CASE REPORT

Recurrent medullary breast carcinoma with good response to chemotherapy. A case report and revisit of pathology

Tiew Toot Chaw, MD (RNRMU)[1], Henry Tan Chor Lip, MMED Surgery[1], Raja Norazah Raja Alam Shah, Anatomical Pathology[2], Rahimah Abd Rashid, MPath[2]

[1]Department of General Surgery, Hospital Sultan Ismail, Johor Bahru, Malaysia, [2]Department of Pathology, Hospital Sultanah Aminah, Johor Bahru, Malaysia

SUMMARY

Medullary breast carcinoma (MBC) is an uncommon variant of invasive ductal carcinoma accounting for less than 5% of all the invasive breast carcinomas. Despite its aggressive histopathological features, it has a much better prognosis compared to triple negative breast cancers. Herein, we present a case of a 37-year-old women who presented with right breast lump and diagnosed with invasive breast cancer with medullary features after an elective lumpectomy and axillary dissection. Due to an unplanned pregnancy, planned adjuvant radiotherapy and chemotherapy were withheld after the primary surgery. Following the delivery of her child, she had a local recurrence with distant metastasis evidenced by clinical examination and computerized tomography (CT) scan. Despite the dismal situation, she had a good response to chemotherapy and subsequently underwent an elective mastectomy and repeated axillary dissection. The management and pathology of medullary breast cancer is discussed in this case report.

INTRODUCTION

Breast cancer is the commonest malignancy amongst females worldwide.[1] Among the subtypes of breast cancer, medullary breast carcinoma (MBC) is a rare variant of invasive ductal carcinoma and its reported incidence is fewer than 5% of all invasive breast cancers.[1] MBC is one of the invasive and malignant subtypes.[2] The five key histopathological features of typical MBC include syncytial growth pattern (>75%), without glandular and intraductal structures, diffuse lymphoplasmacytic infiltration in the stroma, moderate or marked nuclear pleomorphism and complete histological circumscription.[3] Recent World Health Organization (WHO) 2019 classification of breast carcinoma has re-categorised MBC as a subtype of invasive breast carcinoma-no special type (IBC-NST) with medullary pattern rather than a distinct morphological subtype of medullary carcinoma.[4] These tumours commonly occur in middle-aged women of 45 to 52 years.

Despite its aggressive histopathological appearance and malignant characteristics, MBC have a favourable prognosis if treated promptly. In this case report, we aim to revisit the histopathological diagnosis and create awareness of a patient diagnosed with recurrent metastatic MBC with good response to palliative chemotherapy.

CASE PRESENTATION

A 37-year-old woman presented to the breast surgery clinic with a right breast lump for 3 months. She was previously well with no significant past medical history or prior admissions. There was no history of oral contraceptive usage, no prior breast surgeries performed and no family history of breast cancer. Apart from a right breast lump, there were no skin changes over the overlying mass. Physical examination showed a firm mass with regular margin at upper inner quadrant, measuring 2 × 1 cm, well circumscribed and not fixed to skin or underlying muscle, no axillary lymph node palpable. Bilateral breast mammography and ultrasound revealed a right breast hypoechoic lesion at 2 o'clock which was radiologically classified as high-risk Breast Imaging-Reporting and Data System (BI-RADS) 4C. Ultrasound guided fine needle aspiration cytology (FNAC) from the lesion showed atypical cells with high suspicion of malignancy. Chest x-ray and ultrasound abdomen showed no evidence of lung and liver metastasis. The patient underwent an elective right parallelogram mastopexy lumpectomy and axillary node dissection. Post-surgery, recovery was uneventful and final histopathology results were consistent with MBC with clear margins (pT1c N0 M0). Arrangements for post-operative chemotherapy and radiotherapy to the breast after breast conserving surgery the during follow-up of 1 month post operation were unsuccessful as the patient had an unplanned pregnancy (Gravida 3 para 2 at 5 weeks of gestation) and unable to proceed for further adjuvant oncological treatments due to possible risks of chemotherapy induced foetal toxicity. The patient had an uneventful delivery and remained asymptomatic after her delivery. However routine health checks during the breast surgery clinic follow-up after the delivery of her baby a year later revealed a right breast lump. She was immediately investigated for recurrence of breast cancer. During this period, a repeated computerized tomography (CT) staging of thorax, abdomen pelvis revealed a suspicious right breast lesion (size measuring 5 × 4.8 cm) with extension to the anterior mediastinum and intrathoracic, bilateral pleural metastasis and multiple liver metastasis (Figure 1). A repeat biopsy of the right breast lump showed benign breast tissue. The case was discussed in the hospital's tumour board meeting and the consensus is to treat this as recurrent metastatic breast cancer despite the negative breast biopsy, for first line palliative chemotherapy with carboplatin and paclitaxel which she completed six cycles. Reassessment staging CT thorax, abdomen and pelvis revealed smaller

This article was accepted:
Corresponding Author: Tiew Toot Chaw
Email: warrentiew@gmail.com

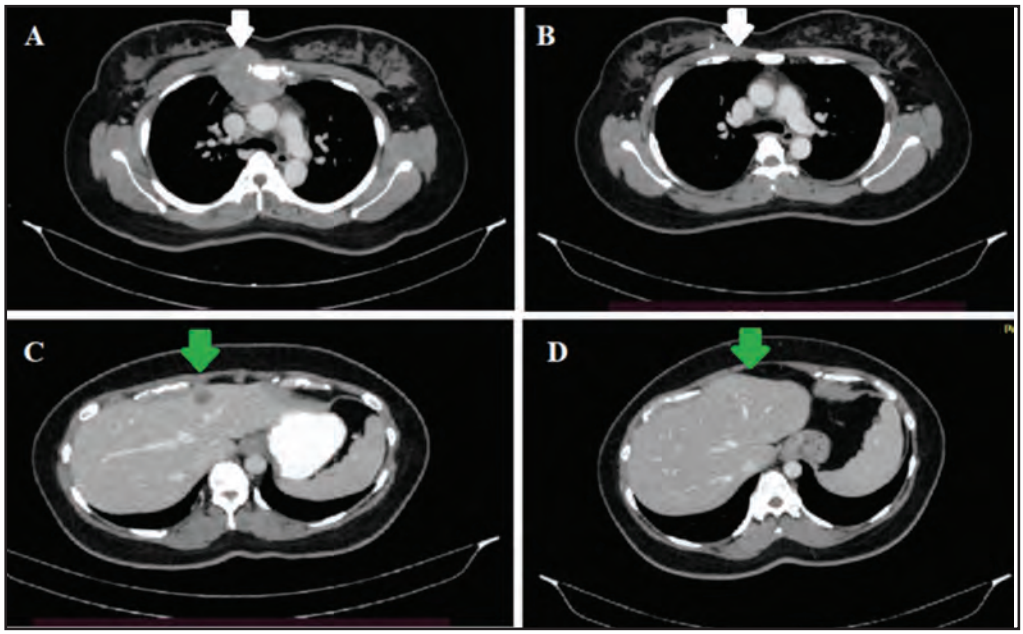

Fig. 1: Contrast enhanced CT thorax and abdomen showing pre- and post-chemotherapy with good response. Figure 1A showing pre-chemotherapy with right breast tumour with extension to the anterior mediastinum and intrathoracic, bilateral pleural metastasis which completely disappears after chemotherapy Figure 1B. Figure 1C which shows liver metastasis pre-chemotherapy (largest at segment II measuring 1.4 × 1.8 cm) which disappears after chemotherapy Figure 1D

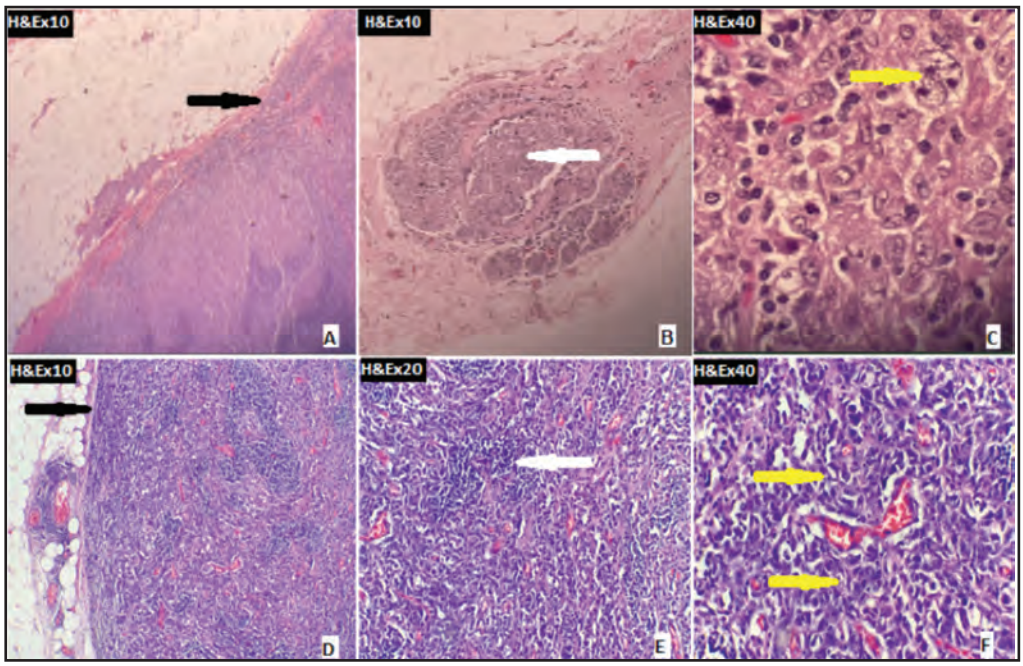

Fig. 2: A,B,C: First surgery right breast lumpectomy microscopic specimen. D,E,F: Second surgery right mastectomy microscopic specimen. A,B,D,E: Syncytial sheets of malignant epithelial cells with poor tubule formation accompanied by marked stromal tumour infiltrating lymphocytes (white arrow) and peripheral circumscription (black arrow). C,F. The tumour cells are large with moderately pleomorphic vesicular nuclei (yellow arrow), prominent nucleoli and moderate to abundant cytoplasm

right breast lesion (size measuring 2 × 1.5 cm) and right axillary lymphadenopathy with complete resolution of intrathoracic, pleural and liver metastasis (Figure 1). The patient underwent an elective right mastectomy and repeat axillary dissection. Post-operative recovery was uneventful, and the patient completed radiotherapy to right chest wall and supraclavicular fossa 40 Gy in 15 fractions for 3 weeks. During follow-up at 6 months post-surgery, the patient remains well with no signs and symptoms of disease recurrence.

First specimen of right breast lumpectomy measured around 85 × 40 × 40 mm, on serial cut sections revealed a tumour measuring 20 × 15 × 20 mm with irregular margin and had

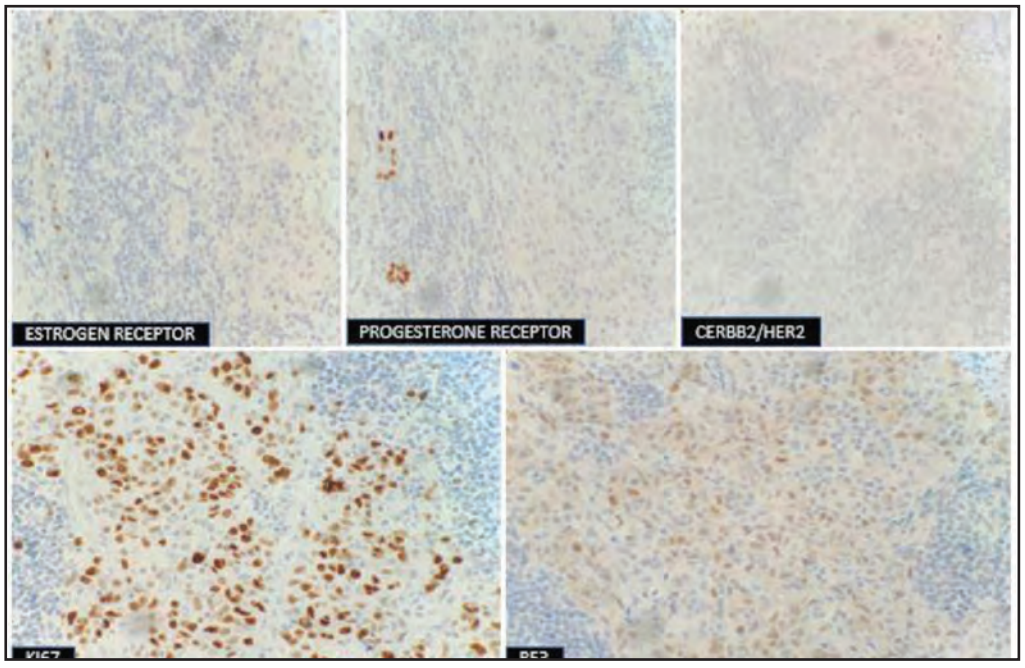

Fig. 3: IHC show negative for ER, PR and CerbB2/Her-2 and positive for Ki-67 (90%) and P53

a lobulated surface. Examinations revealed that the sections from the breast tissue exhibits malignant tumour infiltrates which are arranged in syncytial architecture. The tumour had a pushing border and was circumscribed (Figure 2A). There was also infiltration of lymphoplasmacytic cells within the collagenous stroma and lymphovascular invasion seen (Figure 2B). The tumour cells were pleomorphic with display of vesicular nuclei and prominent nucleoli with indistinct cytoplasmic border (Figure 2C). There were brisk mitoses seen with aberrant forms visualised. Histopathological impression, according to the Modified Bloom and Richardson criteria, was given as medullary carcinoma of breast grade III, with clear margins. All 16 axillary lymph nodes were free from metastasis. On immunohistochemistry study tumour cells were focally positive for CK 5/6 and CK7, negative for estrogen receptors (ER), progesterone receptors (PR), c-erb B2, CK20, p63 and LCA.

The patient underwent a second surgery of right mastectomy and repeated axillary dissection post chemotherapy due to recurrence and distant metastasis. The mastectomy specimen with nipple areola complex and skin were seen attached, measuring 175 × 165 × 50 mm, with well-healed scar seen at upper inner quadrant. Cut sections showed a circumscribed tumour with firm tan cut surface within the lower inner quadrant, measuring 20 × 20 × 15 mm. The histological examination showed similar features with the previous lumpectomy specimen - circumscribed tumour with pushing edges (Figure 2D) composed of malignant ductal epithelial cells arranged in interconnecting sheets, forming a syncytial network accompanied by marked stromal tumour infiltrating lymphocytes (Figure 2E). There was no overt tubule formation visualised. The tumour cells were large with moderately pleomorphic vesicular nuclei, small nucleoli and abundant cytoplasm (Figure 2F). The tumour size was 17 × 14 mm with clear resection margins. Tumour involvement was noted in 2 out of 4 axillary lymph nodes. The immunohistochemical study was positive for Pancytokeratin AE1/AE3, CK5/6 and p53 and negative for ER, PR and c-erb B2. Ki67 proliferative index was approximately 90% (Figure 3).

DISCUSSION

According to WHO, over 1.2 million women are diagnosed with breast cancer every year. Infiltrating ductal carcinoma is a broad entity which comprises tumours that exhibit one or more characteristics of specific types of breast cancers which includes tubular, papillary, medullary or mucinous differentiation.[2] MBC is rare and accounts for less than 5% of all invasive breast cancers.[1] Patients with MBC has an association with *BRCA* gene involvement. One study reported six cases of MBC (19%) among 32 *BRCA1*-associated breast cancers, compared to only one MBC (0.5%) among 200 patients without a family history of breast cancer.[5] This descriptive epidemiology study suggest that MBC is associated with germline mutations in the *BRCA1* gene. Due to the lack of facilities, the authors were not able to proceed with pre-test genetic counselling and germline *BRCA* testing.

Histopathological criteria to diagnose typical MBC include syncytial growth pattern of cells more than 75% of the tumour, well circumscription of microscopic mass, without glandular structures, diffuse lymphoplasmacytic infiltration and presence of marked nuclear pleomorphism with mitosis.[2-3] Sonographically, MBC often shows well circumscribed mass with hypoechoic structures which may mimic benign breast lesions such as fibroadenoma or phyllodes tumour. Thus, histopathologic evaluation is needed for definitive diagnosis. In our case, all the above features were present to clinch the diagnosis.

Compared to other types of breast cancer, triple negative breast cancer is highly invasive with limited treatment options, prone to recurrences, high metastatic potential and

has a poorer prognosis.[6] This is due to the lack of expression of ER, PR, and HER2 receptors making specific endocrine and targeted therapies ineffective. Therefore, chemotherapy has become the mainstay treatment for triple negative breast cancer. According to a report, the reported 5-year overall survival rate for metastatic triple negative breast cancers were 11% and for non-metastatic triple negative breast cancers were 81%.[7] MBC is a rare subtype of invasive ductal cancer and is frequently associated with triple negative breast cancer. However, triple negative MBC has a more favourable clinical outcome compared with the more common triple negative infiltrating ductal carcinoma, despite its aggressive histopathological features. Studies have reported that MBC had a longer 5- and 10-year survival in comparison to other triple negative subtype.[8] Due to the limited reports on MBC, a retrospective study reported a 5-year overall survival rate of 85% which is higher than other triple negative breast cancers.[9] It has been proposed that the presence of infiltration of lymphocytes and plasma cells assists in the suppression of MBC progression.[10] In our case, the patient had a local recurrence with distant metastasis which had good response to chemotherapy.

CONCLUSION

MBC is a rare subtype of infiltrating duct carcinoma which has high grade cytological features but has better prognosis as compared to invasive ductal carcinoma. Even in a metastatic setting, there is a possibility of good response with palliative chemotherapy. Careful histopathological evaluation and strict diagnosis criteria is necessary for definitive diagnosis and subsequent treatment.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient for publication of case report and accompanying images.

AVAILABILITY OF DATA AND MATERIALS

All data related to the outcome are included in the manuscript.

COMPETING INTERESTS

The authors declare that they have no competing interest.

FUNDING

This study was self-funded.

REFERENCES

1. Dendale R, Vincent-Salomon A, Mouret-Fourme E, Savignoni A, Medioni J, et al. Medullary breast carcinoma: prognostic implications of p53 expression. Int J Biol Markers. 2003; 18(2): 99-105.
2. Ridolfi RL, Rosen PP, Port A, Kinne D, Miké V. Medullary carcinoma of the breast: a clinicopathologic study with 10 year follow-up. Cancer. 1977; 40(4): 1365-85.
3. Kleer CG. Carcinoma of the breast with medullary-like features: diagnostic challenges and relationship with BRCA1 and EZH2 functions. Arch Pathol Lab Med. 2009; 133(11): 1822-5.
4. Tan PH, Ellis I, Allison K, Brogi E, Fox SB, Lakhani S, et al. WHO Classification of Tumours Editorial Board. The 2019 World Health Organization classification of tumours of the breast. Histopathology. 2020; 77(2): 181-5.
5. Eisinger F, Jacquemier J, Charpin C, Stoppa-Lyonnet D, Bressac-de Paillerets B, Peyrat JP, et al. Mutations at BRCA1: the medullary breast carcinoma revisited. Cancer Res. 1998; 58(8): 1588-92.
6. Yin L, Duan JJ, Bian XW, Yu SC. Triple-negative breast cancer molecular subtyping and treatment progress. Breast Cancer Res. 2020; 22(1): 61.
7. Hsu, JY., Chang, CJ. & Cheng, JS. Survival, treatment regimens and medical costs of women newly diagnosed with metastatic triple-negative breast cancer. Sci Rep 2022; 12, 729.
8. Budzik MP, Sobieraj MT, Sobol M, Patera J, Czerw A, Deptała A, et al. Medullary breast cancer is a predominantly triple-negative breast cancer - histopathological analysis and comparison with invasive ductal breast cancer. Arch Med Sci. 2019; 18(2): 432-9.
9. Khomsi F, Ben Bachouche W, Bouzaiene H, Chargui R, Ben Hassouna J, Mtaalah MH, et al. Carcinome médullaire typique du sein : étude rétrospective à propos de 33 cas [Typical medullary carcinoma of the breast: a retrospective study about 33 cases]. Gynecol Obstet Fertil. 2007; 35(11): 1117-22.
10. Kuroda H, Tamaru J, Sakamoto G, Ohnisi K, Itoyama S. Immunophenotype of lymphocytic infiltration in medullary carcinoma of the breast. Virchows Arch. 2005; 446(1): 10-4.