous cell carcinoma in the epithelial component and carcinoma including osteosarcomatous field in the mesenchymal component are present. The patient applied with a complaint of a palpable mass that was measured as 6 cm in diameter which is over the 4 cm specification of bad prognostic determination stated in literature. During histopathologic examination, prognostic factor TN was tracked. In addition, p63 staining was positive. Since the case is classified as category 5 according to BIRADS classification, it was highly doubted and advanced diagnosis methods were applied. In many studies, the risk of metastasis to axillary lymph nodes has been reported as high. However, in our case, the patient was diagnosed with MBC has no axillary metastasis. Therefore, MRM was not implemented and simple mastectomy surgery was applied.

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