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Case Report

CASE REPORT

Early HER2-positive breast cancer arising from a fibroadenoma: a case report

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Abstract

Breast cancer arising from fibroadenoma (FA) is rare, in which almost all reported cases are human epidermal growth factor receptor 2 (HER2)-negative. This is the first report to describe a case of HER2-positive breast cancer arising from FA that was treated with chemotherapy plus anti-HER2 therapy. In this early case, upfront surgery outcomes guided the selection of appropriate systemic therapy. A 31-year-old woman previously diagnosed with FA experienced tumor growth. Core needle biopsy and imaging studies confirmed a diagnosis of stage IIA HER2-positive invasive ductal carcinoma (IDC) with no evidence of lymph node metastasis (cT2N0M0). Breast-conserving surgery was performed. Pathological diagnosis revealed stage IA IDC with a predominant intraductal component (pT1aN0M0), arising from FA. In conclusion, we encountered an extremely rare case of HER2-positive breast cancer arising from FA in which pathological infiltration was difficult to predict based on preoperative imaging.

INTRODUCTION

Fibroadenoma (FA) is one of the most common benign breast tumors with a peak age of onset between 15 and 35 years [1]. Breast cancer rarely arises from FA and is detected only in 0.02–0.125% of FA-related cases, usually in patients over 40 years of age [2]. Furthermore, clinical, sonographic and mammographic findings are similar to those of FA alone [3], thereby complicating cancer detection. There is no consensus on subtypes distribution of this disease, and hormone receptor-positive rates may not differ significantly from common breast cancer (estrogen receptor (ER)-positive, 68.8%; progesterone receptor (PgR)-positive, 62.5%) [4, 5]. However, almost all cases, in which subtypes have been reported are of luminal or triple-negative types, were negative for human epidermal growth factor receptor 2 (HER2). Herein, we report a rare case of HER2-positive early breast cancer arising from FA.

CASE REPORT

A 31-year-old woman presented without any medical or family history of cancer. Approximately, 1 year before her current presentation, a 13-mm-sized left breast mass was detected on breast screening (Fig. 1a and b), classified as Breast Imaging Reporting and Data System category 3. The patient was diagnosed with FA based on imaging alone. Follow-up imaging revealed mass enlargement and presence of new calcifications (Fig. 1c and d), which prompted core needle biopsy. Invasive ductal carcinoma (IDC) was diagnosed, and immunohistochemical staining revealed an HER2 score of 3+ (HER2-positive), without ER or PgR expression. Fine-needle aspiration cytology (FNAC) of axillary lymph nodes suggested no evidence of metastasis. Magnetic resonance imaging revealed a maximum lesion diameter of 22 mm. Positron emission tomography-computed tomography revealed absence of distant metastasis. Thus, stage

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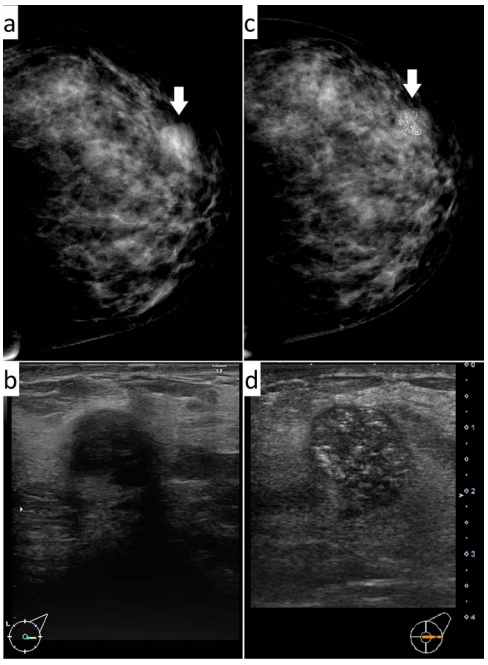

Figure 1: Comparison between images of the left breast tumor taken 1 year earlier (**a** and **b**) and before the current operation (**c** and **d**) (a, c, mammogram (cranio-caudal view); b, d, ultrasonography). (a) An oval-shaped mass with partially obscured margins (arrow). (b) A well-circumscribed hypoechoic tumor. (c) New-onset coarse heterogeneous calcifications in the mass (arrow). (d) Enlargement of the tumor accompanied by multiple hyperechoic spots.

IIA HER2-positive IDC (cT2N0M0) was diagnosed. Although neoadjuvant chemotherapy (NAC) was considered, upfront breast-conserving surgery and sentinel lymph node biopsy were performed based on the patient's preference. The patient refused genetic testing for hereditary cancers. The excised specimen surface contained a relatively well-circumscribed, grey-white and solid 19-mm tumor (Fig. 2a–c). Histologically, this lobulated lesion had predominantly intraductal solid growth patterns of large carcinoma cells with marked coagulation necroses and calcium depositions (Fig. 3a and b). Carcinoma cells were polygonal, showing high nuclear/cytoplasmic ratios and irregular nuclei with distinct nucleoli. Infiltrating elements of histological grade 3, up to 4 mm, were observed in the lesion (Fig. 3c), with scattered microinvasive foci (Fig. 3b). On immunohistochemical examination, neoplastic cells were negative for ER and PgR (total Allred scores: 0 and 0, respectively) (Fig. 3d and e). The HER2 score was estimated to be 3+ in invasive and intraductal neoplastic cells (Fig. 3f), and the Ki67 (MIB-1) labeling index was 58.7%. Myoepithelial cells, positive for p63 and CD10, were identified in intraductal components. Based on these pathological findings, an invasive carcinoma of no special type, HER2 immuno-subtype, with a predominant intraductal component, derived from an intracanalicular FA was diagnosed. Since sentinel lymph node biopsy revealed absence of metastasis, the final diagnosis was stage IA IDC (pT1aN0M0). Pathological findings guided selection of weekly paclitaxel and trastuzumab as adjuvant systemic therapy. Additionally, the patient underwent radiotherapy of the whole left breast (42.56 Gy) and tumor-bed boost irradiation (10.64 Gy), considering her age. Approximately 6 months following surgery, no apparent recurrence was noted.

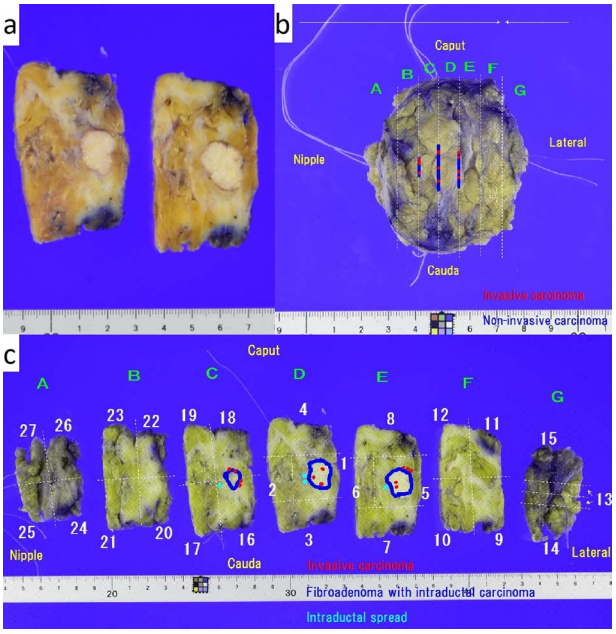

Figure 2: Macroscopic findings of the specimen and pathological mapping of carcinoma. (**a**) Cut surfaces of the excised specimen. (**b**) Multiple invasive components are marked in red, and *in situ* components (fibroadenoma with intraductal carcinoma) are in blue. (**c**) Cut surfaces of the mapping; several *in situ* components extend outside the tumor (marked in light blue).

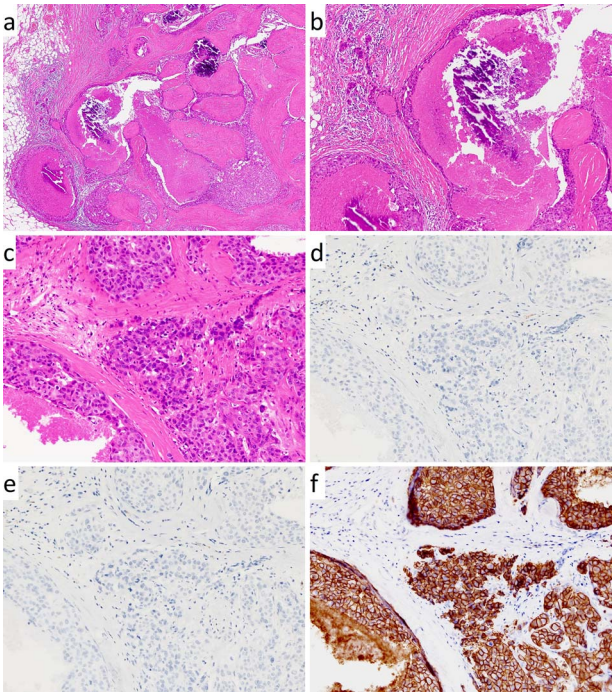

Figure 3: Histopathological findings of invasive ductal carcinoma arising from a fibroadenoma. (**a**) Lobulated mass showing an intracanalicular pattern with fibrous stroma and predominantly intraductal, epithelial proliferation (HE, ×100). (**b**) High-grade ductal carcinoma in situ with comedo-like necroses, coarse calcifications, and small focus of stromal invasion (left side) (HE, ×100). (**c**) Infiltrating and intraductal components have eosinophilic cytoplasm and hyperchromatic nuclei (HE, ×200). (**d–f**) Immunostaining shows no expression of the estrogen (d) and progesterone (e) receptors, whereas HER2 is diffusely positive (f) (×200).

DISCUSSION

This case highlights two crucial clinical findings. First, breast cancer arising from FA could involve HER2-positive type; thus, chemotherapy with targeted therapy should be considered. Second, upfront surgery may be a useful guide for selecting appropriate systemic therapy.

To the best of our knowledge, this is the first report to describe an HER2-positive breast cancer arising from FA treated with adjuvant chemotherapy and anti-HER2 therapy. We conducted literature searches with PubMed using the keywords 'fibroadenoma' and 'carcinoma' to collect articles in English published between February 2013 and June 2021; for literature published between January 1986 and January 2013, we referred to the review by Wu *et al*. [5]. HER2-positive breast cancer arising from FA is extremely rare, with only one reported case [6]. Moreover, a somewhat different case of coexistence of HER2-positive breast cancer, phyllodes tumor and FA has been reported [7]. However, to date, no cases have mentioned a systemic treatment strategy.

Currently, chemotherapy with anti-HER2 therapy is generally considered for HER2-positive invasive breast cancer. The number of patients receiving NAC has recently increased due to the potential for improving breast preservation rate and achieving pathological complete response with good prognosis [8]. However, chemotherapy de-escalation is another significant issue. Using non-anthracycline regimens has become a common option for low-risk patients because anthracycline-based regimens could cause cardiotoxicity and secondary leukemia [9].

Chemotherapy regimen is generally selected by considering the infiltration diameter of the tumor. However, since the histological type of this disease is mainly carcinoma *in situ* or early invasive breast cancer, it is difficult to base this regimen selection on preoperative imaging findings [4]. Wu *et al*. reported a mean tumor diameter of breast cancer within FA of 2.46 cm. However, 33.3% of cases were pTis, and those with a known infiltration diameter were pT1a or pT1b [5]. In our case, the actual infiltration diameter was only up to 4 mm (pT1a). However, the imaging-based tumor diameter was 22 mm (cT2). Therefore, upfront surgery could help in guiding the selection of a less intense non-anthracycline regimen. Furthermore, it may be a reasonable choice to avoid chemotherapy altogether.

It should be noted that even tumors with small infiltration diameter (pT1mi or pT1a) may involve lymph node metastasis [5, 10]. FNAC should be performed, if possible, since NAC may be a better approach when lymph node metastasis is detected. In our case, although mild lymphadenopathy was observed, FNAC did not reveal metastasis.

In conclusion, breast cancer arising from FA could present as an HER2-positive type; hence, chemotherapy with anti-HER2 therapy should be considered. Upfront surgery may be useful in guiding selection of an appropriate adjuvant therapy, owing to difficulty in predicting infiltration diameter through preoperative imaging alone. It is unclear how breast cancers arise from FA and why these cases tend to more frequently involve HER2-negative subtype, and further research is required.

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CONFLICT OF INTEREST STATEMENT

The authors' COI are not related to this work.

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None to declare.

ETHICAL APPROVAL

This case report did not require review by the Ethics Committee of Saitama Medical University International Medical Center, Hidaka, Saitama, Japan.

CONSENT

Informed consent was obtained from the patient included in the case report.

GUARANTOR

Akihiro Fujimoto.

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