

Contralateral Breast Cancer Adjacent to a Fibroadenoma: Report of a Case

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Abstract

A 64-year-old woman noticed a lump of the right breast and consulted our outpatient clinic. She had undergone multiple excisional biopsies of fibroadenomas in both breasts and mastectomy for invasive ductal carcinoma (IDC) of the left breast. After completing 5 years of treatment with adjuvant tamoxifen, she had undergone screening with annual physical examinations and occasional computed tomography. She was declared recurrence-free 13 years after breast cancer surgery, although lumps were detected in the right breast, probably due to fibroadenomas. Mammography, ultrasonography, and magnetic resonance imaging revealed that the lump was irregularly shaped, 2 cm in diameter, and adjacent to a fibroadenoma with macrocalcification. Two axillary lymph nodes were enlarged and suggestive of metastasis. A core needle biopsy revealed IDC of the right breast. She underwent a right partial mastectomy with axillary lymph node dissection. The IDC was 2 cm in diameter, of nuclear grade 2, and adjacent to a 0.7-cm fibroadenoma with a macrocalcification. The margins of the IDC close to the fibroadenoma were clearly demarcated by the fibrous capsule of the fibroadenoma. Four axillary lymph nodes were positive for metastasis. In the present case the presence of fibroadenoma might have interfered with the early detection of the contralateral IDC. The history of multiple excisions of fibroadenomas and mastectomy for breast cancer suggests an increased risk of contralateral breast cancer for the patient's entire life; therefore, regular annual follow-up, such as physical examinations and mammography, is recommended. (J Nippon Med Sch 2014; 81: 168–172)

Key words: breast cancer, fibroadenoma, macrocalcification

Introduction

Annual screening with physical examination and

mammography is recommended, for women with breast cancer who have undergone mastectomy, to find early-stage locoregional recurrence or contralateral breast cancer¹. Abdalla et al.² have

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reported that in their series contralateral breast cancer was smaller (2.0 cm vs 3.0 cm) and was associated with a lower incidence of axillary lymph node involvement (29% vs 52%) than was primary breast cancer. However, patient with contralateral breast cancer had worse outcomes than did patients without contralateral breast cancer. In their study, the annual incidence of contralateral breast cancer remained constant at an average rate of 0.23%. In Japanese women with pTis or pT1mi breast cancer treated with surgery, the incidence of contralateral breast cancer is 0.51% without endocrine therapy and 0.36% with endocrine therapy³. The incidence of contralateral breast cancer is almost the same between American patients and Japanese patients. Although the risk of contralateral breast cancer decreases with adjuvant tamoxifen therapy^{3,4}, it remains elevated for 10 years or more after surgery⁴.

Fibroadenoma is the most common benign breast disease and is most often diagnosed when patients are in their 20s or 30s. Dupont et al.⁵ have reported that the risk of invasive breast cancer is 2.17 times higher among patients with fibroadenoma than among control subjects and remains elevated for more than 30 years after the initial diagnosis.

We report a case of a contralateral invasive ductal carcinoma (IDC) of the breast adjacent to one of multiple fibroadenomas with macrocalcifications more than 13 years after mastectomy for the primary IDC.

Case Report

A 64-year-old woman noticed a lump of the right breast and consulted our outpatient clinic. She had undergone multiple biopsies, all of which revealed fibroadenoma of the right breast at 20 years of age and of the left breast at 35 years and 44 years of age. In addition, IDC of the left breast was diagnosed at 50 years of age. She underwent mastectomy and axillary lymph node dissection and was treated with adjuvant tamoxifen for 5 years. After completing 5 years of adjuvant treatment with tamoxifen she had undergone screening with annual physical examinations and occasional computed

tomography (CT). No contrast agents were used because of an allergy to iodine-based contrast media. She was declared recurrence-free 13 years after breast cancer surgery on the basis of physical examination and CT, although lumps were detected in the right breast, probably due to fibroadenomas. The CT showed macrocalcifications without malignancy (**Fig. 1**).

Six months after the last screening the patient noticed a lump of the right breast and consulted our outpatient clinic. In the outer part of the right breast, a firm 2-cm lump was detected. Two other firm 1-cm lumps were also palpated in the upper outer quadrant and the upper inner quadrant of the right breast. The right axillary lymph nodes were palpable, and 2 were found with mammography and CT to be enlarged, a finding compatible with axillary nodal metastasis.

Mammography revealed an irregularly shaped, isodense mass with microlobulated margins adjacent to one of the macrocalcifications of the fibroadenomas (**Fig. 2**). Ultrasonography revealed a 1-cm hypoechoic mass with irregular margins adjacent to a fibroadenoma, with the macrocalcification showing a strong acoustic shadow (**Fig. 3**). Magnetic resonance imaging showed an irregularly shaped, enhanced 2-cm tumor adjacent to an unenhanced fibroadenoma (**Fig. 4**). A core needle biopsy revealed an IDC of the breast.

Partial mastectomy with axillary lymph node dissection was performed. Pathological findings of the contralateral breast cancer were as follows (**Fig. 5**). The IDC of the breast was 2 cm in diameter and of nuclear grade 2. It was positive for the presence of lymphovascular invasion and estrogen receptors (95%), negative for progesterone receptors (0%) and HER2 (score 0), and had low proliferation (Ki-67 index <1%). Four axillary lymph nodes were positive for metastasis. The IDC was adjacent to a 0.7-cm fibroadenoma with macrocalcification. The margins of the IDC close to the fibroadenoma were clearly demarcated by the fibrous capsule of the fibroadenoma. The IDC is believed to have arisen from tissue adjacent to the fibroadenoma and to have been unable to invade its capsule.

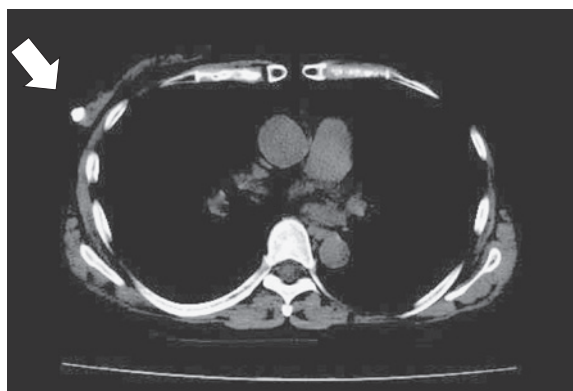


Fig. 1 Computed tomography of the right breast shows a macrocalcification due to fibroadenoma but no abnormal findings that may indicate breast cancer.

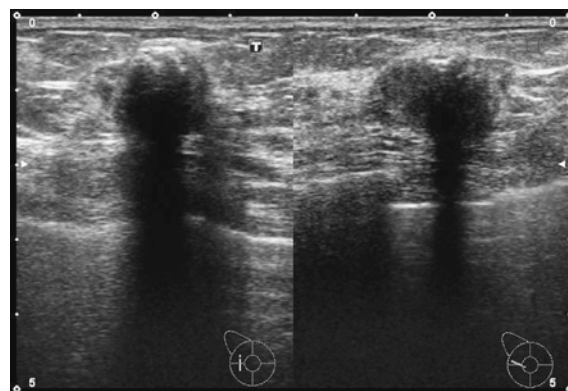


Fig. 3 Ultrasonography revealed a 1-cm hypoechoic mass with irregular margins adjacent to a macrocalcification with an acoustic shadow due to the macrocalcification.

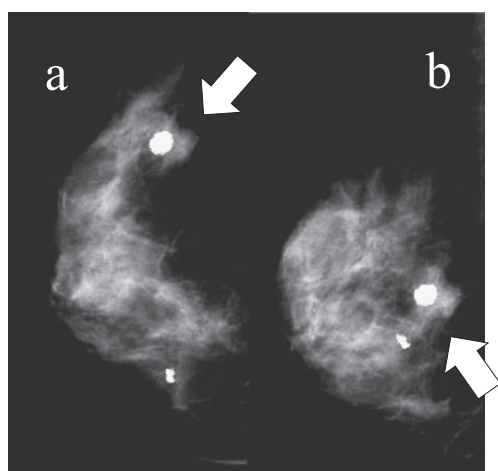


Fig. 2 Mammogram of the right breast shows an irregularly shaped, isodense mass with microlobulated margins adjacent to a macrocalcification of a fibroadenoma. (a: craniocaudal; b: mediolateral oblique)



Fig. 4 Magnetic resonance imaging showed an irregularly shaped, 2-cm enhanced tumor adjacent to an unenhanced fibroadenoma.

Discussion

We believe this case report is important for the following reasons. First, the contralateral breast cancer arose from tissue adjacent to a fibroadenoma with macrocalcification, and the presence of the fibroadenoma interfered with its early detection. The contralateral breast cancer might have been present and undetected for a long time because of its low proliferative features. We must be cautious in examining women with large, palpable fibroadenomas. If mammography were performed

annually according to the American Society of Clinical Oncology guideline¹, the contralateral breast cancer might have been detected earlier. Second, fibroadenoma is a risk factor for breast cancer, and the risk remains elevated for decades after the initial diagnosis⁵. In addition, if fibroadenoma is diagnosed with imaging studies but not with a pathological examination, it is uncertain whether such fibroadenomas are a risk factor of breast cancer because no data are available. The history of multiple excisions of fibroadenomas and mastectomy for breast cancer in this case suggest an increased

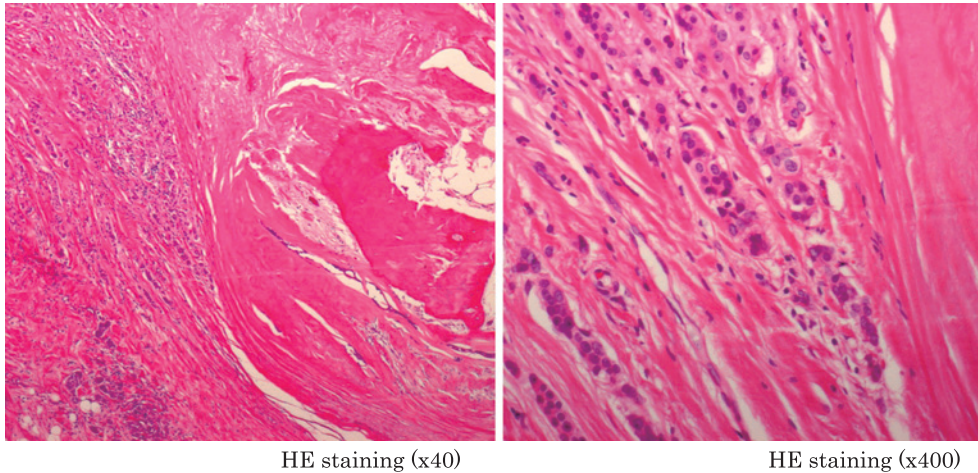


Fig. 5 Invasive ductal carcinoma in the tissue adjacent to the fibroadenoma was 2 cm in diameter and of nuclear grade 2. The margins of the invasive ductal carcinoma were clearly demarcated by the capsule of the fibroadenoma.

risk of contralateral breast cancer for the patient's entire life.

Dupont et al.⁵ have reported that fibroadenomas can be classified as complex if they contain cysts greater than 3 mm in diameter, sclerosing adenosis, epithelial calcifications, or papillary apocrine changes. When sufficient parenchyma adjacent to the fibroadenoma is available for pathological evaluation, it can be classified as being free of proliferative disease, as having proliferative disease without atypia, or as having atypical hyperplasia⁵. According to these classifications, the risk of IDC is elevated by a factor of 1.48 to 7.29⁵. In the present case, there was a history of multiple excisions of fibroadenomas but whether these fibroadenomas were complex and whether proliferative disease was present in the adjacent tissue are unknown. In other words, no other information, except that multiple fibroadenomas were excised, was obtained in this case; the exact risk of IDC of the breast following excision of the fibroadenomas could not be determined. However, the risk of IDC was considered to be high.

Although fibroadenoma is a risk factor for breast cancer, breast cancer rarely arises from an epithelial component of fibroadenoma. Previous reviews suggest that most carcinomas in fibroadenomas are lobular carcinomas in situ or ductal carcinomas in situ^{6,7}. In contrast, IDCs detected after the diagnosis of fibroadenoma usually arise from the tissue outside

the fibroadenoma, as in the present case.

Conclusion

In the present case, the presence of fibroadenoma might have interfered with the early detection of contralateral breast cancer, which arose from tissue adjacent to the fibroadenoma. The history of multiple excisions of fibroadenomas and mastectomy for breast cancer suggest an increased risk of contralateral breast cancer for the patient's entire life; therefore, regular follow-up, such as annual physical examination and mammography, is recommended.

Conflict of Interest: None declared.

References

1. Khatcheressian JL, Hurley P, Bantug E, et al: Breast cancer follow-up and management after primary treatment: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol* 2013; 31: 961–965.
2. Abdalla I, Thisted RA, Heimann R: The impact of contralateral breast cancer on the outcome of breast cancer patients treated by mastectomy. *Cancer J* 2000; 6: 266–272.
3. Aihara T, Tanaka S, Sagara Y, et al: Incidence of contralateral breast cancer in Japanese patients with unilateral minimum-risk primary breast cancer, and the benefits of endocrine therapy and radiotherapy. *Breast Cancer* 2012 Oct 4. [Epub ahead of print].
4. Davies C, Pan H, Dodwin J, et al., for the Adjuvant

- Tamoxifen: Longer Against Shorter (ATLAS) Collaborative Group: Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. *Lancet* 2013; 381: 805–816.
5. Dupont WD, Page DL, Parl FF, et al: Long-term risk of breast cancer in women with fibroadenoma. *N Engl J Med* 1994; 331: 10–15.
 6. Yoshida Y, Takaoka M, Fukumoto M: Carcinoma arising in fibroadenoma: case report and review of the world literature. *J Surg Oncol* 1985; 29: 132–140.
 7. Diaz NM, Palmer JO, McDivitt RW: Carcinoma arising within fibroadenomas of the breast. A clinicopathologic study of 105 patients. *Am J Clin Pathol* 1991; 95: 614–622.

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