

Persistent Extensive Microcalcifications After Neoadjuvant Chemotherapy: Benign or Malignant?

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ABSTRACT

Neoadjuvant chemotherapy is increasingly used for breast cancer due to its several benefits. Assessment of the response to neoadjuvant chemotherapy plays a key role in the management of the disease. Although magnetic resonance imaging is the most accurate method, evaluation of the response to neoadjuvant chemotherapy may be challenging especially in the presence of residual microcalcifications. The presence of residual microcalcifications may not always suggest the residual viable tumor.

In this case, a 48-year-old patient with breast cancer who had persistent extensive microcalcifications after neoadjuvant chemotherapy is presented. Magnetic resonance imaging demonstrated a complete response with the absence of any residual enhancement. Final histopathological results after breast-conserving surgery revealed pathological complete response which is consistent with magnetic resonance imaging and inconsistent with mammography findings. Mammography images showed residual malignant-type microcalcification after surgery, although most of them were excised. However, microcalcifications haven't progressed and recurrent cancer hasn't been observed on MRI and mammography images during the 10-year follow-up.

Keywords: Neoadjuvant chemotherapy, microcalcifications, magnetic resonance imaging, mammography.

INTRODUCTION

Neoadjuvant chemotherapy (NAC) for the treatment of breast cancer has been increasingly used due to several advantages. NAC can decrease tumor size and axillary metastatic nodes before surgery and allow breast-conserving surgery (BCS) and omission of full axillary lymph node dissection (ALND). Furthermore, NAC can provide direct observation of treatment efficacy [1].

Pre- and post-treatment imaging methods including ultrasonography (US), mammography, and magnetic resonance imaging (MRI) are used to assess response to NAC and play a key role in the management of the disease. MRI is superior to other imaging modalities in the evaluation of residual

disease after NAC [1,2]. The overall diagnostic accuracy of MRI in predicting pathological response is reported to be 84% [3]. On the other hand, evaluation of malignant microcalcifications after NAC is challenging as they are not observed on MRI, and the presence of residual microcalcifications doesn't always show the viable tumor. So, the decision on surgical approach may become controversial.

Here, a patient with breast cancer who had persistent extensive microcalcifications after NAC is presented. Histopathological results after BCS revealed pathological complete response (pCR) which is consistent with MRI and inconsistent with

mammography findings. While mammography images show residual malignant-type microcalcification after surgery, microcalcifications haven't progressed and recurrent cancer hasn't been observed on MRI and mammography images during the 10-year follow-up.

CASE PRESENTATION

A 48-year-old female patient was admitted to the hospital with complaints of palpable mass within her left breast. Mammography images demonstrated extensive pleomorphic malignant-type microcalcifications and skin thickening in the left breast. Masses could not be observed on mammography secondary to dense fibroglandular tissue (Fig 1a and 1b.) US revealed hypoechoic irregular masses with echogenic foci corresponding to microcalcifications. Contrast-enhanced breast MRI detected non-mass enhancement with type 3 dynamic curve and extensive distribution involving

nearly all of the right upper and lower outer quadrants of the breast (Fig 1c). Enlarged lymph nodes without fatty hilum were detected on the right axilla. US-guided core biopsy was performed and pathology results showed both grade 3 invasive ductal carcinoma and ductal carcinoma in situ (DCIS) with comedo necrosis. The tumor was estrogen receptor (ER) positive (50%) with negative progesterone receptor (PR) and positive human epidermal growth factor receptor 2 (HER 2) expression.

The patient underwent four cycles of NAC with cyclophosphamide and adriamycin. Subsequent paclitaxel and trastuzumab treatment was performed for 12 weeks. After NAC treatment, follow-up mammography images showed persistent extensive microcalcifications while MRI demonstrated complete response with the absence of any residual enhancement (Fig 2a, 2b, and 2c). Despite extensive microcalcifications in the right breast, the patient underwent BCS

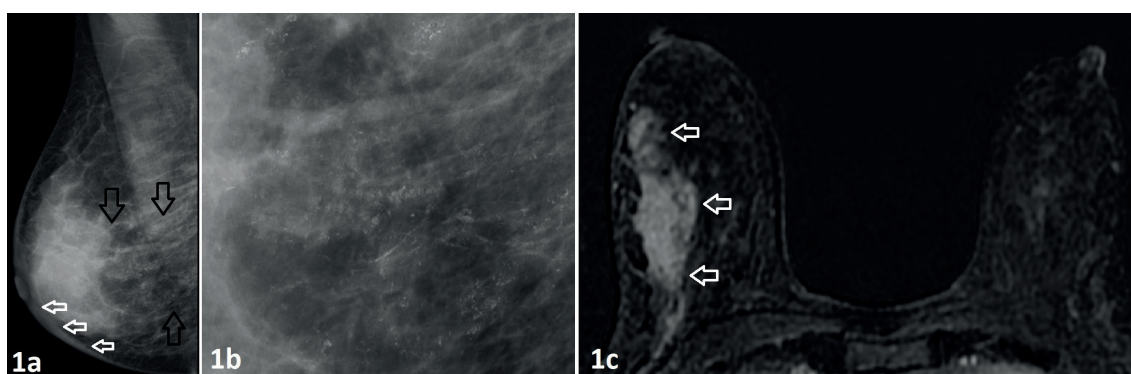


Figure 1. Radiological images of the patient before neoadjuvant chemotherapy.

Mediolateral oblique (MLO) mammography (1a) shows skin thickening (white arrows) and widespread malignant pleomorphic microcalcifications (black arrows). Zoomed image of mammography (1b) demonstrates microcalcifications better. MRI (1c) depicts contrast enhancement in the outer half of the breast (white arrows).

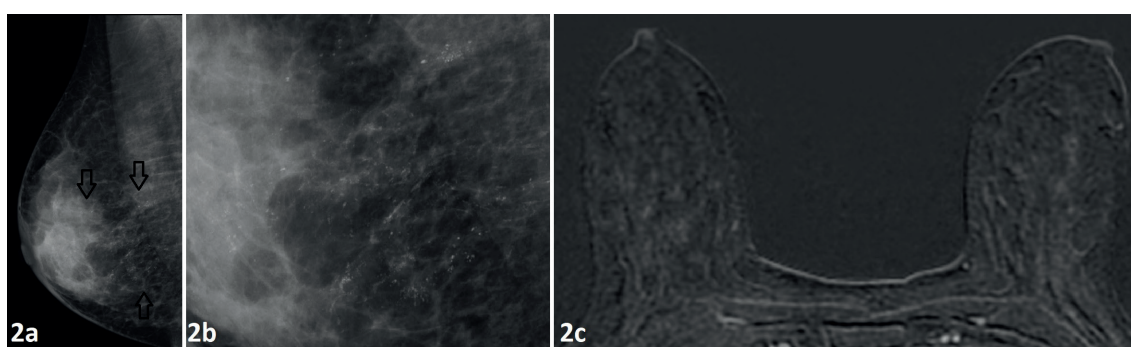


Figure 2. Radiological images of the patient after neoadjuvant chemotherapy.

Mediolateral oblique (MLO) mammography (2a) demonstrates extensive residual pleomorphic microcalcifications (black arrows). Zoomed image of mammography (2b) shows residual microcalcifications better. Complete response with the absence of any residual enhancement is observed on MRI (2c).

upon her preference. Histopathological results of BCS and axillary lymph node dissection revealed the complete disappearance of the invasive and in situ cancer. After surgery, residual malignant-type microcalcifications were observed on mammography images, although most of them were excised (Fig 3a and 3c). But, it was decided to follow up the microcalcifications with imaging methods because of the complete response in the pathology results. During a 10-year follow-up, mammography images did not depict increased microcalcifications and suspicious enhancement was not observed on MRI (Fig 3b and 3d). The follow-up of the patient is still ongoing.

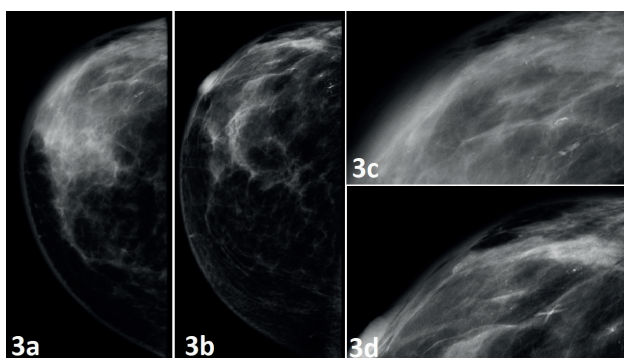


Figure 3. Post-surgical and follow-up mammography images of the patient.

Craniocaudal (CC) mammography (3a) and zoomed mammography (3c) images after surgery demonstrate decreased residual microcalcifications. Residual microcalcifications are still seen on the 10th year follow-up CC mammography image (3b) and zoomed mammography image (3d).

DISCUSSION

In the present case, a patient with breast cancer had persistent extensive microcalcifications on mammography images and did not show any enhancement on MRI after NAC. Histopathological results were consistent with MRI results and showed pCR. Also, residual malignant-type microcalcifications after BCS have not shown malignant transformation during the 10-year follow-up period.

NAC has usually been used for locally advanced breast cancer. NAC can downstage breast cancer and allow BCS, rather than mastectomy. NAC can also avoid the morbidities of ALND such as lymphedema and limb disorders as it increases the usage of sentinel lymph node dissection rather

than performing ALND for all node patients before NAC [4]. On the other hand, NAC is increasingly used to evaluate individual tumor response in earlier stage breast cancer. So, NAC can give prognostic information of disease [5]. Although physical examination can be used for assessing tumor response to NAC, its accuracy is inferior to imaging methods [3].

The most accurate imaging method for the evaluation of tumor response to NAC is MRI. The ability to predict the presence of the disease has been found high (93%) while the ability to predict the absence of disease has been detected only mild (65%) according to the final pathology results in a recent study [3]. MRI can underestimate the presence of disease in patients treated with antiangiogenic drugs because of decreasing contrast enhancement [1]. So, complete resolution of contrast enhancement on MRI does not always show the absence of tumor contrary to our case which has a complete response on MRI and at final pathology results. To predict pCR is more difficult when there are accompanying residual microcalcifications on mammography images.

Microcalcifications may decrease or increase after NAC without exact correlation with the presence or absence of residual viable tumor. Residual or newly developed microcalcifications may be the result of necrotic tumor cells, hematoma, fat necrosis, or the development of DCIS [6, 7]. Although residual microcalcifications usually correspond to benign disease such as dystrophic and psammomatous types in histopathological results, complete excision of suspicious microcalcifications are recommended [6, 8]. However, BCS may not be performed in the presence of extensive microcalcification and mastectomy may be needed despite the unwillingness of the patient. BCS was performed due to the preference of the patient in our case. And our patient did not undergo mastectomy with the pCR results despite residual microcalcifications. Regular mammography images did not show increased microcalcifications for 10-year follow-up and any suspicious enhancement was not observed on MRI performed 10 years after the surgery.

In conclusion, persistent malignant-type microcalcifications may not always be indicative of residual disease. MRI is the most accurate imaging method for the evaluation of

response to NAC. Although the excision of the residual microcalcifications after NAC is usually recommended, patients who have no enhancement on MRI and show pCR at final lumpectomy results may be followed-up carefully.

Author contribution

Study conception and design: GD; data collection: GD; analysis and interpretation of results: GD; draft manuscript preparation: GD. The author reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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