



# A case of lymph node dissection for contralateral axillary lymph node metastasis of ipsilateral breast tumor recurrence after identifying the primary lymphatic drainage by lymphoscintigraphy

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Received: 21 December 2020 / Accepted: 7 January 2021 / Published online: 29 January 2021  
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## Abstract

We report a case of total mastectomy and contralateral axillary lymph node dissection (ALND) in a patient with ipsilateral breast tumor recurrence (IBTR) and contralateral axillary lymph node metastasis (ALNM), with lymphoscintigraphy, confirming that the primary lymphatic flow was directed to the contralateral ALNM. The patient in the present case study is a 63-year-old woman. At the age of 46 years, the patient underwent lumpectomy and sentinel lymph node biopsy (SLNB) for left breast cancer. After surgery, she underwent whole-breast irradiation and hormone therapy (tamoxifen) for 5 years. On follow-up, she did not have recurrence. When she underwent breast ultrasound examination at the 17-year checkup after the initial surgery, she was diagnosed with tumor recurrence in the left conserved breast and with contralateral ALNM, without distant metastasis to any other organ. When re-SLNB is performed in patients with IBTR, the primary lymphatic flow is directed toward a lymph node other than the ipsilateral axillary lymph node (ALN). Therefore, it is necessary to discuss whether or not the contralateral ALNM in our case should be treated as stage IV. Therefore, we performed ALND after confirming that the primary lymphatic flow was directed toward the contralateral ALN as observed on lymphoscintigraphy and considering the contralateral ALNM as a localized lesion. Lymphoscintigraphy and intraoperative fluorescence imaging aid in the identification of the primary lymphatic flow. Lymph node metastases beyond the altered primary lymphatic flow are treated as localized lesions, and aggressive surgery is expected to be effective. There is a need to formulate guidelines on the treatment of IBTR considering changes in primary lymphatic flow.

**Keywords** Aberrant lymphatic drainage · Ipsilateral breast tumor recurrence · Lymphoscintigraphy · Re-sentinel lymph node biopsy · Contralateral axillary lymph node metastasis

## Introduction

It has been more than 20 years since breast-conserving therapy (BCT) has become widespread, and the number of patients with ipsilateral breast tumor recurrence (IBTR) has been increasing. Some clinical practice guidelines for breast cancer recommend total mastectomy for IBTR and axillary lymph node dissection (ALND) for axillary lymph

node (ALN) recurrence. In addition, re-sentinel lymph node biopsy (SLNB) for IBTR patients who have had a SLNB may also be considered. However, there is no clear evidence for the treatment of contralateral axillary lymph node metastasis (ALNM) due to aberrant lymphatic drainage of IBTR. In the present study, we report a case of total mastectomy and contralateral ALND in a patient with IBTR and contralateral ALNM, with lymphoscintigraphy, confirming that primary lymphatic flow was directed to the contralateral ALN.

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## Case report

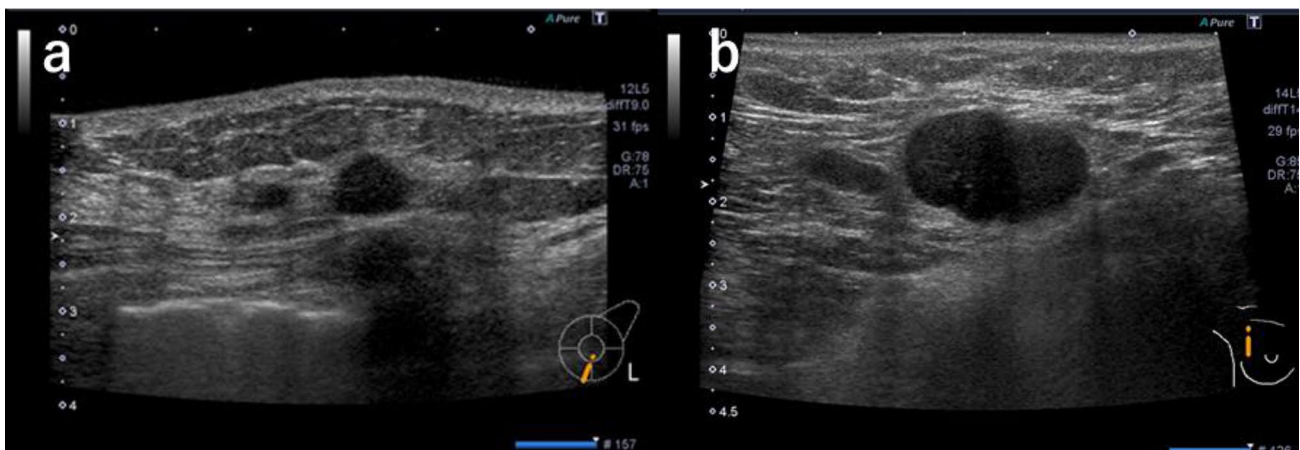
The patient was a 63-year-old woman. Seventeen years prior, she underwent lumpectomy and SLNB for left breast cancer. After the operation, she underwent whole-breast irradiation (WBI) and received tamoxifen orally for 5 years, and on follow-up, the patient did not have recurrence. Breast ultrasonography performed during breast cancer screening revealed the presence of a mass in the left conserved breast and swelling of the right ALN. Fine-needle biopsy revealed that both the left breast tumor and right ALN were malignant. The patient was referred to our hospital for treatment and underwent detailed examination, including mammography, ultrasonography, and contrast-enhanced (CE) magnetic resonance imaging (MRI). Palpation revealed the presence of a 10-mm mass at the 7 o'clock position in the left breast and a 15-mm mass in the right axilla. Surgical scars were found at the 9 o'clock position in the left breast and the left axilla. Mammography showed no significant findings due to the deformity associated with partial resection of the left breast. Breast ultrasound revealed a 10-mm mass in the left breast at the 7 o'clock position and a 24-mm lobulated hypoechoic mass in the right axilla (Fig. 1). CE-MRI also revealed 10 mm of early contrast-agent staining and a late-washout mass in the inner-lower part of the left conserved breast. Lymphadenopathy with a 15-mm contrast effect was observed at level I of the right axilla. No obvious findings were detected in the right breast or the left axilla (Fig. 2).

Pathological diagnosis of the left breast tumor based on the core needle biopsy was invasive ductal carcinoma (IDC), which was estrogen receptor (ER)-positive, progesterone receptor (PgR)-positive, and human epidermal growth factor receptor 2 (HER2)-negative

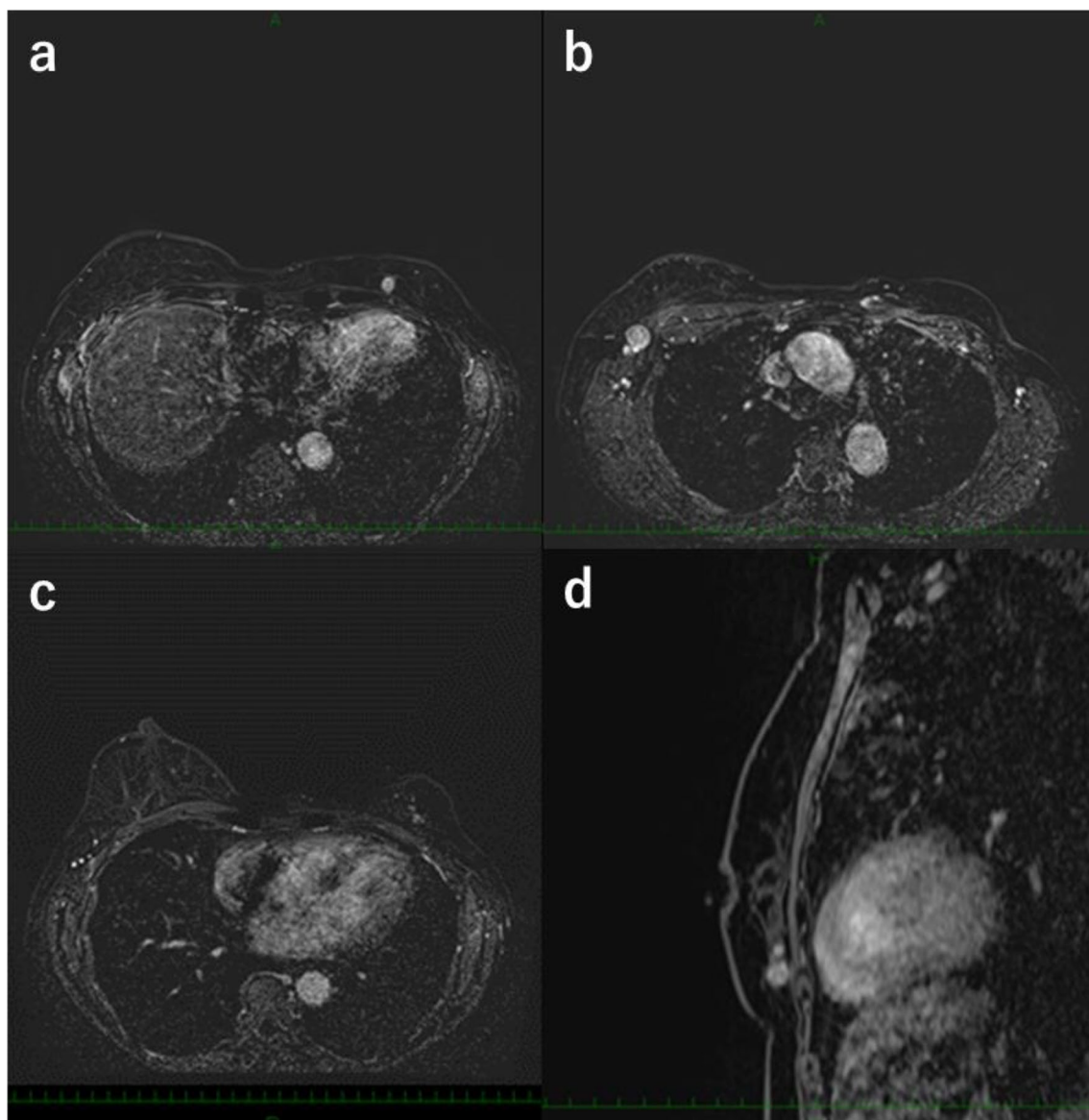
(Immunohistochemistry (IHC) 2+, FISH negative), with a Ki-67 of 16%. The right ALN was an adenocarcinoma, which was ER positive, PgR positive, and HER2 equivocal (IHC 2+, FISH equivocal), with a Ki-67 of 15.3%. The pathological features of the two tumors were highly similar. Therefore, this suggested that there was a possibility of direct metastasis of the left breast cancer to the right ALN.

On the day before surgery,  $^{99m}\text{Tc}$ -phytate was injected just above the left breast tumor, and images were captured 3 h later by lymphoscintigraphy. We observed the accumulation of  $^{99m}\text{Tc}$ -phytate in the contralateral right ALN, but not in the ipsilateral left ALN or other regional lymph nodes (Fig. 3). On the day of surgery, when a  $\gamma$  probe that responded to  $^{99m}\text{Tc}$ -phytate was brought close to both axillae, the probe responded to the right axilla but not to the left axilla. Moreover, 1 cc of indocyanine green (ICG) was injected directly above the left breast tumor, and the flow was observed on intraoperative fluorescence imaging; lymphatic flow from the left breast to the contralateral right axilla was observed. No flow to the left axilla was observed (Fig. 4). We noted that the primary lymphatic flow of IBTR had changed to the contralateral axilla. Therefore, we performed left breast mastectomy and right ALND for IBTR and contralateral ALNM.

The final pathological diagnosis was IDC, histological grade 2, ER positive, PgR positive, HER2 negative (IHC 2+, FISH negative), with a Ki-67 of 22%. ALN was positive for metastasis ( $n = 6/15$ ), which was ER positive, PgR positive, and HER2 negative (IHC 2+, FISH negative), with a Ki-67 of 19.9%. After the operation, four cycles of adriamycin and cyclophosphamide (AC) combination therapy, followed by paclitaxel weekly, was administered as adjuvant chemotherapy, following which adjuvant radiotherapy was planned.



**Fig. 1** Breast ultrasound revealed a 10-mm mass in the left breast (a) and a 24-mm swollen lymph node in the right axilla (b)



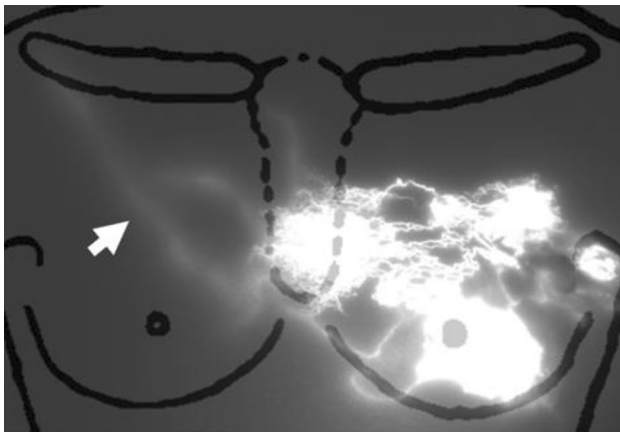
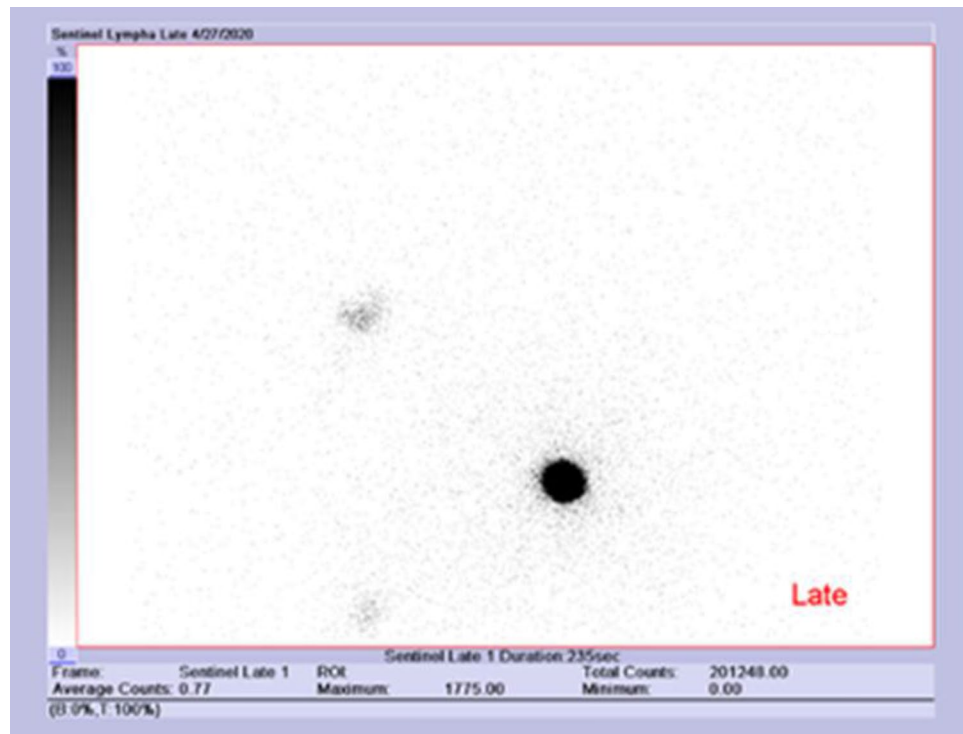
**Fig. 2** Magnetic resonance imaging detected contrast-stained mass in the left conserved breast (**a, d**), and lymphadenopathy with contrast effect at level I of the right axilla (**b**). No obvious findings were detected in the right breast (**c**). T1-weighted images

## Discussion

We encountered a case of ALND for the diagnosis of contralateral ALNM of IBTR after confirmation that the contralateral ALN drainage was sentinel lymphatic drainage as observed on lymphoscintigraphy. The Japanese Breast Cancer Society clinical practice guidelines and National Comprehensive Cancer Network Guideline suggest that SLNB with IBTR could be considered when axillary dissection was not performed in the initial surgery, but when ALND was performed in the initial surgery it remains controversial [1, 2].

In a meta-analysis of 692 cases that examined the benefit of re-SLNB, the overall identification rate was 65.3% in all patients, 81.0% in those who underwent SLNB in the initial surgery, and 52.2% with ALND in the initial surgery [3]. According to the Sentinel Node and Recurrent Breast Cancer (SNARB) study, the overall identification rate of re-SLNB was 63.3% [4]. This means that we can adequately identify primary lymphatic drainage by SLNB procedures even in cases of IBTR. In addition, SLNs are sometimes identified outside the ipsilateral axillary region by re-SLNB, which occurs more often after ALND than after SLNB. A meta-analysis reported that SLNs were identified by re-SLNB in the aberrant region in 69.2% of cases in which ALND was

**Fig. 3** Lymphoscintigraphy showed accumulation in the contralateral right axillary lymph node, but any accumulation was not observed in the ipsilateral left axillary lymph node or other regional lymph nodes



**Fig. 4** Intraoperative fluorescence imaging shows the lymphatic flow (arrow) from the left breast tumor to the contralateral right axilla lymph node

performed in the initial surgery and 17.4% of cases in which SLNB was performed in the initial surgery [3]. The SNARB study reported that re-SLNB was identified in an aberrant region in 79.3% of cases in which ALND was performed in the initial surgery and 25.0% of cases in which SLNB was performed in the initial surgery [4]. This finding emphasizes the usefulness of lymphoscintigraphy for SLN identification [5, 6]. Frequent locations of aberrant SLNs are internal mammary (46.3%), contralateral axilla (34.3%), and supra-/infraclavicular (14.3%) [3]. Other studies have suggested

that the most common aberrant lymph node basins are the contralateral axilla and ipsilateral internal mammary chain [7]. Alterations in lymphatic flow are reportedly caused by the effects of initial surgery and fibrosis in the mammary tissue at irradiation sites due to postoperative radiotherapy [7, 8]. In this case, the initial left BCT, including WBI, might have altered the lymphatic flow.

In this case, the right ALNM had already been identified based on the preoperative core needle biopsy. The following four hypotheses could be considered for this situation: (1) The primary lymphatic flow from the left IBTR was directed to the contralateral right ALN as local recurrence (N1). (2) The primary lymphatic flow from the left IBTR was directed to the ipsilateral left ALN as usual, and metastasis to the contralateral right ALN occurred as distant metastasis (M1). (3) Another visualized tumor was present simultaneously in the contralateral right breast along with the right ALNM (bilateral breast cancer). (4) The presence of right occult breast cancer along with right ALNM was observed. We denied bilateral breast cancer because there were no findings in the right breast in any preoperative image. Although ruling out occult breast cancer was difficult, it was most important to distinguish between localized lesions and stage-IV lesions because performing right ALND without confirming the first lymphatic flow might lead to overtreatment in the case of stage-IV lesions. According to the cancer staging guidelines of the American Joint Committee on Cancer, contralateral ALNM is categorized as M1 [9]. However, when the primary lymphatic flow is directed toward the contralateral



ALN, as seen in this case, it is appropriate to identify it as N1, not M1 [10, 11]. In a systematic review, 79.2% of patients with contralateral axillary metastases underwent operation, and 89.5% of them, without any reason, such as micro-metastasis, underwent contralateral ALND. Although postoperative follow-up was available for only about half of the patients, the overall survival and disease-free survival rates at a median follow-up of 50.3 months were 82.6% and 65.2%, respectively, which is generally acceptable [12]. Therefore, reoperation and postoperative therapy for local control should be considered just the same as those for ipsilateral axillary recurrence.

In this case, we performed lymphoscintigraphy and intraoperative fluorescence imaging to identify primary lymphatic flow, and the flow directed toward the contralateral right axilla was visualized, which could be regarded as the primary lymphatic flow. The postoperative pathology of both the left breast tumor and right ALN was very similar. Finally, we observed that the right ALNM had a localized lesion from the left IBTR. There have been scattered reports of altered lymphatic flow after re-SLNB for IBTR, but treatment strategies for clear contralateral ALNM have not been discussed. Therefore, reliable guidelines for the treatment of IBTR that consider changes in primary lymphatic flow are needed.

**Acknowledgements** We would like to thank Editage ([www.editage.com](http://www.editage.com)) for English language editing.

### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Informed consent** Informed consent was obtained from the patient in this report.

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