



Metachronous Contralateral Axillary Lymph Node Metastasis from Invasive Breast Carcinoma: A Case Report with Imaging Findings

침윤성 유방암의 이시성 반대쪽 액와 림프절 전이: 영상 소견을 포함한 증례 보고

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Contralateral axillary lymph node metastasis is a rare entity in breast cancer and is currently classified as a distant metastasis; however, recent studies have proposed aggressive curative treatment since this entity may manifest as a locoregional disease. Herein, we report a rare case of contralateral axillary lymph node metastasis that presented with imaging findings 22 months after the initial breast cancer diagnosis in a 67-year-old female. The patient underwent lymph node dissection of the axilla with adjuvant chemotherapy and radiotherapy. A follow-up examination 6 months after surgery showed no evidence of tumor recurrence or metastasis.

Index terms Breast; Lymph Node Metastasis; Mammography; Ultrasonography; Magnetic Resonance Imaging

INTRODUCTION

Contralateral axillary lymph node metastasis (CAM) is a rare clinical condition, accounting for 1.9%–6% of breast cancer cases (1, 2). Although it is uncommon, identification of CAM is clinically important because lymph node metastasis is the most crucial prognostic factor in breast cancer. CAM is currently classified as distant metastasis, or stage IV disease; however, recent studies have proposed that it is a locoregional dis-

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ease and recommended multidisciplinary and more aggressive curative treatment (1, 3, 4). Herein, we report a rare case of metachronous CAM of invasive breast carcinoma with various imaging findings. A brief review of the relevant literature is also provided.

CASE REPORT

A 67-year-old female was referred to our hospital because of an outside biopsy-proven malignancy in the left breast. She had no specific past medical or family history. Ultrasonography (US) performed at the outside hospital showed an irregular hypoechoic mass with indistinct margins (Fig. 1A) and increased vascularity on the color Doppler image. Several enlarged lymph nodes were seen in the left axilla (Fig. 1A). Dynamic contrast-enhanced MRI of the breast showed an oval-shaped mass with circumscribed margins and heterogeneous enhancement in the upper outer quadrant of the left breast and enlarged lymph nodes in the left axilla (Fig. 1B). ^{18}F -fluorodeoxyglucose (FDG)-PET showed focal avid FDG uptake in the left breast, left axilla, and left supraclavicular fossa with a maximum standardized uptake value (SUV) of 7.1, 13.4, and 5.1, respectively (Fig. 1C).

The patient underwent breast conserving surgery and lymph node dissection. Histopathological examination confirmed a poorly differentiated invasive ductal carcinoma with medullary features (Fig. 1D), 1.8 cm \times 1.5 cm in size with a clear resection margin. There were metastatic ductal carcinomas in 14 out of 17 lymph nodes, with the largest metastatic tumor measuring 6.0 cm in size. The tumor was negative for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2); however, it had a diffuse strong membranous positive for epidermal growth factor receptor (EGFR) expressing the immunophenotype of triple negative basal-like type (Fig. 1D).

At the time of diagnosis of left breast cancer, there was a small suspicious mass on the right subareolar area. The mass was excised and confirmed as a benign fibrocystic change. After surgery, the patient received adjuvant chemotherapy consisting of four cycles of doxorubicin and cyclophosphamide, as well as four cycles of docetaxel. Subsequently, the patient received radiation therapy to the left breast, left axilla, and left supraclavicular fossa. After completion of treatment, the patient underwent regular imaging follow-up including mammography (MG), US, and CT of the chest and abdomen-pelvis without evidence of tumor recurrence.

Twenty-two months after the initial diagnosis, MG showed enlarged lymph nodes in the right axilla (Fig. 1E). US showed enlarged lymph nodes with loss of the fatty hilum in the right axilla (Fig. 1E) and an irregular hypoechoic mass with indistinct margins at the 10 o'clock direction of the right breast. We assessed this mass as Breast Imaging Reporting and Data System category 4A low suspicion for malignancy. US-guided fine needle aspiration was performed at the lymph node of the right axilla, and the result was metastatic carcinoma. US-guided core needle biopsy was performed at the right breast mass, which was confirmed as fibrocystic change. Breast MRI showed enlarged lymph nodes in the right axilla without any abnormally enhancing lesion in the breast (Fig. 1E). ^{18}F -FDG PET/CT showed focal avid FDG uptake in the right axilla with a SUV of 5.8. The patient underwent right axillary lymph node dissection and excision of the right breast mass. Eight of the nine resected lymph nodes

revealed metastases. These metastatic lymph nodes had the same triple negative basal like immunophenotype, showing negativity of ER, PR, HER2 and diffuse strong EGFR expression (Fig. 1F). The right breast mass was confirmed as a benign fibrocystic change with a small fo-

Fig. 1. Imaging and pathologic findings of metachronous controlateral axillary lymph node metastasis from invasive ductal carcinoma in a 67-year-old female.

A. Transverse ultrasonography of the left breast shows an irregular hypoechoic mass with indistinct margins (arrows), and transverse ultrasonography of the left axilla shows an enlarged lymph node.

B. MIP image shows an oval-shaped mass with circumscribed margins and heterogeneous enhancement in the upper outer quadrant of the left breast and enlarged lymph nodes in the left axilla (dashed arrows).

C. ¹⁸F-FDG PET/CT shows multifocal avid FDG uptake in the left breast, left axilla, and left supraclavicular fossa (arrowheads).

D. Primary left breast cancer shows medullary features with tumor clusters arranged in a syncytial growth pattern, highly pleomorphic nuclear atypia, conspicuous mitotic activity, and prominent lymphoplasmacytic infiltrates (H&E stain, × 200). Prominent membranous expression of EGFR is noted in immunohistochemical staining (EGFR, × 200).

EGFR = epidermal growth factor receptor, FDG = fluorodeoxyglucose, H&E = hematoxylin and eosin, MIP = maximal intensity projection

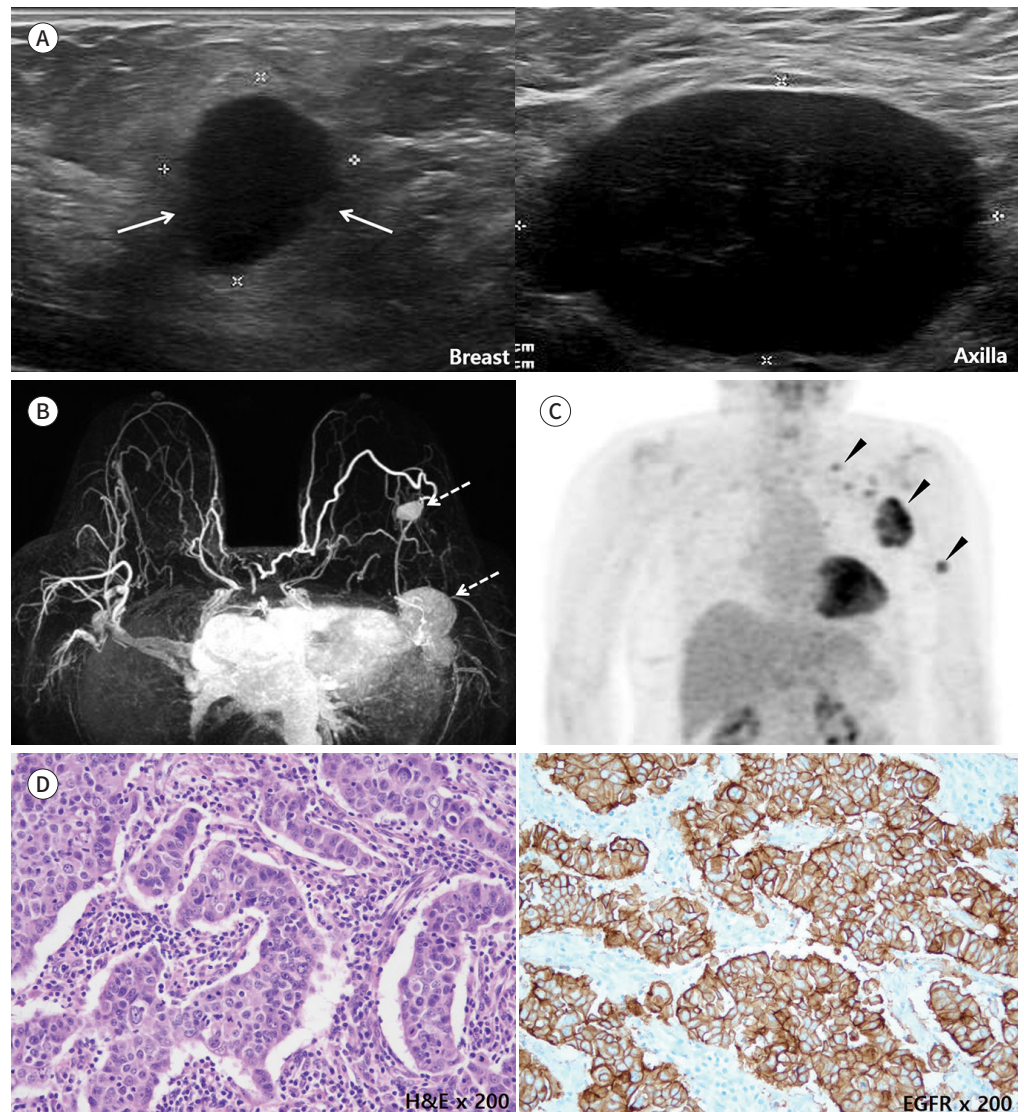
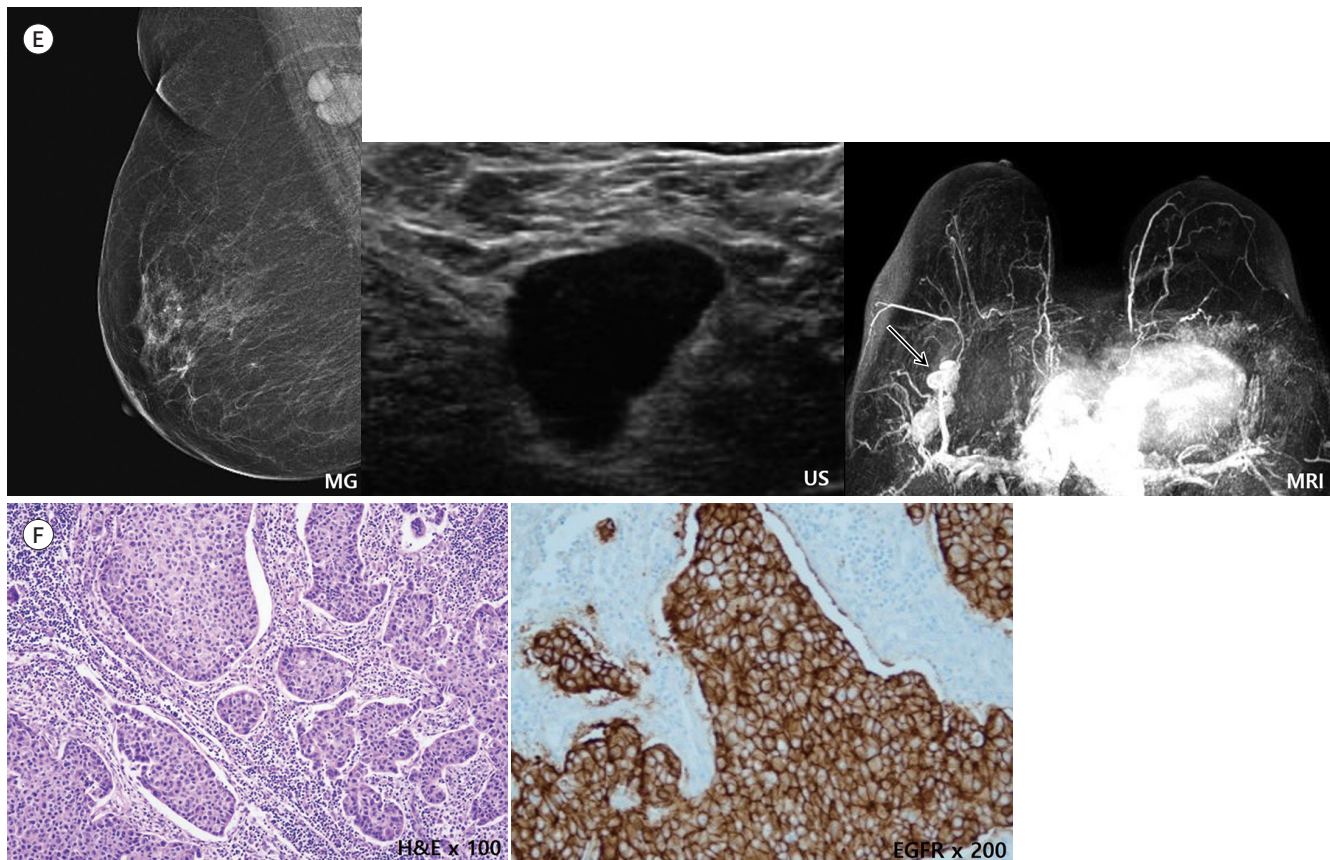


Fig. 1. Imaging and pathologic findings of metachronous controlateral axillary lymph node metastasis from invasive ductal carcinoma in a 67-year-old female.

E. At 22 months after the initial breast cancer diagnosis, mediolateral oblique MG of the right breast shows enlarged lymph nodes in the right axilla. Transverse US of the right axilla shows an enlarged lymph node. MIP image shows enlarged lymph nodes at the right axilla (arrow) without any abnormally enhancing lesion in the breast.

F. The contralateral right axillary lymph node shows metastatic ductal carcinoma composed of tumor clusters of highly pleomorphic nuclear atypia (H&E stain, $\times 100$), and diffuse strong EGFR immunohistochemistry membranous staining (EGFR, $\times 200$).

EGFR = epidermal growth factor receptor, H&E = hematoxylin and eosin, MG = mammography, US = ultrasonography, MIP = maximal intensity projection



cus of atypical lobular hyperplasia with a clear resection margin.

Following surgery, the patient received adjuvant chemotherapy with six cycles of paclitaxel and cisplatin and radiation therapy to the right breast and right axilla. A 6 months after surgery, there was no evidence of tumor recurrence or metastasis on follow-up examination.

This study was approved by the Institutional Review Board of our institution (IRB No. 2021-02-002). Informed consent was waived due to the retrospective nature of the study.

DISCUSSION

Ipsilateral axillary lymph node metastasis in breast cancer is a common finding; however, CAM is quite uncommon. CAM is divided into two different types: synchronous, when CAM occurs at the same time of diagnosis of the primary breast cancer, or metachronous, when CAM appears after the previous breast cancer has been treated with adjuvant therapy (3).

Metachronous CAM is more common than synchronous CAM. The true incidence of CAM is difficult to estimate, because there are cases of overestimation due to lack of full evaluation of occult contralateral breast cancer or extramammary malignancy. On the other hand, there are cases of underestimation due to failure of adequate follow-up study (1).

One of the main pathophysiologies of CAM is aberrant drainage due to blockage of normal lymphatic routes, resulting in the redirection of lymph flow to other nodal basins. Known factors that cause destruction of the ipsilateral lymphatic networks include large breast tumors, extensive tumor burden in the ipsilateral axilla, previous breast, chest wall, or axillary surgery, and radiotherapy to the breast or axilla (4, 5). In a lymphoscintigraphy of patients who have previously undergone breast or axillary surgery and radiotherapy, lymph drainage to the contralateral axilla, internal mammary chain, or supra/infraclavicular area frequently occurs (6, 7). This suggests that CAM could be caused by direct aberrant drainage and represents a locoregional disease rather than a distant metastatic disease. However, untreated breast cancer cases have different mechanisms of CAM, that CAM means dissemination as distant metastasis beyond the locoregional area. In addition, Morcos et al. (2) reported that CAM is associated with aggressive histopathological features of primary breast tumors such as higher tumor grade, lymphovascular invasion, large tumor size, ER negativity, and HER2 overexpression. In this case, the primary breast tumor showed high grade invasive ductal carcinoma of the breast, presence of lymphovascular invasion, ER negativity, extensive tumor burden to the ipsilateral lymphatic chains, and a history of breast and axillary surgery with radiotherapy to the ipsilateral side. These aggressive histopathological factors may have affected the presentation of CAM in our case.

To determine the origin of CAM, whether primary breast cancer, occult contralateral breast cancer, or extramammary malignancy, is the first step. Management of patients with CAM is a dilemma when there is no other metastatic disease. To exclude occult contralateral breast cancer, MRI has been proposed as a good imaging modality to evaluate breast lesions. According to de Bresser et al. (8) systemic review study, breast MRI can detect occult breast cancer in more than two thirds of patients showing high sensitivity but lower specificity, and 80% of patients in whom that MRI detected breast lesions could be localized by subsequent US study. On the other hand, metachronous CAM often simultaneously occurs with ipsilateral breast cancer recurrence (IBCR) or chest wall recurrence (6). Therefore, when IBCR is diagnosed, evaluation including exact physical examination and imaging workup including MG, US, MRI, or PET should be performed on the contralateral axilla to rule out CAM.

The American Joint Committee on Cancer 8th edition classifies CAM as stage IV disease and a distant metastasis (9). However, several previous publications have questioned this classification, suggesting that CAM should be considered an N3 disease, and should be treated with multidisciplinary and curative therapy as a locoregional spread of breast cancer (1, 3, 4). Magnoni et al. (3) recent study reported that metachronous CAM patients without any distant metastasis received curative surgery and chemotherapy with radiotherapy, and showed better overall survival and disease free survival rates (72% and 61% at 5 years with 5.4 years median follow-up time, respectively) than other distant dissemination. Moosdorff et al. (6) systemic review showed an 82.6% overall survival rate and 65.2% disease free survival rate with 50.3 months mean follow-up time in CAM patients who received surgery (89.5%) and

adjuvant chemotherapy (77.8%). A previous study suggested that radiotherapy could be effective (10). Radiotherapy can treat any occult contralateral breast cancer and eradicate microscopic tumor cells along the dermal lymphatics that could have spread from the ipsilateral primary breast cancer or IBCR. In this case, the patient also underwent axillary dissection and adjuvant chemotherapy with radiotherapy with curative intent.

In conclusion, CAM is a rare and challenging situation for proper therapy. We have reported a case of metachronous CAM with various imaging findings including MG, US, MRI, and PET. With a history of previous breast and axillary surgery and radiotherapy, our case also supports that the alteration of the normal lymphatic networks and subsequent development of aberrant lymphatic routes could result in CAM as suggested in previous studies. Aggressive histopathological factors may also be affected in this case.

Author Contributions

Conceptualization, J.H.K.; investigation, K.J.; supervision, J.H.K.; visualization, K.W.; writing—original draft, K.J.; and writing—review & editing, J.H.K., K.W.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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침윤성 유방암의 이시성 반대쪽 액와 림프절 전이: 영상 소견을 포함한 증례 보고

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이시성 반대쪽 액와 림프절 전이는 유방암에서 드물게 발생하며, 현재 원격 전이로 분류되어 있다. 그러나 최근 연구들은 이것이 국소 질환으로 간주될 수 있기 때문에 적극적으로 완치를 위한 치료를 할 것을 제안했다. 이에 저자들은 유방암을 진단받은 지 22개월 후에 반대쪽 액와 림프절 전이가 확인된 67세 여성의 증례를 영상 소견과 함께 보고하고자 한다. 환자는 액와 림프절 절제 수술 후 보조 항암화학요법 및 방사선치료를 받았다. 수술 6개월 후 추적 검사에서 종양 재발이나 전이의 증거는 없었다.

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