

Multicentric breast cancer comprising of three different histopathological types: a case report

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Abstract: Multicentric breast cancers are rare and variable types of histopathology are even less documented. We report a case of a 57-year-old lady with multicentric breast cancer comprising of three different histopathological types. She presented with a left breast lump progressively increasing in size. She was not on oral contraceptives or hormone replacement therapy. There was no family history of breast cancer or other malignancies in her family. Physical examination showed a lobulated swelling of the left breast with multiple satellite nodules. Multiple mobile left axillary lymph nodes were palpable. The right breast was normal and there were no signs of metastases. Bilateral breast ultrasound demonstrated a large lobulated mass at the left lower region extending to the sub areolar with small nodules adjacent to the mass. There was also extensive edema with multiple lymphadenopathies at left axillary region. Contrast enhanced computed tomography (CECT) demonstrated multicentric left breast lesion and core biopsy revealed an invasive carcinoma. Clinical staging was T4bN1M0. She underwent chemotherapy followed by mastectomy and axillary clearance. Biopsy confirmed mixed mucinous carcinoma, invasive ductal carcinoma and carcinoma with neuroendocrine features with high lymph nodes positivities. Estrogen receptor and progesterone receptor protein were positive. Diagnosis of mucinous carcinoma, carcinoma with neuroendocrine feature and mixed mucinous carcinoma (mucinous type and no special type) with modified Bloom and Richardson grade 2 was given. Whole body bone scan indicated skeletal metastasis. She was then referred to oncologist for further management but refused for further treatment. Breast conserving surgery is a safe surgical option for multicentric breast cancer however the prognosis is usually poor due to advanced presentation and its tumor biology.

Keywords: Multicentric breast cancer; histopathological types; case report

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Introduction

Breast cancers are defined as multicentric when it originates from different duct collecting systems with two or more synchronous ipsilateral neoplasms, separated by benign tissue located within different quadrant of the breast (1). The incidence of unilateral multiple breast cancer has

been reported to account for approximately 5% of all breast cancers (2). We, herein, report a rare case of a post-menopausal lady with a unilateral multicentric breast cancer comprising of three different histopathological types. We present the following article in accordance with the CARE reporting checklist (available at <http://dx.doi.org/10.21037/abs-19-101>).

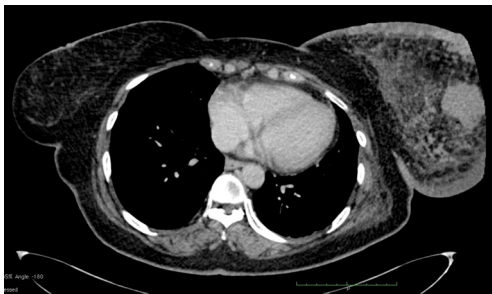


Figure 1 Reconstructed MPR images of the computer tomography scan showing mass at left inner quadrant of left breast infiltrating the overlying skin. Noted the contra-lateral right breast is normal. There is a large, enhancing irregular nodule at LIQ measuring 5.2 cm × 4.2 cm × 5.9 cm in size, infiltrating the overlying skin. MPR, multiplanar reformation; LIQ, lower inner quadrant.



Figure 2 Sagittal reconstructed computer tomography image showing multiple other irregular left breast nodules with axillary lymphadenopathies. There are also multiple irregular enhancing nodules at central and UIQ of left breasts with marked thickening of the adjacent Cooper's ligaments. Multiple enlarged left axillary lymph nodes noted. Contralateral right breast is normal. There is no nodule detected in the liver, spleen and lung to suggest distant organ metastases. UIQ, upper inner quadrant.

Case presentation

A 57-year-old lady presented with a left breast lump for 1 year. The lump was progressively increasing in size and there was no associated nipple discharge. She attained menarche at the age of 15 years old and menopause at the

age of 52. She is married and blessed with 4 children. There was neither history of taking oral contraceptives nor any hormone replacement therapy. She denies smoking and alcohol intake. There was no family history of breast cancer or other malignancies in her family.

Physical examination demonstrated a lobulated swelling of the left breast with multiple satellite nodules and erythematous skin changes. The swelling was mobile, hard in consistency and the nipple was distorted. Multiple mobile left axillary lymph nodes were palpable. The right breast was normal and there were no signs of metastases.

A bilateral breast ultrasound demonstrated a large lobulated mass at the left lower region extending to the sub areolar with small nodules adjacent to the mass. There was also extensive edema with multiple lymphadenopathies at left axillary region.

Subsequently, contrast enhanced computed tomography (CECT) (*Figures 1,2*) showed multicentric left breast lesion, most likely breast carcinoma with regional axillary lymph nodes involvement. Histopathological examination of a core biopsy over the left breast lesion revealed an invasive carcinoma. Clinical staging was T4bN1M0.

The patient underwent six cycles of neo-adjuvant chemotherapy, FEC regime (5-fluorouracil, epirubicin, cyclophosphamide), followed by mastectomy and axillary dissection after its completion. Histopathological examination of mastectomy specimen showed mixed mucinous carcinoma (mucinous component 40%), invasive ductal carcinoma (40%) and carcinoma with neuroendocrine features (20%) (*Figures 3-5*).

Morphologically, the largest breast lesion [upper outer quadrant (UOQ)] showed malignant cells in interconnecting sheets, trabeculae and cords (*Figure 5A*) with 15% glandular formation. In less than 30% of the areas, mucinous extravasation was noted. The malignant cells were moderate to markedly pleomorphic and have vesicular nuclei. There were occasional prominent nucleoli and moderate amount of cytoplasm. Signet ring cells were also noted. Mitosis was 1 in 10 high power fields.

The second largest breast lesion [upper inner quadrant (UIQ)] showed interconnecting sheets of malignant cells (*Figure 5B*) with very minimal glandular formation. The malignant cells were mild to moderately pleomorphic and have hyperchromatic nuclei, inconspicuous nucleoli and moderate amount of granular cytoplasm. Occasional bizarre malignant cells were also noted. They were positive toward synaptophysin+ (*Figure 5C*) but negative for chromogranin-. Mitosis was absent.



Figure 3 Grossly, the overlying skin was unremarkable. The nipple appeared normal. There were three multicentric breast lesions identified. The largest lesion was located at UOQ of the breast and measuring 40×35×30 mm. The tumor border was ill-defined and infiltrative. It has dirty white solid cut surface with brownish nodular appearance at the periphery. The other lesion at UIQ of the breast (*Figure 1*) has also similar gross findings and measured 20×28×30 mm. UOQ, upper outer quadrant; UIQ, upper inner quadrant.



Figure 4 The smallest breast lesion was located at LIQ of the breast (*Figure 2*) and measuring 11×11×11 mm. It has well defined border with gelatinous solid cut surface. LIQ, lower inner quadrant.

The smallest breast lesion [lower inner quadrant (LIQ)] showed extensive mucinous extravasation with floating malignant cells in small nest and trabeculae (*Figure 5D*). The malignant cells were moderate to markedly pleomorphic and have vesicular nuclei and prominent nucleoli and moderate amount of cytoplasm. Overall, the stroma was fibrotic. Lymphovascular invasion and dermal lymphovascular were present. Ductal carcinoma *in situ* (DCIS) of high nuclear grade, usual ductal hyperplasia and benign ductal papilloma were also noted. No Paget's disease

of the nipple or direct skin involvement was identified. The malignant tumor involved at superior margin. In total, 21 reactive lymph nodes were examined. Nineteen out of these lymph nodes were involved by malignant cells. Extranodal extension was also present. The malignant tumors expressed estrogen receptor and progesterone receptor protein. Her2 protein expression was negative. Diagnosis of mucinous carcinoma, carcinoma with neuroendocrine feature and mixed mucinous carcinoma (mucinous type and no special type) with modified Bloom and Richardson grade 2 (score 6–7) was given.

Later, whole body bone scan however showed increased tracer uptake in the left parietal bone, right shoulder, left sternoclavicular joint, left 2nd rib (anterior), left 3rd rib (posterior), T11 vertebra, L4/L5 vertebrae, left ischium, sacroiliac joints, and sacrum is due HDP-avid skeletal metastasis. She was then referred to Oncologist for further management unfortunately refused for further treatment.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient.

Discussion

Breast cancer with multiple simultaneous foci has been a well-known issue for decades (2). When there is more than one distinct tumor within the same quadrant of the breast it is defined as multifocal and when multiple cancers develop in different quadrants of the breast it is defined as multicentric (3).

The diagnosis of unilateral multifocal breast cancer is usually made following a detailed histological examination of the dissected specimens. CECT (4) and magnetic resonance imaging (MRI) (5) have been reported to reveal a unilateral multiple breast cancer prior to surgery. Similarly demonstrated in our patient where preoperative CECT showed multicentric left breast lesion.

Based on recent studies, surgical options on multicentric or multifocal breast cancer (MMBC) women may undergo breast-conserving surgery as long as the principles of negative margins, appropriate radiotherapy and acceptable cosmesis are met (6-9). Most of them reported a loco-regional recurrence range of 3.0% to 5.1% at a 6-year follow-up in MMBC women with breast conservation, and there was no difference from the patients with unifocal tumor. Furthermore, they did not find any apparent

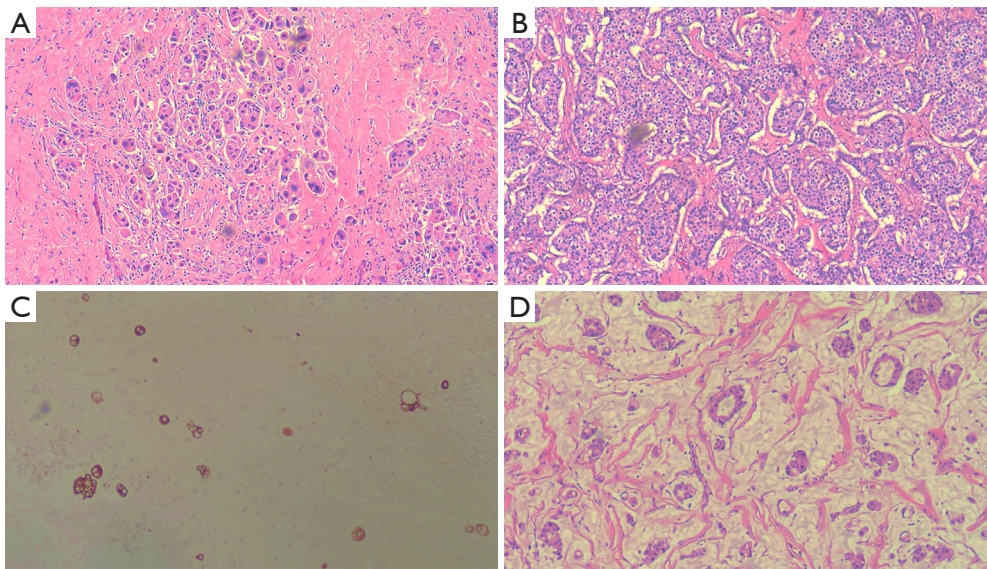


Figure 5 Histology showing three different features. (A) Malignant cells in interconnecting sheets, trabeculae and cords with 15% glandular formation at upper outer quadrant (haematoxylin and eosin, 10×). (B) Malignant cells arranged in interconnecting sheets of malignant cells with very minimal glandular formation at upper inner quadrant (haematoxylin and eosin, 10×). (C,D) Extensive mucinous extravasation with floating malignant cells in small nest and trabeculae at lower inner quadrant (haematoxylin and eosin, 10×).

differences in terms of disease-free survival or cosmetic result between MMBC patients and women with unifocal breast cancer after breast-conserving treatment. Hence, breast-conserving surgery is an option and effective for MMBC patients. Another study concluded that breast conserving surgery was a safe option in selected MMBC cases, particularly those women aged 50–69 years old with small multifocal tumor (<1 cm) and without an extensive DCIS component (10).

Multicentric breast cancers have a negative impact on prognosis. They are related to higher loco-regional and distant relapse independently from the type of surgery performed. Multicentric tumors have a worse biological behavior and that the presence of multiple foci should be considered in planning adjuvant treatments (11).

Conclusions

Multicentric breast cancer comprising of three different histopathological types are rare. Breast conserving surgery is a safe surgical option for multicentric breast cancer however the prognosis is usually poor due to advanced presentation and its tumor biology.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/abs-19-101>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki

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