



Case report

Contralateral axillary lymph node metastasis in primary breast cancer: A case report

Kimiyasu Yoneyama^{*}, Motohito Nakagawa, Asuka Hara

Department of Breast Surgery, Hiratsuka City Hospital, Hiratsuka, Japan

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ABSTRACT

Introduction: Contralateral axillary lymph node metastasis (CAM) is rare, especially in primary breast cancer.

Presentation of case: A 71-year-old woman visited our hospital after noticing a mass in her right breast. A mass of 5 cm in diameter with skin infiltration was palpable on the medial side of the right breast. She underwent a needle biopsy and was diagnosed with invasive ductal carcinoma. On various imaging modalities, there were no distant metastases but bilateral axillary lymph node metastases were found. She underwent preoperative chemotherapy and showed a clinical partial response. After thorough discussion, she opted for surgery and underwent partial mastectomy of the right breast and bilateral axillary lymph node dissection. Histopathological examination revealed residual breast tumor and one metastatic axillary lymph node on each side. Postoperative radiotherapy and hormone therapy were performed. The patient is alive and recurrence-free as of 1 year after the start of treatment.

Conclusion: CAM is often regarded as distant metastasis, but can be considered curable if there is no distant metastasis to other organs. CAM without distant metastasis to other organs should be treated with curative intent in order to avoid a disadvantage to the patient.

1. Introduction

The spread of sentinel lymph node biopsy for clinically node-negative breast cancer has led to dramatic advances in our understanding of the lymphatics of the breast [1]. Most lymph flows into the ipsilateral axillary lymph nodes, but some flows into the supraclavicular, cervical, and internal thoracic lymph nodes. Flow to the contralateral axillary lymph nodes can occur but is extremely rare.

Contralateral axillary lymph node metastasis (CAM) is rare in breast cancer patients [2]. CAM has conventionally been regarded as distant metastasis and has therefore been treated with systemic therapy (chemotherapy or hormone therapy) [3]. CAM can be divided into synchronous CAM at the diagnosis of primary breast cancer and metachronous CAM at recurrence after treatment for breast cancer [4]. In previous reports, most cases of CAM are metachronous and few are synchronous. Most reported cases of CAM are due to recurrence following breast surgery or axillary surgery. Here we report a case of a 71-year-old woman with true primary breast cancer who had CAM and ipsilateral axillary lymph node metastasis.

This work was written in accordance with SCARE criteria [5].

2. Presentation of case

A 71-year-old postmenopausal woman visited our breast clinic after noticing a mass in the upper medial quadrant of her right breast. A mass of 5 cm in diameter with skin infiltration was palpable in the right breast. Breast ultrasound confirmed a 5-cm diameter mass in the right breast, and axillary ultrasound revealed multiple enlarged lymph nodes with a maximum diameter of 3 cm on both the ipsilateral and contralateral sides. Ultrasound-guided core needle biopsy was performed on the mass of the right breast. Histopathological examination revealed invasive ductal carcinoma with Grade 3 nuclear atypia (Fig. 1). The tumor was estrogen receptor-positive, progesterone receptor-negative, and HER2-negative. Contrast-enhanced CT showed the mass in the right breast with skin infiltration and the enlarged bilateral axillary lymph nodes, but no distant metastases to other organs. The left end of the tumor had invaded the contralateral breast (Fig. 2-a, b, c). Bone scintigraphy showed no bone metastases. The preoperative diagnosis was cT4bN1M1 (LYM).

The patient was treated with chemotherapy consisting of 4 cycles of epirubicin and cyclophosphamide every 3 weeks followed by 4 cycles of

^{*} Corresponding author at: 1-19-1 Minamihara, Hiratsuka-shi, Kanagawa 254-0065, Japan.

E-mail address: key13213@yahoo.co.jp (K. Yoneyama).

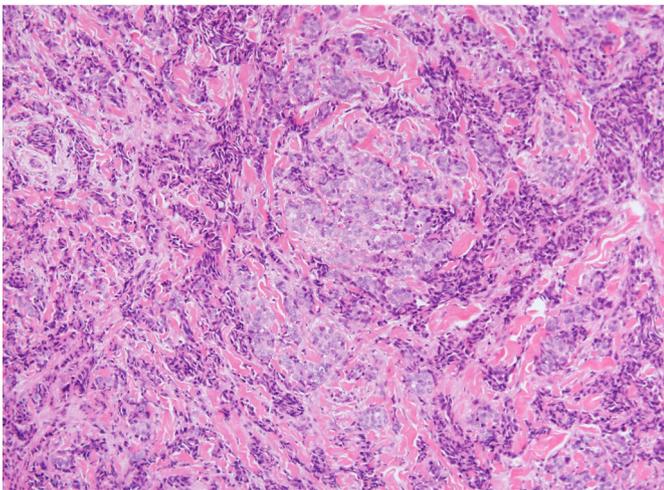


Fig. 1. Atypical cells with swollen nuclei infiltrating the dermis. The diagnosis is invasive ductal carcinoma with skin infiltration.

docetaxel every 3 weeks.

She showed a clinical partial response (Fig. 3-a, b, c). After thorough discussion, the patient opted for partial mastectomy of the right breast and bilateral axillary lymph node dissection. The postoperative course was favorable.

Histopathological examination revealed that the tumor in the right breast was invasive lobular carcinoma with a diameter of 4.2 cm. Lymphatic invasion (LVI) was positive. The histological therapeutic effect was Grade 2a. In total, 15 lymph nodes were removed from the right axilla and 10 from the left axilla. There was 1 metastatic node on each side, which measured 6 mm and 2 mm, respectively.

After surgery, she received local radiation therapy to the remaining right breast at a total dose of 60 Gy in daily fractions of 2 Gy. The supraclavicular and parasternal lymph node areas were also included in the radiation field. After discussing the risks and benefits of adjuvant hormone therapy, she was started on letrozole. The patient is alive without recurrence as of 1 year after the start of this multimodal treatment.

3. Discussion

Lymphatic scintigraphy has dramatically advanced our understanding of the lymphatics of the breast. Primary lymphatic drainage of the breast is to the ipsilateral axillary lymph nodes, but drainage to other sites such as the supraclavicular or internal mammary lymph nodes can occur in up to 30% of women [6]. Lizarraga et al. reported that lymphatic flow to the contralateral axillary lymph nodes occurs in only 0.3% of women [7]. Pasta et al. observed lymphatic drainage to the contralateral axilla in 2.8% of women who had previously undergone breast cancer surgery [8]. Using different tracers to examine other possible routes, Haagensen demonstrated that tumor cells could spread to the contralateral axillary lymph nodes by penetrating the deep lymphatic plexus of the chest wall [9]. Taken together, these previous studies show that lymph can flow to the contralateral axilla. Therefore, CAM can occur depending on the site of the tumor and the anatomy of the patient. In our patient, we speculate that the lymphatic flow was directed contralaterally because the tumor was located in the medial part of the right breast.

CAM is rarely found at the diagnosis of primary breast cancer. The reported frequency of CAM is 1.9% to 6% [2]. Most reported cases are metachronous CAM following breast surgery or axillary surgery. The reason for this is that axillary surgery or radiation therapy alters the lymphatics of the breast. Devitt et al. reported that only 2 of 52 patients with CAM had synchronous CAM at the primary diagnosis, with most

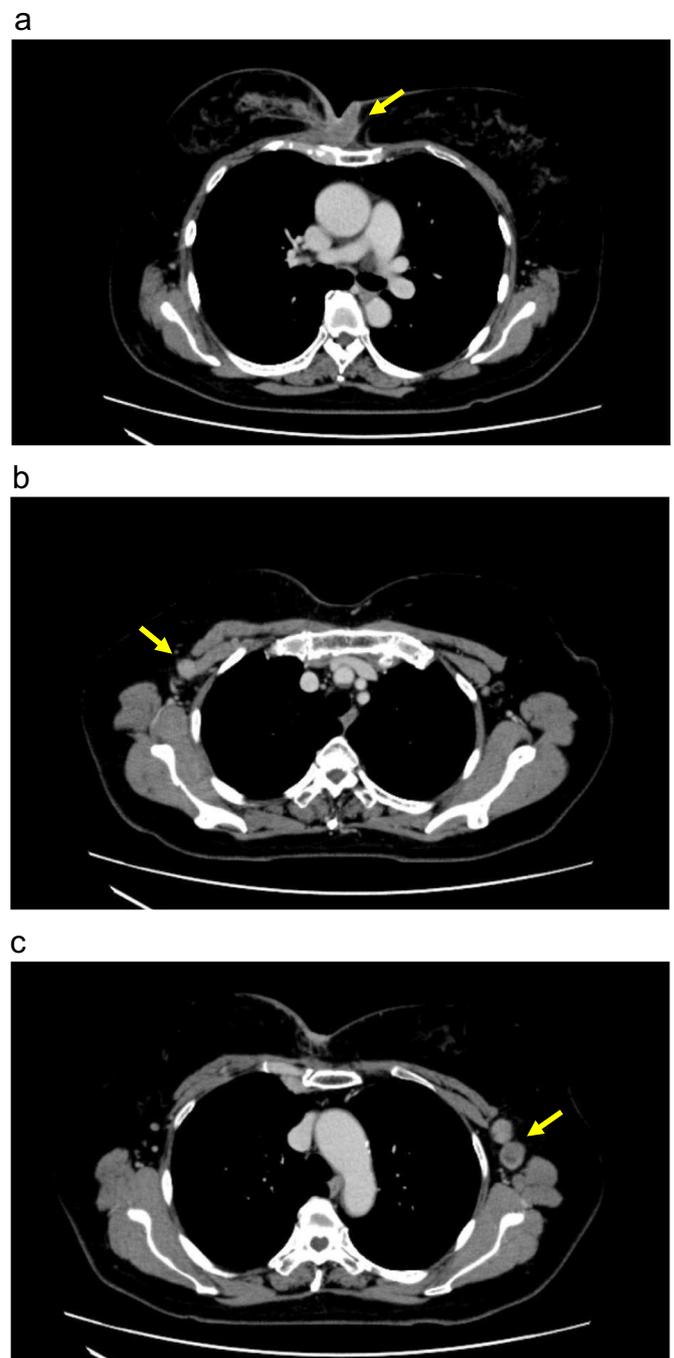


Fig. 2. Contrast-enhanced CT imaging at the first visit.

(a) A tumor with skin infiltration is found in the medial part right breast. The left end of the tumor is invading the contralateral breast (arrow).

(b) Swelling of the right axillary lymph nodes is observed (arrow).

(c) Enlargement of multiple contralateral axillary lymph nodes is noted (arrow).

patients developing metachronous CAM 12 to 32 months later [10]. Moreover, Morcos et al. reported that 10 of 21 patients with CAM had synchronous CAM at the primary diagnosis [11], and in a case series reported by Huston et al., only 1 of 7 patients with CAM had synchronous CAM [12]. Therefore, the actual incidence of CAM, especially synchronous CAM, is probably much lower than reported in the literature.

Indeed, CAM is rare and a controversial topic. In addition, the uncertain laterality of the cancer that causes CAM complicates the staging of the overall disease and poses a management dilemma for clinicians.

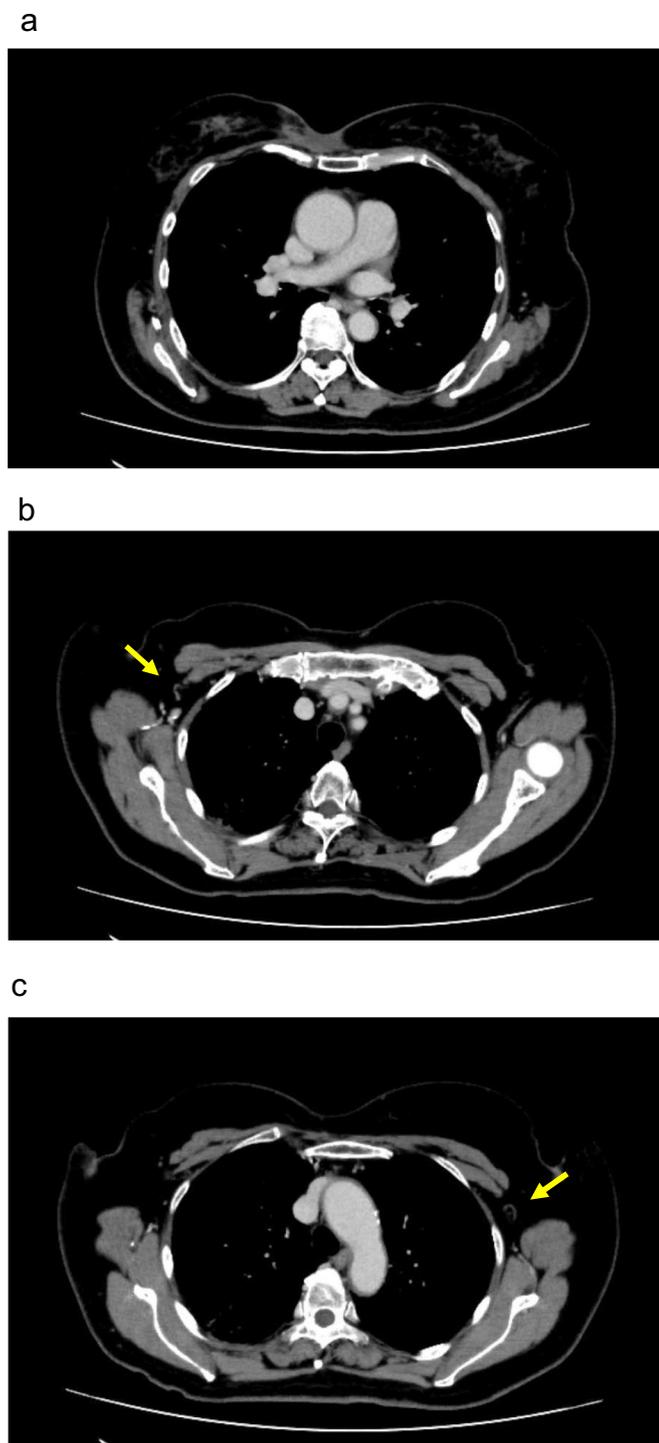


Fig. 3. Contrast-enhanced CT imaging after preoperative chemotherapy. (a) The main tumor has shrunk but still remains. Although difficult to see on CT, the skin infiltration has disappeared. (b) The right axillary lymph nodes have shrunk (arrow). (c) The contralateral axillary lymph nodes have also shrunk (arrow).

Controversy remains as to whether CAM should be regarded as distant metastasis or local spread. If CAM is present at the initial diagnosis, it is conventionally thought to be the result of systemic spread. CAM is not included in the current version of the AJCC Cancer Staging Manual but was previously classified as distant metastasis. In Japan as well, CAM is regarded as distant metastasis but is not clearly described in guidelines.

Although the precise mechanism of CAM is not known, three possible factors can be considered.

- 1: Metastasis of contralateral breast cancer.
- 2: Metastasis of latent breast cancer on the ipsilateral side.
- 3: Metastasis from other organs.

In the present case, we ruled out 2 and 3 using various imaging modalities.

The development of CAM is associated with aggressive histopathological features of primary breast tumors. Morcos et al. retrospectively analyzed 21 breast cancer patients with CAM and 401 without CAM, and found that the patients with CAM had higher tumor grade (81% grade 3), more frequent LVI (81%), larger primary tumors (95% cT3/cT4), more frequent ER-negative status (52%), and more frequent HER2 overexpression (42%) [11].

Thus, the histopathological features were significantly worse in patients with CAM.

Not all of these histopathological features were present in our case, underscoring the variety of tumors that can cause CAM. Our patient had advanced cancer (cT4) and LVI, but the tumor was ER-positive and HER2-negative.

In addition to aggressive histopathological features, changes in lymphatic flow from the tumor to the contralateral axilla can contribute to the development of CAM. For example, radiation or axillary surgery can damage lymphatic vessels leading to changes in lymphatic flow [13]. In our case, however, CAM was observed at the primary diagnosis, prior to surgery and radiation.

As mentioned above, it remains an open question whether CAM should be regarded as distant metastasis or local spread. However, in recent years, there have been some reports in which CAM without distant metastasis to other organs was treated with the aim of radical cure [4,14]. Many of those reports do not describe CAM in terms of distant metastasis.

Yet, even if CAM is not regarded as distant metastasis, the lymph node stage would then be N3, which is still advanced disease, and poor prognosis would be expected. However, good prognosis has been reported in some cases.

To avoid a disadvantage to patients, especially those with primary breast cancer, CAM without distant metastasis to other organs should be treated with curative intent.

4. Conclusion

We reported a rare case of synchronous CAM from primary breast cancer in a 71-year-old woman. This case suggests that CAM without distant metastasis to other organs should be treated with curative intent in order to avoid a disadvantage to the patient.

Author contributions

Kimiyasu Yoneyama: Conceptualization, Investigation, Resources, Writing – Original draft preparation, Writing – Review and editing.

Asuka Hara: Conceptualization, Investigation.

Motohito Nakagawa: Administration, Review.

Ethical approval

Our institution does not require ethical approval for case reports that are deidentified and collected retrospectively.

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Consent

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

Registration of research studies

This is a case report, and no database approval was applied.

Guarantor

Kimiyasu Yoneyama.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

None.

References

- [1] S.H. Estourgie, O.E. Nieweg, R.A.V. Olmos, E.J.T. Ruggers, B.B.R. Kroon, Lymphatic drainage patterns from the breast, *Ann. Surg.* 239 (2004) 232–237.
- [2] W. Wang, P. Yuan, J. Wang, F. Ma, P. Zhang, Q. Li, et al., Management of contralateral axillary lymph node metastasis from breast cancer: a clinical dilemma, *Tumori* 100 (2014) 600–604.
- [3] C. Zhou, M.C. Richir, M.W.H. Leenders, B.L.A.M. Langenhorst, H.P. Knol, W. H. Schreurs, Contralateral axillary lymph node metastasis at the time of primary breast cancer diagnosis: curative or palliative intent? *Case Rep. Surg.* 2013 (2013), 389013.
- [4] J. Gingerich, E. Kapenhas, J. Morgani, A. Heimann, Contralateral axillary lymph node metastasis in second primary breast cancer: case report and review of the literature, *Int. J. Surg. Case Rep.* 40 (2017) 47–49.
- [5] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, for the SCARE Group, The SCARE 2020 guideline: updating consensus Surgical CAse REport (SCARE) guidelines, *Int. J. Surg.* 84 (2020) 226–230.
- [6] O.E. Nieweg, Lymphatics of the breast and the rationale for different injection techniques, *Ann. Surg. Oncol.* 8 (9 Suppl.) (2001) 71–73.
- [7] I.M. Lizarraga, C.E.H. Scott-Conner, S. Muzahir, R.J. Weigel, M.M. Graham, S. L. Sugg, Management of contralateral axillary sentinel lymph nodes detected on lymphoscintigraphy for breast cancer, *Ann. Surg. Oncol.* 20 (2013) 3317–3322.
- [8] V. Pasta, F. Monteleone, V. D’Orazi, L. Del Vecchio, D. Sottile, S. Iacobelli, et al., Typical and atypical lymphatic flows in breast carcinoma, *Ann. Ital. Chir.* 86 (2015) 311–316.
- [9] C. Haagensen, *The lymphatics in cancer*, Saunders, Philadelphia, 1972.
- [10] J.E. Devitt, A.W. Michalchuk, Significance of contralateral axillary metastasis in carcinoma of the breast, *Can. J. Surg.* 12 (1969) 178–180.
- [11] B. Morcos, I. Jaradat, M. El-Ghanem, Characteristics of and therapeutic options for contralateral axillary lymph node metastasis in breast cancer, *Eur. J. Surg. Oncol.* 37 (2011) 418–421.
- [12] T.L. Huston, P.I. Pressman, A. Moore, L. Vahdat, S.A. Hoda, M. Kato, et al., The presentation of contralateral axillary lymph node metastasis from breast carcinoma: a clinical management dilemma, *Breast J.* 13 (2007) 158–164.
- [13] C.I. Perre, C.A. Hoefnagel, B.B. Kroon, F.A. Zoetmulder, E.J. Rutgers, Altered lymphatic drainage after lymphadenectomy or radiotherapy of the axilla in patients with breast cancer, *Br. J. Surg.* 83 (1996) 1258.
- [14] A. Strazzanti, S. Gangi, C. Trovato, N. Pacini, F. Basile, Contralateral lymph node metastasis in a woman with new primary breast cancer: systemic disease or locoregional diffusion? *Int. J. Surg. Case Rep.* 53 (2018) 400–402.