

Case Report



Multicentric Breast Cancer of the Axillary and Pectoral Breasts: A Case Report and Literature Review

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ABSTRACT

Multicentric cancer of the pectoral and ectopic breasts is extremely rare, and diagnosing this malignancy remains challenging because axillary breast cancer is easily misdiagnosed as lymph node metastasis. Moreover, there are no established treatment guidelines for this disease. We present our experience with a multicentric breast cancer patient who showed different responses to neoadjuvant chemotherapy (NAC) and underwent surgical treatments that differed from those in previous studies. In our case, the preoperative imaging of both lesions and subsequent core needle biopsy of each lesion were crucial, as these procedures confirm the diagnosis and help decide the chemotherapy regimen based on the subtype. After NAC, the patient underwent right breast-conserving surgery, sentinel lymph node biopsy (SLNB), and excision of accessory breast tissue in the right axilla. SLNB should be the initial step in staging multicentric breast cancer, unless imaging scan shows evidence of lymph node metastasis.

Keywords: Axilla; Breast Neoplasms; Neoplasms, Multiple Primary

INTRODUCTION

An extra breast (polymastia) or nipple (polythelia) is reported in approximately 0.2%–5.6% of the female population [1], and accessory breast tissue cancer is a rare entity representing approximately 0.3%–0.6% of all breast cancer cases [2]. Multicentric cancers of the pectoral and ectopic breasts are more rare, with only 4 published studies reporting 5 cases since 2006 [3-6]. Diagnosing multicentric breast cancer is challenging because accessory breast cancer of the axilla can be misdiagnosed as a lymph node metastasis. In addition, there are no established treatment guidelines for synchronous accessory and pectoral breast cancers [7]. We present a case of multicentric cancer of the pectoral and axillary breasts that responded differently to neoadjuvant chemotherapy (NAC).

Conflict of Interest

The authors declare that they have no competing interests.

Author Contributions

Conceptualization: Ko EY; Data curation: Han BK, Kim JY; Formal analysis: Han BK, Kim JY; Investigation: Kim H, Kim JY; Methodology: Chae BJ, Lee H; Resources: Chae BJ, Lee H; Supervision: Ko EY; Writing - original draft: Kim H; Writing - review & editing: Kim H, Ko EY.

CASE REPORT

A 41-year-old woman was referred to our hospital for breast cancer detected during a routine screening test. The patient was a married woman with no pregnancy history. Menarche occurred at the age of 15 years, and the patient was premenopausal at the time of diagnosis. The patient had no family history of breast cancer. On physical examination, the mass in the right breast and regional presumed lymph nodes in the right axilla were palpable.

On mammography, the breasts were heterogeneously dense, and there were no suspicious findings suggestive of malignancy in either breast. The accessory breasts were found in both axillae, and a nodular lesion was suspected in the right axillary breast (**Figure 1A**). Breast ultrasonography (US) (**Figure 1B**) revealed a 1.1-cm hypoechoic mass with indistinct margins in the right inner breast in the 3 o'clock direction. An accessory breast was detected in the right axilla, and 2 small, irregular, low-echoic masses less than 0.6 cm in size with nonparallel orientation were found in the axillary breast tissue. On physical examination, the palpable mass in the right axilla were suspected to be arising from the axillary breast. Doppler US revealed increased vascularity in all 3 masses in the pectoral and axillary breasts. Magnetic resonance imaging (MRI) revealed an irregular mass measuring > 1 cm in size with persistent enhancement in the right inner breast (**Figure 1C**). The accessory breast tissue was found in both axillae, and 2 small irregular masses corresponding to those observed on US were detected in the right axillary breast tissue. The lymph nodes in the axillary fossa appeared normal in size and shape. Taken together, multicentric breast cancer in the pectoral and axillary breasts was suspected rather than pectoral breast cancer with ipsilateral lymph node metastasis.

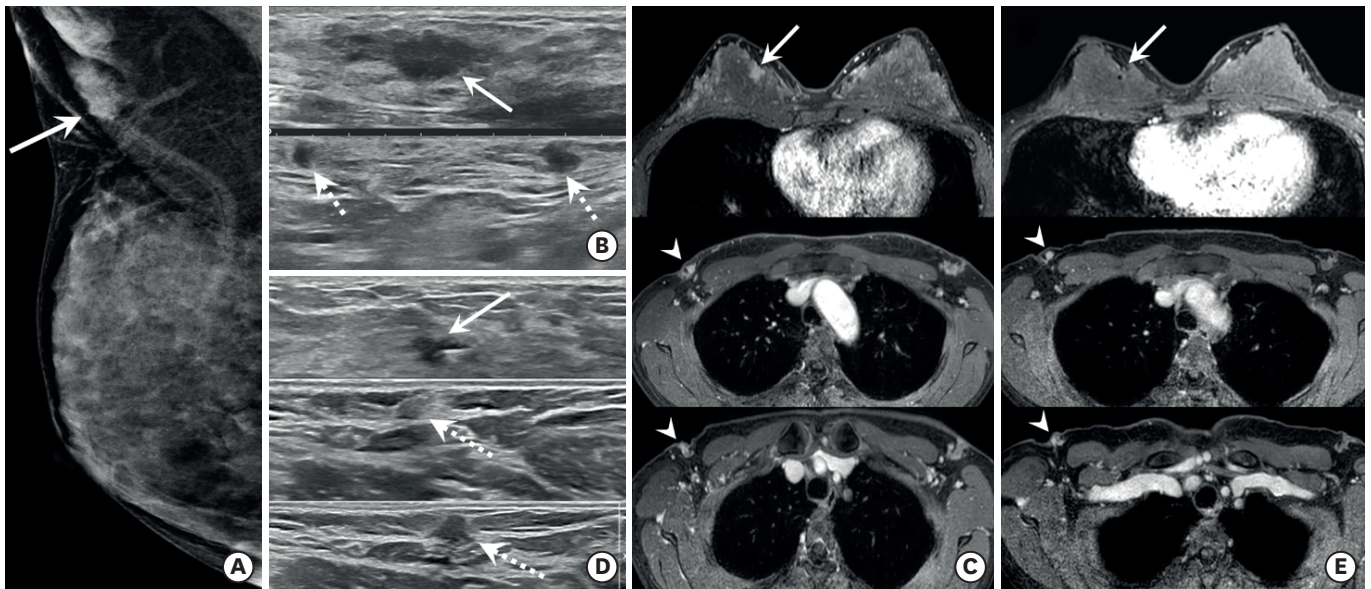


Figure 1. Preoperative images before neoadjuvant chemotherapy (A-C) and preoperative images after the completion of neoadjuvant chemotherapy (D, E). (A) Screening mammography shows extremely dense parenchyma without visible mass in right breast. A 1.5-cm hyperdense mass-like lesion similar to the dense parenchyma is noted in the right axilla (arrow). (B) Breast US shows a 1.1-cm mass in the right breast (solid arrow). In the right axilla, 2 small masses of less than 0.6 cm in size, with non-parallel orientation (dotted arrows), are visible within the axillary breast tissue. (C) MRI shows an irregular mass of approximately 1 cm in size in the right inner breast (arrow). Two small, irregular masses corresponding to the masses detected on US (arrowheads) are visible in the right axillary breast tissue. Lymph nodes in the axillary fossa appear normal in size and shape. (D) US reveals a reduction in the pectoral breast lesion size to 0.5 cm and appeared as a low-echoic mass surrounding the clip (solid arrow); meanwhile, the 2 masses (dotted arrows) in the axillary breast show no significant interval change. (E) MRI shows no definite enhancement around the clip in the right inner breast (arrow), and the masses (arrowheads) in the right axillary breast show no significant interval change.

US = ultrasonography; MRI = magnetic resonance imaging.

Core needle biopsy of the breast and right axillary masses was performed. Pathological examination of the breast lesion revealed intermediate-grade invasive ductal carcinoma, which was positive for estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and Ki-67 (60%). With the pathological features of the axillary lesion, invasive carcinoma with well-formed tubules was observed in the benign breast tissue and adipose tissue, thus confirming multicentric breast cancer in both the pectoral and axillary breasts. Chest and abdominal computed tomography and whole-body bone scans revealed the absence of distant metastases. Genomic analysis revealed the absence of BRCA mutations. In our case, additional biopsy of the axillary breast lesion for immunohistochemistry was not performed at the time of diagnosis because the pectoral breast lesion was more than 1 cm and positive for HER2, which were sufficient indications for NAC regardless of the subtype of axillary lesions according to the European Society for Medical Oncology guidelines for early-stage breast cancer [8]. After 6 cycles of NAC with docetaxel, carboplatin, trastuzumab, and pertuzumab, the lesion in the pectoral breast decreased in size from 1.1 cm to 0.5 cm, whereas no significant interval change was observed in the 2 lesions in the axillary breast on US (**Figure 1D**). Follow-up MRI (**Figure 1E**) showed no residual tumor in the right pectoral breast, whereas the axillary lesions did not show a significant interval change.

After the completion of NAC therapy, the patient underwent right breast-conserving surgery and sentinel lymph node biopsy (SLNB), along with excision of the accessory breast tissue in the right axilla. A pathology report revealed a residual 0.5-cm Bloom-Richardson grade I invasive ductal carcinoma in the right pectoral breast without lymphovascular invasion or an extensive intraductal component. The 2 lesions in the axillary breast were 0.5-cm and 0.3-cm Bloom-Richardson grade I tubular carcinomas, respectively, without lymphovascular invasion or extensive intraductal components. Four sentinel lymph nodes were sampled, and no metastases or therapeutic changes were observed. Results of the immunohistochemical analysis of the pectoral breast lesions revealed expressions of ER, PR, and HER2 (**Figure 2A-D**). The Ki-67 rate decreased to 1%. The axillary lesions were positive for ER but negative for PR and HER2, with a Ki-67 rate of less than 5% (**Figure 2E-H**). After the surgery, the patient was prescribed with hormone therapy with tamoxifen and goserelin for the next 5 years. The patient received complementary radiotherapy in the right breast and was clinically stable without disease recurrence within 1 year after surgery.

Informed consent

This study was approved by the Institutional Review Board (IRB) of Samsung Medical Center with a waiver of informed consent (IRB No. 2022-01-102).

DISCUSSION

The intriguing and unusual findings of our case can be summarized as follows: 1) preoperative imaging diagnosis of axillary breast cancer, which was distinguished from lymph node metastasis; 2) different responses to treatment of histologically different multicentric breast cancers; and 3) the first case of multicentric breast cancer in the pectoral and axillary breasts, in which SLNB without axillary lymph node dissection (ALND) was performed. The published case reports of multicentric breast cancer in the pectoral and ectopic breasts are summarized in **Table 1**. A few studies provide detailed documentation of the imaging findings and treatment of this condition. Appropriate diagnosis is even more challenging due to the lack of established diagnostic procedures and therapeutic management for accessory breast cancer.

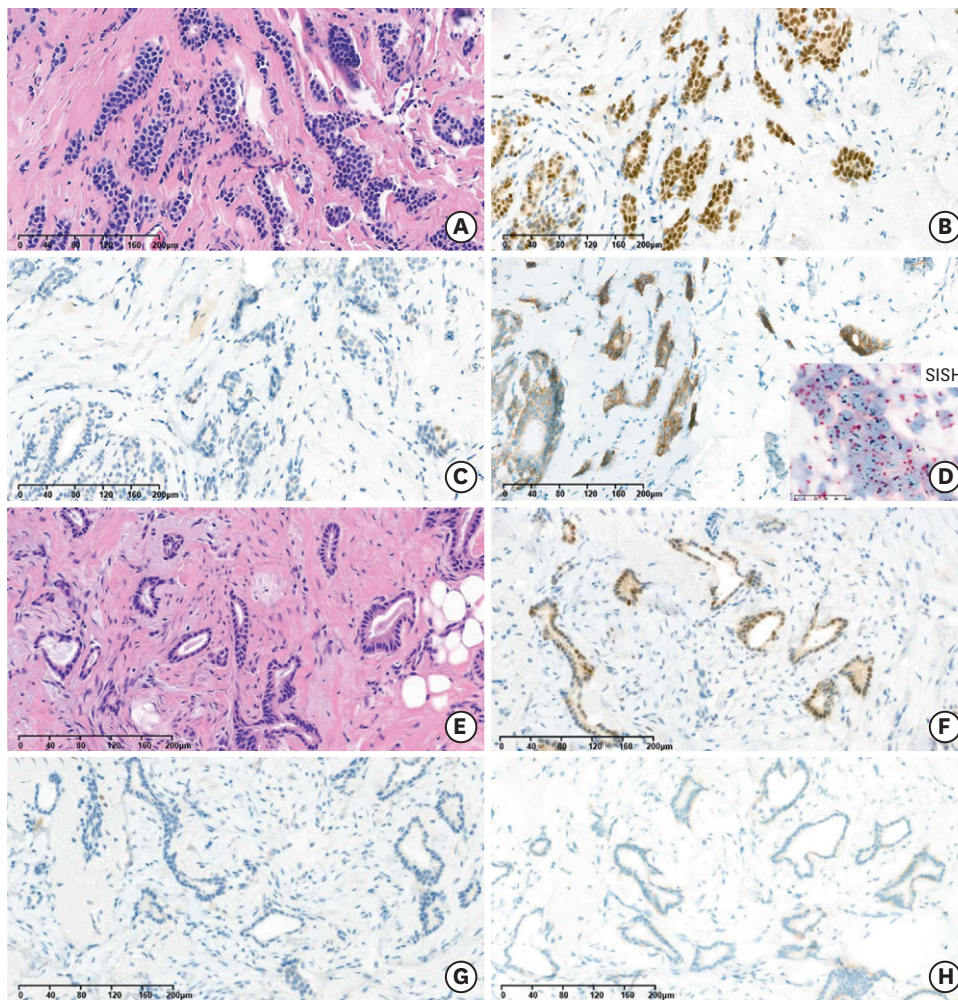


Figure 2. Histology of pectoral breast lesion (A-D) and axillary lesion (E-H). (A) H&E-stained section of pectoral breast lesion shows invasive ductal carcinoma with low-grade nucleus. The carcinoma is positive for ER (B) and HER2 confirmed by silver-enhanced *in situ* hybridization (D). About 1%-10% of tumor cells are positive for PR (C). H&E-stained section of axillary lesion shows tubular carcinoma with well-formed tubules and low-grade nucleus (E). The carcinoma is positive for ER (F), but negative for PR (G) and HER2 (H). H&E = hematoxylin and eosin; ER = estrogen receptor; HER2 = human epidermal growth factor receptor 2; PR = progesterone receptor.

Table 1. Reported cases of multicentric breast cancer in both pectoral and ectopic breast tissue

Case No.	Author (yr)	Age (yr)/ Sex	Extent (Pectoral breast/Ectopic breast)	LN metastasis	Pathologic diagnosis (Pectoral breast/Ectopic breast)	Surgery (Pectoral breast/ Ectopic breast)	NAC	Adjuvant chemotherapy/ Hormone therapy/ Radiotherapy	Outcome
1	Intra et al. (2006) [3]	53/F	Left/Vulva	(-)	DCIS/IDC	Radio-guided breast resection/Hemivulvectomy with both inguinal SLNB	(-)	(-)/(+)/(+)	Uneventful
2	Hao et al. (2012) [4]	43/F	Bilateral/Left axilla	Right axilla	IDC/IDC	Bilateral MRM	(-)	(+)/(-)/(-)	NA
3	Hao et al. (2012) [4]	53/F	Bilateral/Right axilla	Both axilla	Apocrine carcinoma/IDC	Bilateral MRM	(+)	(+)/(-)/(-)	NA
4	Oh et al. (2017) [5]	61/F	Left/Right axilla	Right axilla	DCIS/Micropapillary carcinoma	BCS/Wide excision and regional lymph node dissection	(-)	(+)/(+)/(+)	Uneventful and no recurrence for 1 yr
5	Shinseki et al. (2020) [6]	50/F	Left/Right axilla	(-)	IDC/IDC	Left mastectomy and sentinel LN biopsy/Wide excision and level I axillary dissection	NA	NA	NA

The patient had a strong family history of breast cancer and chose elective bilateral mastectomy after the diagnosis of adenoid cystic carcinoma of the left breast. F = female; NAC = neoadjuvant chemotherapy; DCIS = ductal carcinoma in situ; IDC = invasive ductal carcinoma; LN = lymph node; SLNB = sentinel lymph node biopsy; MRM = modified radical mastectomy; NA = not available; BCS = breast-conserving surgery.

Distinguishing accessory breast cancer from lymph node metastasis using imaging plays a crucial role in establishing a treatment plan. If breast cancer and axillary masses are simultaneously detected, cancer staging and surgical treatment are determined based on the diagnosis of the axillary mass. In the present case, the patient was diagnosed with T1N0M0 breast cancer and underwent SLNB. However, if the axillary mass is diagnosed as lymph node metastasis, the cancer staging would be T1N1 or T1N2, requiring ALND, which increases morbidity, including lymphedema, shoulder motion limitation, and sensory discomfort [9,10]. Therefore, it is important to accurately diagnose cancer in the axillary breast, which is distinct from axillary lymph node metastasis.

Distinguishing axillary masses from axillary lymph nodes solely by palpation may be challenging, and biopsy may not always facilitate the diagnosis. Imaging, especially mammography and US, may facilitate the differential diagnosis. Axillary breast cancers can be distinguished based on their location. Lymph nodes are usually located in the axillary fossa alongside the axillary vessels, whereas axillary breast masses are located more superficially within the accessory breast tissue, just beneath the skin. On US, the accessory breast shows a texture identical to that of the pectoral breast tissue [11]. In some cases, when the metastatic lymph node is nearly replaced with tumor cells, the lymph node structures may not be distinguishable and can be mistaken for an axillary mass. However, in such cases, the adjacent structures or the presence of surrounding breast tissue can help in the differential diagnosis.

All previously reported cases of multicentric breast cancer showed different histological types of ectopic and pectoral breast lesions. In multicentric breast cancer with different molecular subtypes, the treatment regimen suggested at our institution depends on the presence or absence of triple-negative breast cancer (TNBC) and breast cancer with HER2 overexpression. If one or more HER2-positive tumors were present, the chemotherapy regimen included trastuzumab. If one tumor was TNBC and the other was hormone positive, and none of them exhibited HER2 overexpression, a specific chemotherapy regimen for TNBC was selected. In addition, (neo)adjuvant chemotherapy is recommended for all HER2-positive early breast cancers, except for selected cases with very low risk such as T1aNO breast cancer [8]. In our case, pectoral and axillary cancers had different molecular subtypes and histology, that is, invasive ductal carcinoma and tubular carcinoma, respectively. Although immunohistochemical analysis of the tumor before NAC was conducted only in pectoral breast lesions, confirmation of the presence of HER2-positive cancer is a sufficient indication for NAC regimens, including trastuzumab. Because tubular carcinomas in the axillary breast were negative for HER2, they showed different responses from pectoral breast lesions after NAC. Based on our case, biopsy and molecular subtype assessment of each synchronous breast cancer before NAC are recommended to accurately determine the specific chemotherapy regimen and predict the treatment responses.

ALND in accessory breast cancer has been advocated because of its expected lymphatic drainage to the axillary lymph nodes and high rate of nodal metastasis, measuring up to 46%–51.8% [12-15]. All 4 patients with multicentric breast cancer in the pectoral and axillary breasts reported in previous studies underwent ALND (**Table 1**). However, as ALND increases the patient's morbidity, its clinical necessity should be carefully reviewed. Visconti et al. [15] reported that axillary breast cancer did not demonstrate a higher incidence of axillary nodal metastasis compared with pectoral breast cancer, whereas Munrós et al. [16] suggested the performance of SLNB for lymph node staging of ectopic breast cancer. Our patient had stage I disease and was the first patient with multicentric breast cancer in the pectoral and

axillary breasts, in which SLNB without ALND was performed. The risk stratification of nodal metastasis in axillary breast cancer is yet to be studied, but ALND may not be required in the early stage without imaging evidence of nodal metastasis. Further studies investigating the risk of nodal metastasis and the specific treatment options for accessory breast cancer are necessary to address this issue.

In conclusion, in patients with multicentric breast cancers in the pectoral and axillary breasts, differential diagnosis between cancer in the axillary breast and axillary lymph node metastasis may be challenging but is extremely crucial. The accurate imaging diagnosis and biopsy of both pectoral and axillary lesions to confirm the molecular subtype can help determine the appropriate chemotherapy regimen and surgical treatment. This study presents the first case report of different treatment responses of tumors after NAC and a less invasive surgical approach for multicentric breast cancer. In addition, SLNB should be the initial step in staging multicentric breast cancer, unless imaging examination shows evidence of lymph node metastasis. We believe that this report will help in the management of multicentric breast cancers in the pectoral and accessory breasts.

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