

A case of synchronous bilateral invasive lobular carcinoma of breast

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Abstract: Breast cancer is the most common malignancy in female, accounting for nearly 22.9% of all malignancy in female worldwide. However, bilateral breast cancer is rare and sometimes missed. We reported a 44 year old lady presented with late presentation of bilateral invasive lobular breast carcinoma, focusing on her risk factors and treatment strategy.

Keyword: Bilateral Breast Cancer, Invasive Lobular Carcinoma

1. Case Summary

A 44 year old lady presented to our department with 7 months history of painless left breast lump, gradually increasing in size and reducing mobility, associated with constitutional symptoms such as loss of weight (17 kg for past 1 year) and loss of appetite. She started having backache about 2 months prior to admission. She is still menstruating and has 4 previous pregnancies. Her elder birth sister has breast cancer. She has no other comorbidities.

Clinically, she has a large 10cm x 10cm central breast lump which is hard and fixed to the skin, with skin dimpling, peau d'orange and nipple retraction, but not fixed to chest wall. There is presence of hard and fixed left axillary lymphadenopathy.

During the course of work-up, clinical breast examination revealed another asymptomatic right upper outer quadrant breast lump approximately 5cm x 5cm which is mobile without involvement of skin and nipples, and right mobile axillary lymph nodes palpable.

FNAC done on left breast lump revealed infiltrating ductal carcinoma. Computer Tomography (CT) of Chest and Abdomen reveals multilevel sclerotic vertebral bone lesions, left breast lesion infiltrating skin with multiple left axillary lymph nodes. There is enhancement of left pectoralis muscles which most probably signifies chest wall infiltration. There was no evidence of liver or lung

metastasis on CT. Serum calcium level was normal. Bone scan was not yet available to confirm bone metastasis (figure 1).

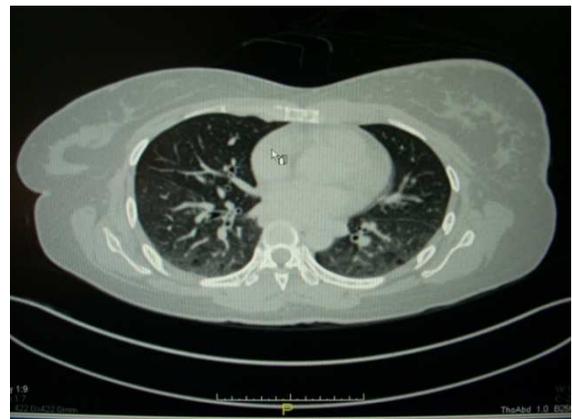


Figure 1. Thickened and irregular pectoralis major muscle on the left side suggestive of infiltration.

Treatment is planned as for locally advanced bilateral breast cancer at this stage. She was counseled for mastectomy with axillary clearance. In view that tissue biopsy for right breast lump may delay surgery; intra-operative right breast lump incisional biopsy was taken for frozen section histopathological examination, which was reported as infiltrating lobular carcinoma. Decision was made intra-operatively, with prior consent from patient to

proceed with bilateral mastectomy and bilateral axillary clearance up to level II (figure 2 and 3). It was also found that left breast tumour does not adhere to chest wall muscles, in contrary to CT scan findings. Otherwise, other operative findings were consistent with clinical findings. Post-operative recovery was uneventful.

Final histopathological examination report is summarized as follow:

Right breast: Infiltrative Lobular Carcinoma, pT3 and N2. Tumour size measures 10cm x 3cm x 7cm. Surgical margins are clear for right side. 13 lymph nodes sampled from right axilla were all positive for metastatic lesions. Left breast: Infiltrative Lobular Carcinoma, pT3. Tumour size measures 6cm x 2cm x 6cm. Unable to assess N as no lymph nodes where sampled but axillary fat tissue contains scattered foci of tumour deposits. Surgical margins are clear except for inferior margin 3mm and deep margin 2mm from tumour. Both side tumours have lymphovascular permeation, and are Cyclin D1, Estrogen receptor & Progesterone receptor positive. E-cadherin and Cerb B2 are negative for both.(figure 4)

Final diagnosis was bilateral infiltrative lobular carcinoma of breast, pT3 N2 Mx. Bone metastasis was suggestive based on CT scan but not yet confirmed by bone scan. Post-operatively she recovered well. Drains on both site were removed after 5 days and she did not have any post-operative complications.

2. Discussion

Between 2% and 11% of women with an initial primary invasive breast cancer develops contralateral breast cancer in their lifetime , with several studies demonstrated annual risk of developing contralateral breast cancer to be around 0.5% to 0.8% (1). Synchronous bilateral breast cancer accounts for only 1.1% of all breast cancer. Synchronous breast cancer is defined as second primary breast cancer detected within 1 year of the diagnosis of the primary breast cancer (1). Even though infiltrating lobular carcinoma accounts for about 5-10% of all invasive breast cancers, it is recognized that nearly 8.7% of patients diagnosed with invasive lobular carcinoma have bilateral breast disease as compared to 0.5% in invasive ductal carcinoma (2).

It is important to be able to identify the relatively small proportion of women at risk of having bilateral breast cancer or having a second contralateral primary breast cancer, so that close surveillance and appropriate adjuvant therapies can be considered. Commonly recognized risk factors associated with bilateral breast cancer are age of onset of first primary breast cancer, histopathology of lobular carcinoma, positive family history of breast cancer and presence of genetic predisposition.

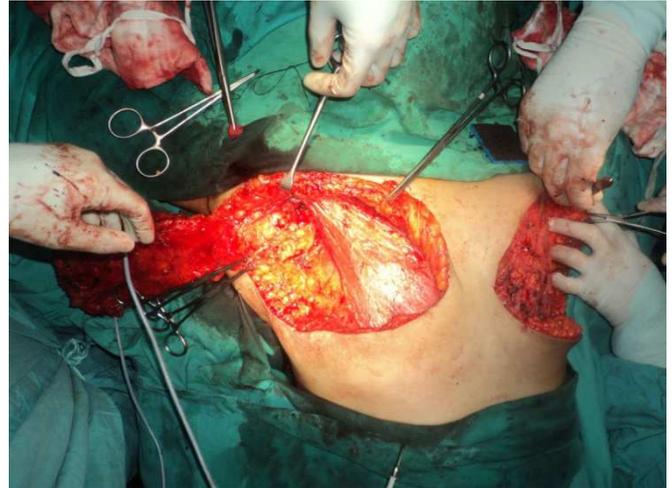


Figure 2. bilateral mastectomies were done during the same setting.



Figure 3. The appearance of the surgical scar after the mastectomy.

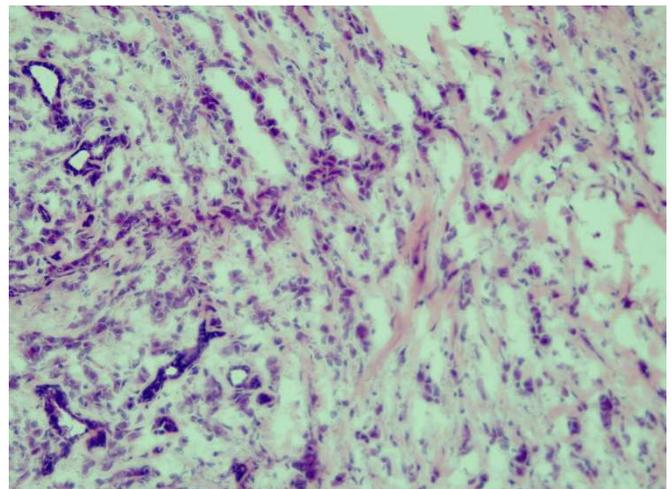


Figure 4. microscopic appearance of right breast tissue in haematoxyline and eosin showing heavily malignant cell infiltration.

In this case, we are dealing with a young lady with synchronous bilateral breast cancer. She presented late with a left breast lump, which clinical examination subsequently detected a smaller asymptomatic lesion on the right breast.

Initial report of invasive ductal carcinoma via FNAC from left breast tumour was later confirmed as invasive lobular carcinoma which is identical to the right breast histopathology.

Many studies have concluded that age of onset of the primary breast cancer is related to increased risk of developing a second primary breast cancer. Chen Y et al confirmed that women who developed primary breast cancer at the age below 40 years old is associated with a 17 fold risk of developing a second primary breast cancer compared to the risk of developing primary breast cancer in general population (1). Some concludes that this risk factor is the most important predictor for contralateral breast cancer. This may be explained by the fact that younger patients have longer life expectancy, and young onset of breast cancer is associated with positive family history and mutation of BRCA 1 and 2 genes (1,3).

BRCA 1 and 2 mutation carriers diagnosed with breast cancer have a strong lifetime risk of developing contralateral breast cancer. The risk is 53% among gene mutation carriers compared to 2% among non-carriers. This group of individuals also presents at significantly younger age (mean age of 42 years old) and has strong family history of breast cancer (4).

Studies have showed that positive family history of breast cancer is associated with increased risk of developing contralateral breast cancer. The effect of family history was particularly noted among women with an affected first-degree relative. There is also data showing that having a sister with breast cancer incurs a greater risk of contralateral breast cancer compared to having a mother with breast cancer (5). In this case, our patient has a biological sister who was also diagnosed with breast cancer. However, no genetic screening was performed to neither her nor her family members.

In term of histology, it is well documented that invasive lobular histology type is significantly associated with nearly 2 fold increased risk of contralateral breast cancer, and that this increased risk is only found among cases of synchronous tumours rather than asynchronous cases (5). Bilateral breast cancers are now accepted to be of two events of independent origin instead of metastatic lesion from the initial breast cancer. First tumour appears to be unrelated to time of appearance and biological characteristic of the second (3). In our case, both lesions are primary breast cancers arising independently from a single lobule and shows typical infiltrative pattern. It is suggested that the high frequency of bilaterality of lobular carcinoma is related to greater hormonal sensitivity of terminal duct – lobular unit compared to more proximal ducts. Therefore, bilateral synchronous lobular carcinoma is frequently associated with bilateral hormone receptor positive as in our case (3).

Traditionally, invasive lobular carcinoma was considered to be a bilateral breast disease due to its tendency for multifocality and bilaterality. Mastectomy was a standard practice on the affected breast regardless of the size of

tumour. To increase early detection of contralateral breast cancer, it was previously a normal practice to perform clinical or mammogram guided biopsy of the contralateral breast or even prophylactic mastectomy of the contralateral breast. Random blind biopsy and prophylactic mastectomy of contralateral breast is no longer recommended (6). However, several recent studies have proved that invasive lobular carcinoma can be treated surgically with the same principles applied to invasive ductal carcinoma.

Principles of management for this lady are based on agreed consensus on locally advanced breast cancer (6,7). Pre-operatively, clinical staging for her left breast cancer was T4c and N2 whereas her right breast disease was assessed as T3 and N1. Metastatic disease to the bone was confirmed on CT scan. She had adequate skin cover for primary closure post-mastectomy on the left side. In view of tumour clinically involving skin, nipple areolar complex and chest wall, she had clear indications for left mastectomy with axillary clearance, followed by adjuvant radio-chemotherapy (6).

Discovery of right breast lump was late. Tissue biopsy for right breast lump and mammogram assessment was not available. Frozen section biopsy intra-operatively for right breast lump is an alternative for tissue confirmation of malignancy. In absence of mammogram assessment for multifocal lesions, breast conserving surgery is not a suitable option. Therefore, once frozen section confirmed invasive breast cancer, the best surgical option was a right mastectomy and axillary clearance to reduce the risk of local recurrence. Surgical removal of primary tumour was associated with longer survival in stage IV breast cancer (7).

With presence of 13 lymph nodes with metastatic depositions on right axilla, presence of large tumour (more than 2cm) with lymphovascular permeation on both side and left mastectomy deep margin is 2mm from tumour, there are clear indications for both adjuvant chest wall radiotherapy and chemotherapy. Hormonal therapy with Tamoxifen for 5 years is also indicated with presence of Estrogen receptor and Progesterone receptor positive in a premenopausal woman (7). Breast cancers are both moderate radiosensitive and chemosensitive tumour. However, numerous studies have proven that adjuvant local radiotherapy is associated with lower local recurrence rates, whereas adjuvant chemotherapy and hormonal therapy are associated with prolonged relapse-free survival and overall survival (7).

3. Summary

In conclusion, synchronous bilateral breast cancer is uncommon. Various studies consistently confirms several important risk factors, namely age of onset of first primary breast cancer, first cancer of lobular histology, positive family history and presence of BRCA 1 and 2 mutation. Presence of these risk factors should alert clinician to actively search for contralateral breast cancer to ensure full work-up and pre-operative preparations are made

adequately. Treatment options of invasive lobular carcinoma are similar to other histological types. Frozen section biopsy intra-operatively is useful in diagnosis and defining treatment strategy in selected cases. In this case, bilateral mastectomy and axillary clearance was the surgical treatment of choice, followed by adjuvant local and systemic therapies.

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