Case Report
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Long-term Breast Tumor Control with Brachytherapy and External Beam Radiotherapy: A Case Report

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Abstract

While surgical resection of the primary tumour and regional nodes is part of the standard algorithm for the treatment of early-stage invasive breast carcinomas, not all patients are surgical candidates or agree for surgery. This case report is about one such patient who refused surgery for a biopsy confirmed in the 7th edition of the tumour, nodes, metastases (TNM) Classification System (TNM7) T2N1M0 left breast infiltrative ductal carcinoma with estrogen receptor/ progesterone receptor positive and human epidermal growth factor receptor 2 negative for personal reasons.

A 39-year-old lady presented with left breast mass at upper outer quadrant, which confirmed to be infiltrative ductal carcinoma with Luminal A sub-type from the biopsy report. Despite the early stage of breast cancer, she refused for surgery because of personal reasons. Therefore, she underwent 12 cycles of chemotherapy followed by radiotherapy to the left breast and regional nodes to a dose of 50 Gy in 25 fractions (fx) and further high dose rate (HDR) brachytherapy boost of 16 Gy in 1 fx to the 2.0 × 2.0 cm residual lesion. After the completion of the treatment, the patient was on 20 mg tablet Tamoxifen daily.

During follow-up, there was a residual fibrotic lesion in the left breast from the computed tomography scan, and there was a doubt on the nature of the lesion. Thus, the patient was subjected to excision of the lesion and regional nodes, which showed a pathological complete response of three years after the completion of HDR brachytherapy. While surgery is the standard of care, this case report shows that definitive HDR brachytherapy has a role in patients not suitable for surgery.

Keywords: Carcinoma, Ductal, Breast, Brachytherapy, Radiotherapy

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Introduction

The outcome of early, non-metastatic breast cancer patients in terms of both local or locoregional recurrence and overall survival has improved markedly with the advancement in the multimodality treatment algorithm that consists of surgery, chemotherapy, radiotherapy, and at times molecular targeted therapy. However, despite the known effectiveness of the current treatment approach, there are still a small number of patients who are unable to undergo radical treatment or, in some circumstances, refuse the established treatment algorithm.

In patients who refuse definitive surgery for the local tumor in the breast, local ablative techniques may result in a good local control. The known local ablative techniques used in other tumor sites in the body include: thermal ablation such as radiofrequency ablation (RFA), microwave ablation, cryoablation, high-intensity focused ultrasound, laser ablation, and radiation modality such as stereotactic body radiotherapy (SBRT) and high-dose rate interstitial brachytherapy (HDR IBT).[1]

While radiation modality is a promising approach in definitive treatment of breast lesions, the evidence in the literature is scanty. A publication in 2023 by Shibamoto et al. showed very good local control rate and cosmetic outcome with definitive radiotherapy.[2] The present case report describes a patient who had a complete pathological response after a course of chemotherapy, external beam radiotherapy (EBRT), and HDR IBT for left breast cancer.

Case Presentation

A 39-year-old lady initially presented with a 4.0 × 3.0 cm painless left upper outer quadrant breast lump, which had been slowly increasing in size for the past two years in 2014. Tru-cut biopsy of the lesion confirmed infiltrative ductal carcinoma, Bloom Richardson grade 3 with 90% staining of estrogen receptor (ER), 75% staining of progesterone receptor (PR), and human epidermal growth factor receptor 2 (Her2) negative. Magnetic resonance imaging (MRI) of both breasts showed a 2.2 × 1.6 × 1.3 cm spiculated lesion in the upper outer quadrant. There was architectural distortion of nearby tissue, and two intramammary lymph nodes were seen posterior to the lesion with significant contrast uptake and the presence of a choline peak in one of the lesions (Figures 1A and 1B). Ultrasound demonstrated an ill-defined spiculated hypoechoic lesion at 2-3 o'clock position with posterior shadowing and internal vascularity correlating with the lesion seen on MRI (Figures 2A and 2B). Subsequent staging computed tomography (CT) scans of the thorax, abdomen, and pelvis showed the left upper outer quadrant left breast lesion measuring 2.3 × 1.8 cm (Figure 3A) with no evidence of distant metastatic disease. The patient was counselled for wide local excision and axillary dissection followed by chemotherapy and radiotherapy. However, despite extensive

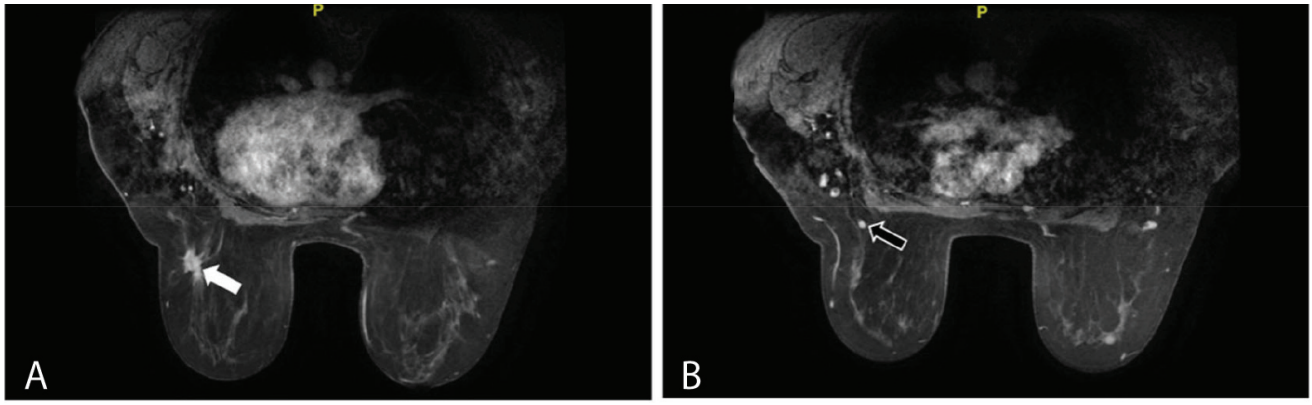

Figure 1. This figure shows: (A) Axial magnetic resonance of both breasts with contrast demonstrating a 1.6 × 1.3 × 2.2 cm enhancing spiculated lesion (white arrow) located directly 8 cm posterior to the base of left nipple on image. (B) There is architectural distortion of nearby tissue with no obvious skin thickening. Two intramammary lymph nodes were seen posterior to the lesion with the one further away (black arrow) showing significant contrast uptake.

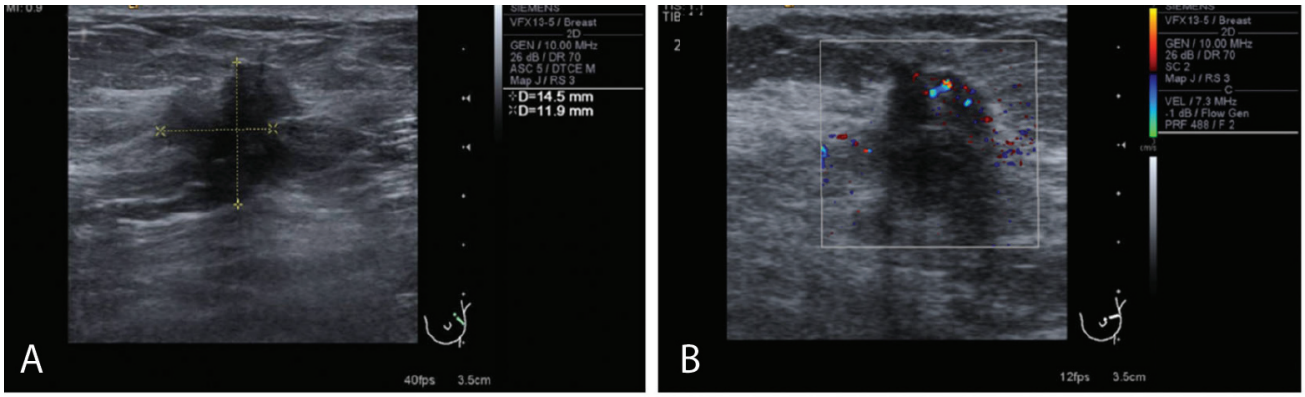

Figure 2. This figure shows the ultrasound of left breast showing ill-defined spiculated taller than wider hypoechoic lesion at 2-3 O'clock position on image A with posterior shadowing and internal vascularity (image B) correlating with lesion seen on MRI.
MRI: Magnetic resonance imaging

counselling, the patient was worried about the cosmetic outcome and did not wish to have any scars on her breast. She was planning to get married within six months.

Otherwise, the patient agreed to undergo chemotherapy, radiotherapy, and hormonal therapy. The patient was subjected to 4 cycles of adriamycin and cyclophosphamide every 3 weeks, followed by 12 cycles of weekly paclitaxel chemotherapy. Upon the completion of the chemotherapy, the lesion in the left breast reduced to 2.0 × 2.0 cm on clinical assessment. Thereafter, the patient underwent EBRT to the left breast and regional nodes. Radiotherapy dose prescription to the left breast was 50 Gy in 25 daily fractions (fx), 5 times a week, using tangential fields to cover the left breast. A direct anterior field was used to cover the supraclavicular fossa and left axilla, delivering 45 Gy in 25 daily fx (Figure 2). After the completion of EBRT, treatment with HDR IBT for the residual lesion was proposed to the patient. The patient agreed and consented to the treatment while acknowledging that there is limited data in the literature.

One week after completing the course of EBRT, the patient underwent HDR IBT for the residual lesion in the left breast. The procedure was performed under mild sedation and local anesthesia. A flexible 6 French (F) needle catheter (ProGuide Sharp Needle; Nucletron an Elekta Company, Veenendaal, The Netherlands) was inserted through a small skin incision under ultrasound guidance to penetrate at the center of the tumor. The applicator was further advanced around 2 cm beyond the tumor to ensure good dose coverage. The patient was CT simulated with IV contrast, and the tumor margins were manually contoured in the CT images. Brachytherapy dose planning was performed using the Oncentra MasterPlan v5.2 brachytherapy

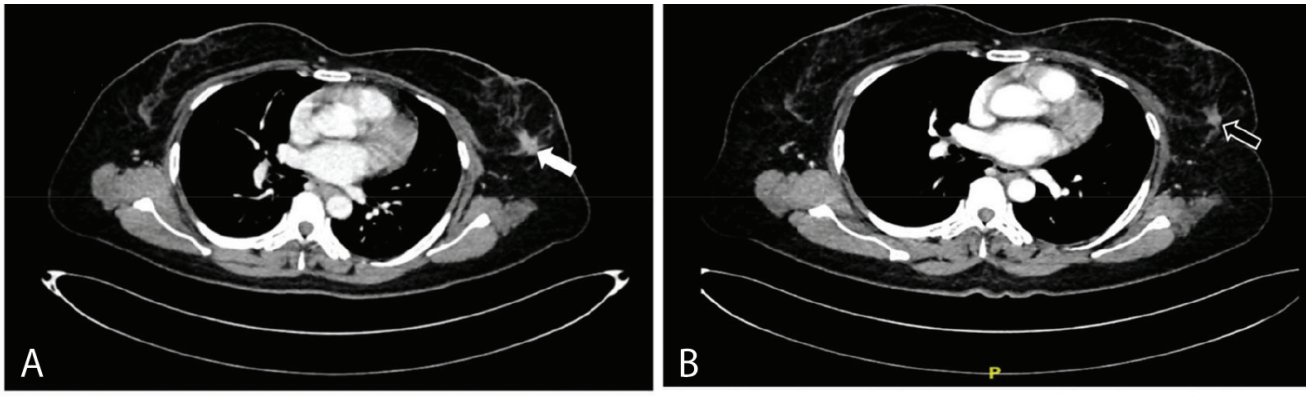

Figure 3. This figure shows: (A) Axial computed tomography of thorax with contrast demonstrating a 2.3 × 1.8 cm enhancing spiculated lesion (white arrow) in the upper outer quadrant of the left breast prior to treatment on image. (B) 3 years after completing the treatment, the similar lesion appears to be smaller in size measuring 1.2 × 0.9 cm on image.

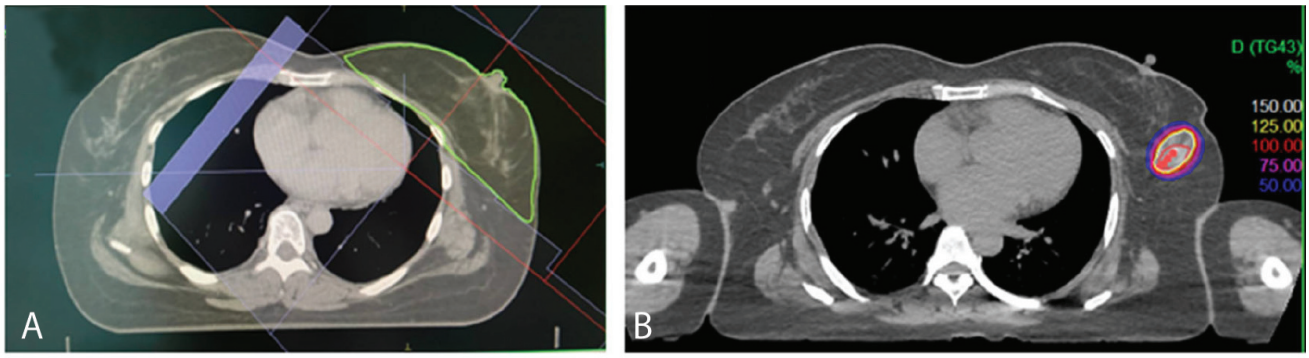

Figure 4. This figure shows: (A) Axial tangential EBRT plan of the left breast and (B) brachytherapy plan to the residual lesion. EBRT: external beam radiotherapy

computerized treatment planning system. The prescribed dose was 16 Gy in single fx to the periphery of the tumor, and 95% of the tumor received at least 20 Gy (Figure 4).

The patient had been on regular three-monthly follow-up with the breast surgeon with no active complaints throughout the period. A repeat CT thorax, abdomen, and pelvis at three years after completing the treatment showed a 1.2 × 0.9 cm lesion with ill-defined margins in the left breast (Figure 3B) corresponding to the earlier lesion. This time the patient was counselled again, and she agreed and underwent wide local excision and axillary dissection.

Intraoperatively, the tumor location was confirmed with on table ultrasound. Periareolar methylene blue injection did not show any discoloration of the breast mass or axillary nodes. Axillary lymph node dissection and wide local excision of the tumor through the axillary scar were performed. The thoracodorsal, long thoracic, and intercostobrachial nerves were preserved. There was no significant fibrosis intraoperatively, and postoperative recovery was uneventful. The tissue was sent for a frozen section, which showed more than a 6 cm margin in all directions from the fibrotic lesion. Further histopathological examination showed no viable cancer cells, and all 12 identified lymph nodes were clear of metastatic disease. The pathological staging was ypT0N0. The timeline of the major events is summarized in (Figure 5).

On our last follow-up in July 2024, the patient was clinically disease-free with normal mammogram findings, the tumor marker (CA15.3) was within the normal range, and the patient was satisfied with the cosmetic outcome of her left breast. The patient consented to the use of her

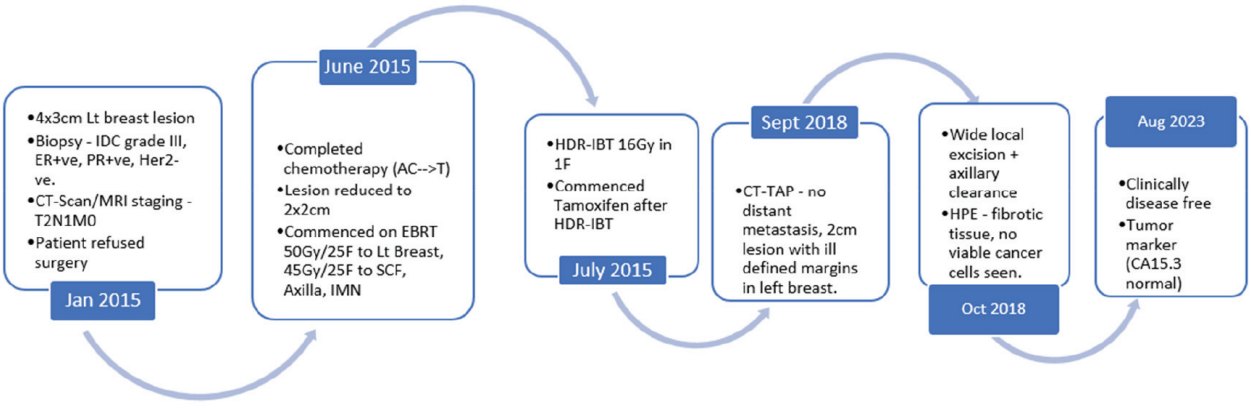

Figure 5. Timeline of major events from January 2015 to August 2023

Jan: January; IDC: invasive ductal carcinoma; ER+ve: estrogen receptor positive; PR+ve: progesterone receptor positive; Her2-ve: human epidermal growth factor receptor 2 negative; CT: computed tomography; MRI: magnetic resonance imaging; Lt: Left; IDC: Infiltrating ductal carcinoma; AC-->T: Adriamycin/Cyclophosphamide 3 weekly x 4 cycles followed by weekly Paclitaxel x 12 cycles; EBRT: external beam radiotherapy; Gy: Gray; F: fraction/s; SCF: supraclavicular fossa; IMN: internal mammary lymph node; HDR-IBT: high dose rate interstitial brachytherapy; Sept: September; CT-TAP: CT scan of thorax/ abdomen/ pelvis; Oct: October; HPE: histopathological examination; Aug: August; CA15.3: Cancer Antigen 15.3.

case and radiological images for publication, but she was not keen to have a clinical image of her breast for the purpose of this publication.

The ethical approval was granted from the Human Research Ethics Committee USM (HREC), Universiti Sains Malaysia, with registered ethics code of USM/JEPeM/PP/25050470. The patient was informed about the purpose of the study, her rights, and written consent was obtained.

Discussion

RFA is the most well-studied ablative technique in definitive breast treatment. A phase 2 prospective trial of RFA showed a higher complication rate, such as postprocedural inflammation, infection, and poor cosmetic outcome, and the authors even suggested omitting radiotherapy to reduce the toxicity.[3] While complete ablative rates of 96% confirmed by pathological examination have been reported with RFA, significant toxicity such as skin burn, and muscle burn has been reported.[4]

HDR IBT has distinct advantages such as high radiation tolerance of the skin, the ability to treat larger tumors as seen in other organs or tumor sites, and immune modulatory effects.[5, 6] With the current HDR IBT computerized three dimensional (3D) treatment planning system, significant post-insertion dose manoeuvring is possible to ensure good coverage of the tumor seen in the CT images. The use of radiation in breast cancer treatment has a long history and proven efficacy, whereby omitting it as suggested in the RFA paper can be detrimental.[3] While there had been attempts to use EBRT, either as a single ablative dose with the SBRT technique or as a boost after completing the conventionally fractionated radiotherapy, these techniques are quite complex with the need for accurate positioning and motion management facilities.[7, 8] Compared with SBRT, HDR IBT can produce a better dose conformality while ensuring that the central hypoxic region receives a much higher dose of radiation.[9]

In this patient, the combined dose of EBRT and HDR IBT was around 84 Gy, which resulted in no viable tumor cells in the surgical specimen three years later. The regional nodes, which include the axilla and supraclavicular fossa, were included in the EBRT fields as the patient did not have a nodal sampling before chemotherapy. The internal mammary node was not included as the lesion was in the lateral segment of the breast.

Axillary dissection was performed even though there is no dye uptake, as in the post-chemotherapy setting, sentinel lymph node assessment may not be accurate. Positron emission tomography-CT (PET-CT) scan facility was not available in our center at the time of surgery, and probably surgery would have been avoided in this patient if PET-CT scan had shown complete metabolic response in this patient.

Patient's favorable outcomes may be attributed to molecular subtype of Luminal A, clinical presentation at early stage, and aggressive treatment with chemotherapy, EBRT, and HDR IBT.

Conclusion

The combination of EBRT and HDR IBT to a total cumulative equivalent dose in 2 Gy fx (EqD2) > 84 Gy to the primary lesion induced complete pathological response. HDR IBT has a distinct advantage compared with other local ablative methods and has the potential to become the preferred choice of local treatment in breast cancer patients who are not suitable for surgery.

Informed Consent

The patient gave informed consent.

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Authors' Contribution

GKA, MZAA, HH, SAS, NDR, NHI and NKAK: Study design; data acquisition; data analysis and interpretation; drafting and critical reviewing of the manuscript. KY: Manuscript editing and submission. All authors read and approved the final manuscript version and agreed

with all parts of the work in ensuring that any queries about the accuracy or integrity of any component of the work were appropriately investigated and handled.

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Conflict of Interest

None declared.

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