

Pleomorphic Ductal Carcinoma of Breast: Two Cases and Review Literature

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Abstract- We report two cases of pleomorphic breast carcinoma, a rare variant of high-grade invasive ductal breast carcinoma of no special type, which is a combination of pleomorphic and bizarre giant cells in an adenocarcinoma background. For gaining better insights, available literature is also reviewed.

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Introduction

The most common cancer accounts for 29% of all cancer diagnosis, and the second cause of cancer death among females is breast cancer which is classified into two categories: lobular and ductal (ductal and lobular dominancy). Pleomorphic carcinoma is a rare variant of high-grade invasive ductal carcinoma of the breast with unfavorable prognosis (1,2). It is characterized by more than 50% of pleomorphic and bizarre giant cells in a background of adenocarcinoma with spindle and squamous differentiation based on World Health Organization (WHO) classification (3). Pleomorphism and high mitotic activity with atypical mitosis are the two main features of these cells (4). Due to its unusual morphology, pleomorphic carcinoma may be misdiagnosed with sarcoma; therefore, specific immunostaining for epithelial and mesenchymal markers can be useful in differentiation (5). Based on our knowledge, 84 pleomorphic carcinomas of breast cases have been reported in English.

Herein, we present two cases of pleomorphic carcinoma, and pertinent literature is reviewed.

Case Report

Case 1

A 55-year-old woman had a palpable, itchy, and erythematous mass in her left breast, suspected breast cancer, 4 months earlier. In spite of explaining the process and plan, she did not acquiesce the treatment. During this period of time, the lump became larger, painful, infected,

and ulcerated. Besides losing appetite, she showed significant weight loss. Furthermore, at the time of admission, she complained of purulent, odoriferous discharges from several fistules. In the primary observations, the skin was abnormal, firm with cream-gray colored areas on its surface with the maximum diameter of 13 cm. Additionally, nodules with a 0.5-1 cm diameter were observed.

She underwent a left total mastectomy. The specimen measuring 19×16×8 cm had semifirm consistency and showed total infiltration by tumor with cream-pink colored cut sections. Breast skin was involved, and multiple cutaneous ulcerations were seen. Also, there was no nipple due to malignant destruction. Microscopic examination revealed breast tissue infiltrated diffusely by the malignant highly pleomorphic epithelial neoplasm. The tumor was composed of many mono- and multinucleated giant cells with bizarre vesicular nuclei containing prominent eosinophilic nucleoli. In some regions, streams of tumoral spindle-shaped cells and also brisk mitotic figures with atypical form were present. These pleomorphic tumoral cells were described by immunostaining as strongly positive cells for CKAE1/3, Vimentin, and CD10 and negative for ER, PR, HER2, p53, S-100, CK5/6, and CK7. Ki-67 proliferation index was 40%. At the beginning of the follow-up, the bone scan was normal, and there was not any sign of metastasis. Despite the post-surgical stability, she had severe dry coughs. Chest X-ray demonstrated blunt pleural angles, coarse reticular opacities, and right lower lobe consolidation (70×60 mm). Mycobacterium tuberculosis infection was ruled out. Spiral CT-scan of

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lungs and mediastinum with IV contrast injection was done which revealed bilateral pleural effusion, multiple peripheral and subpleural pulmonary nodules, and partial abnormal alveolar opacities of right lung middle zone and the majority of lower lobes that confirmed diffuse pulmonary metastasis. Multiple metastases to left supraclavicular lymph nodes (largest size 29×23 mm) compressing left subclavian vein were seen in Doppler sonography which caused left-hand edema. Later, she developed wound infection presenting as pruricity, scales and pus discharges. She was expired about two months after the surgery.

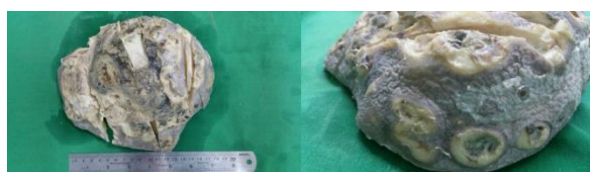


Figure 1. Mastectomy specimen which is totally infiltrated by tumor and shows multiple cutaneous tumoral nodules with ulceration and sinus tracts

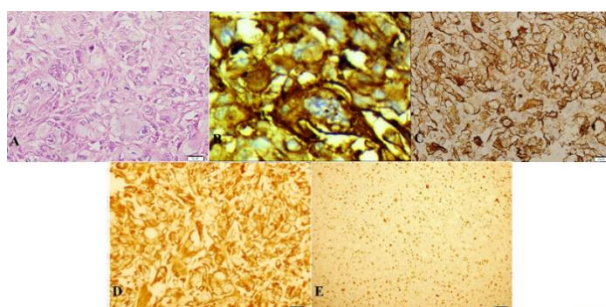


Figure 2. A. H and E. bizarre pleomorphic and giant tumoral cells B. CD10 C. CKEA1/3 D. vimentin E. ki-67

Case 2

A 40-year-old woman presented with a firm, palpable, painless, and non-itching mass in the upper inner quadrant of her left breast from 2.5 years ago which had grown in size. There was not any scale, discharge or nipple retraction on examinations, while peau d'orange

appearance was present. Ultrasonography reported a large, ill-defined hypoechoic lesion at 10-11 O'clock measuring 85×66 mm with central necrotic changes and increased the thickness of the skin. Furthermore, 3 hypoechoic lesions measuring 42×28 mm, 26×19 mm, and 21×14 mm were recognized in the left axillary region. Mammographic observations proved the ultrasonographic findings and noted severe edema and increased the thickness of the subcutaneous tissue. There was not any localized lesion in the areola or subareolar region. These findings were compatible with a malignant lesion with BI-RADS category 5. Primary pathologic observation of core needle biopsy reported a tumoral tissue consisted of cells with severe nuclear pleomorphism, high mitotic activity, and low ductal formation surrounded by fibrotic stroma. Six sessions of chemotherapy were effective, and the tumor size decreased, 4 cm at maximum diameter. Then, she was referred to our hospital for the surgery. The patient underwent total mastectomy with axillary lymph node dissection. All surgical margins, axillary lymph nodes, and nipple were free of tumor. Hematoxylin and Eosin (H and E) staining showed cysts lining with multinucleated bizarre neoplastic cells and filled with a fibrinous material. The cysts were infiltrated by inflammatory cells mostly lymphoplasm cells and hemosiderin-laden macrophages. These pleomorphic cells had large hyperchromatic nuclei with atypical mitosis. Furthermore, Mild fibroadenomatous change was observed. All surgical margins were free of tumor. Immunohistochemistry (IHC) study was performed and was positive for S-100 (some of the cells), Vimentin, CKEA1/3 and, and ER, while negative for HER2 and PR. These findings demonstrated pleomorphic carcinoma. She was discharged with a good condition and referred for the following radiotherapy.

Ten months after the last, 25th, session of radiotherapy, she has not experienced any recur or metastasis.

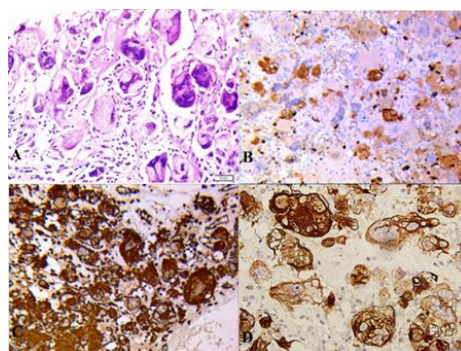


Figure 2. A. H and E B. S100 C. vimentin D. CKEA1/3

Discussion

Breast cancer, the most common cancer with a high mortality rate among women, can be classified into ductal and lobular types. Invasive ductal breast cancer is more common and accounts for about 75-85% of invasive breast cancer and more frequent in lower age groups in comparison with invasive lobular carcinoma (6-8). Although there were reports of pleomorphic bizarre giant cell in breast cancer before 2000 (9-11), Silver and Tavassoli described pleomorphic breast carcinoma as a unique morphological variant of high-grade ductal carcinoma by studying 26 cases and identifying some of their similar morphological features (12) that later led to the new WHO classification of breast tumors (13). In the latest WHO edition, pleomorphic breast carcinoma is a rare variant of high-grade invasive breast carcinoma of no special type that more than half of the texture should be a combination of pleomorphic and bizarre giant cells in a background of adenocarcinoma with a spindle or squamous differentiation (3). Although the entity has a poor prognosis, not all of the reported tumors behave badly. Presence of a spindle cell metaplastic component and tumor size greater than 5 cm in stages I-III disease decreased overall survival.

After presenting with a palpable mass, which is the most common symptom, most of the patients refer within a few weeks. Some others come after a recent increase in the size of a previous stable tumor; however, there are reports of delayed refer to like the first case of our study. In addition, some of the cases are found through mammographic screening or physical examination for other diseases (4,14).

Imaging features of pleomorphic carcinoma can be similar to the benign breast lesions, fibroadenoma, malignant phyllodes tumor, and inflammation. So, pathologic findings play a critical role in the diagnosis (4).

Several cases of pleomorphic carcinoma have been reported to display cyst formation. Yamada *et al.*, suggested 3 mechanisms for this finding: 1) carcinoma cells initially develop in the ductal wall and locally grow intraductally; 2) the cells block the lumen via stromal

involvement; 3) increasing inner pressure and/or possible necrotic changes (15).

Other breast tumors, such as invasive pleomorphic lobular carcinoma, invasive carcinoma with osteoclast-like giant cells, invasive carcinoma with chorioepithelioma features, metaplastic carcinoma with giant cells, mammary sarcoma with giant cells, and metastatic tumors can present pleomorphic tumor cells (13). Pleomorphic lobular carcinoma cells nuclei are hyperchromatic, irregular, and markedly pleomorphic with a tendency to arrange in a linear pattern. Unlike pleomorphic ductal carcinoma, these cells do not express E-Cadherin in IHC study. Moreover, CD68 and CK markers are useful to differentiate pleomorphic ductal carcinoma from invasive ductal carcinoma with osteoclast-like giant cells, which is CD68 positive and CK negative. β -HCG positivity also makes the diagnosis of invasive carcinoma with chorioepithelioma features more likely. Finally, IHC study with CK and EMA, which are epithelial markers, can be applied to differentiate pleomorphic carcinoma from mammary sarcoma. The multicentric pattern of breast involvement in metastatic carcinomas and patient history of a primary tumor can be useful for diagnosis and differentiation from pleomorphic carcinoma (16). IHC study in some of the patients was positive for Vimentin, S100 protein, p53, C-erbB-2. However, there are other markers expressed in a few reported cases (14,17).

Late diagnosis and lack of proper treatment of pleomorphic carcinoma can lead to a catastrophe; the same as our first patient with total breast tissue involvement, multiple sinus tracts, and several metastases. However, timely diagnosis through pathologic examination and specific IHC studies to rule out other similar tumors and appropriate following are associated with a better prognosis and longer survival.

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Table 1. Previous reports of pleomorphic carcinoma of the breast

Author, year	number of cases	age	tumor size/ diameter (cm)	Right /Left	stage/grade	metastasis	treatment
Silver <i>et al.</i> , 2000(14)	26	28-96 (mean=51)	0.5-15 (average, 5.4)	65% right	all stages	lymph nodes	biopsy and/or mastectomy (24) or lumpectomy (2)
Lenicek <i>et al.</i> , 2007(18)	1	83	5.8	right	NR	-	Radical mastectomy
Kurokawa <i>et al.</i> , 2009(19)	1	51	1	left	I	-	mastectomy, adjuvant chemotherapy
Nguyen <i>et al.</i> , 2010(2)	37	23-78 (mean = 52)	1.2-11.6 (average, 3.5)	71% left	all stages	lymph nodes, lung, brain, liver, bone, skin, sort tissue	total mastectomy (22) BCS (9) No surgery (3) Unknown (3)
Yamaguchi <i>et al.</i> , 2010(17)	1	17	7.6	left	T3N2M0/IIIA	lymph nodes, lung	mastectomy, chemotherapy, radiotherapy
Zhao <i>et al.</i> , 2010(4)	10	33-76 (mean = 50)	1-15 (average, 4.3)	60% right	I, II, IIb	lymph nodes, lumbar vertebrae, liver, lung, thoracic bone	radical mastectomy (9), conservative surgery (1)
Caruso <i>et al.</i> , 2011(20)	1 male	65	2.5	left	pT2 N1aMx/III	lymph nodes	mastectomy
Tacchini <i>et al.</i> , 2011(21)	1	44	1.2 & 0.6			-	
Cordoba <i>et al.</i> , 2012(5)	2	76, 46	5, <1	right, Both	NR	NR	total mastectomy, Segmental resection of breast
Tang <i>et al.</i> , 2014(22)	1	45	3.5	left	T2N1M0 IIB	lymph node	radical mastectomy, chemotherapy
Yamada <i>et al.</i> , 2013(15)	1	55	3.5	right	pT2N0M0 IIA	-	adjuvant chemotherapy, radiotherapy
Shousha, 2014 (23)	1	NR	5	left	III	-	mastectomy
Arasi <i>et al.</i> , 2016(16)	1	57	5.6×2.5	left	-	lymph node	modified radical mastectomy
Moghimi <i>et al.</i> , 2017	2	55, 40	19×16×8,	Both left	IV, IIIB	Lung, -	total mastectomy, neoadjuvant chemotherapy

L= lobular D= ductal NR= not reported

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