



## Coexistence of malignant phyllodes tumor and her2-positive locally advanced breast cancer in distinct breasts: A case report



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### ABSTRACT

**INTRODUCTION:** Phyllodes tumor of the breast is a rare biphasic neoplasm, accounting for less than 1% of all breast tumors. Coexistence of phyllodes tumor and breast cancer in distinct breasts is extremely rare.

**CASE PRESENTATION:** A 47-year-old Japanese woman presented with bilateral breast lumps. A HER2-positive, unresectable invasive carcinoma in the right breast and fibroadenoma in the left were diagnosed via core needle biopsy. During chemotherapy with anti-HER2 therapy, the breast cancer shrank quickly, while the left breast lump suddenly enlarged. Under a diagnosis of malignant neoplasm of the breast, left mastectomy was performed. Malignant phyllodes tumor was diagnosed by postoperative histological examination and recurred in multiple areas as early as 2 months after surgery.

**DISCUSSION:** Only 10 cases of coexisting phyllodes tumor and breast cancer in distinct breasts have been reported in the English literature. Phyllodes tumor associated with breast cancer in distinct breasts tends to be malignant. This is the first case of phyllodes tumor rapidly enlarging during anti-HER2 chemotherapy for locally advanced HER2-positive breast cancer.

**CONCLUSION:** Even during effective treatment of advanced or recurrent breast cancer, attention should also be paid to the contralateral breast for the possible association of a second malignancy such as phyllodes tumor.

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### 1. Introduction

Phyllodes tumor of the breast (PT) is a rare biphasic neoplasm composed of epithelial and stromal elements, and accounts for less than 1% of all breast tumors [1]. Although even more uncommon, breast cancer (BC) can occur associated with PT: inside or outside of the PT; synchronously or metachronously; in the same breast or in distinct breasts [2–5]. We report here an extremely rare case of the synchronous coexistence of malignant PT and HER2-positive locally advanced BC in distinct breasts.

### 2. Case presentation

A 47-year-old Japanese woman, who had no notable past medical and familial history, presented with bilateral breast lumps: a 13 cm mass with skin ulceration in the right breast and a 5.5 cm, lobulated mass with a smooth surface in the left. Mammogram of the left side revealed a lobulated mass with a smooth surface in the



**Fig. 1.** Mammogram of the left breast. A lobulated mass with a smooth surface could be seen. Mammogram of the right breast was not performed due to the presence of a huge mass and skin ulceration.

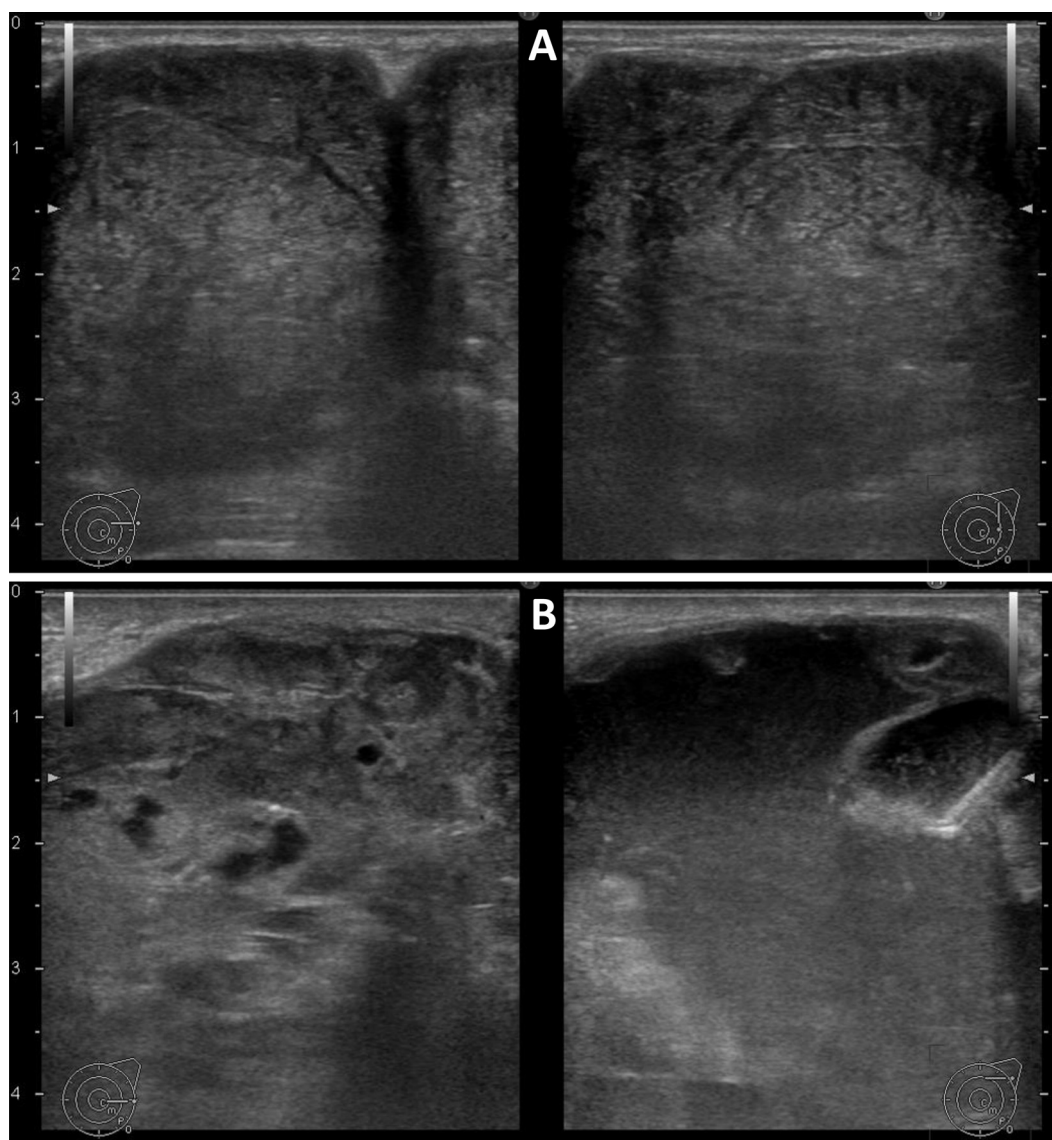
*Abbreviations:* PT, phyllodes tumor; BC, breast cancer; FA, fibroadenoma.

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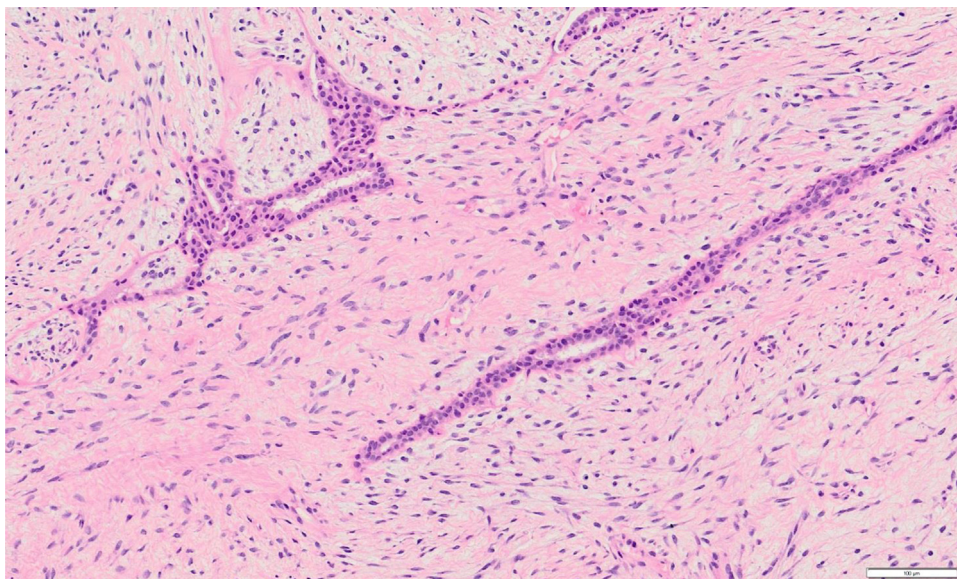
**Fig. 2.** Ultrasonography of the left breast at first presentation (A) and after 3 months of anti-HER2 chemotherapy (B). A well-defined, low-echoic mass with a homogeneous intratumoral echoic pattern could be seen at first presentation (A). After 3 months of anti-HER2 chemotherapy, the mass suddenly enlarged and contained fluid, potentially suggesting intratumoral hemorrhage (B).

upper outer quadrant of the left breast (Fig. 1), but no mammogram of the right side was performed due to the presence of a huge mass with skin ulceration. Ultrasonography of the left breast revealed a well-defined, low-echoic mass with a homogeneous intratumoral echoic pattern, suggesting a benign tumor (Fig. 2A). On the right, there were massive axillary lymph node metastases. HER2-positive invasive carcinoma in the right breast and fibroadenoma (FA) rather than PT in the left were diagnosed by core needle biopsy (Fig. 3). Because the BC in the right breast was unresectable, anti-HER2 therapy with docetaxel, trastuzumab and pertuzumab was initiated. After 3 months, the BC had shrunk markedly and finally disappeared on physical examination and CT, while the mass in the left breast enlarged suddenly (Figs. 2 and 4). Repeated core needle biopsy of the left breast revealed a malignant neoplasm, such as sarcoma, malignant PT or metaplastic carcinoma; therefore, left mastectomy and axillary lymph node sampling were performed. A frozen section of the sampled lymph nodes revealed metastases of adenocarcinoma cells, and left axillary lymphadenectomy was performed. The mass was  $100 \times 90 \times 70$  mm with massive hemorrhagic necrosis (Fig. 5). Histologically, the mass was composed of

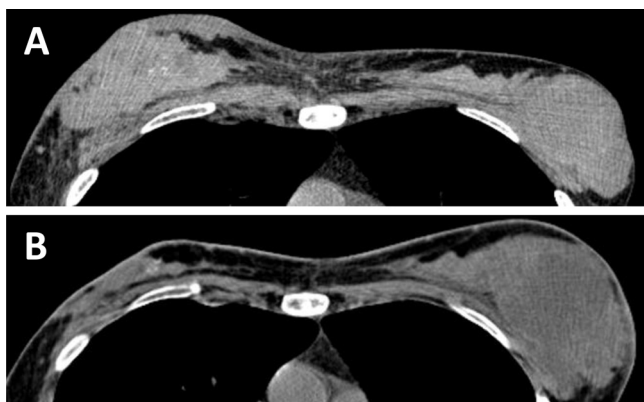
dense atypical spindled mesenchymal cells with numerous mitoses (50 mitoses/10 high-power fields, Fig. 6). Benign PT was also observed next to the malignant component (Fig. 6), and malignant PT was diagnosed. The lymph node metastases were poorly differentiated adenocarcinoma with positive staining for HER2, and therefore metastasis from the contralateral BC was diagnosed. Two months after the operation, multiple lung and liver metastases occurred. Computed tomography-guided core needle lung biopsy revealed PT metastasis. Subsequently, the patient preferred palliative care rather than cytotoxic chemotherapy. She died 9 months after the operation.

### 3. Discussion

Phyllodes tumor is a rare biphasic, fibroepithelial neoplasm, which is sub-classified into benign, borderline and malignant types, based on the following features: degree of stromal cellular atypia, mitotic activity, presence or absence of stromal overgrowth, and infiltrative or circumscribed tumor margin [1]. Most PTs are benign



**Fig. 3.** Histology of the core needle biopsy from the left breast tumor. Fibroadenoma rather than phyllodes tumor was diagnosed due to the absence of a leaf-like pattern, stromal overgrowth or mitosis.

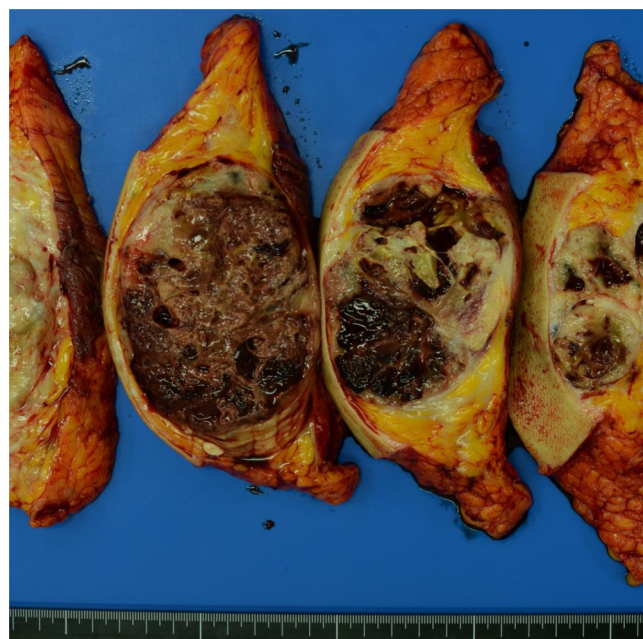


**Fig. 4.** Computed tomography before chemotherapy and anti-HER2 therapy (A) and 3 months after the therapy (B). The right BC had shrunk markedly, but the left breast tumor had enlarged rapidly. Enhanced medium was not used due to allergic reaction.

or borderline, and malignant PT is even less common, accounting for less than 30% [6,7].

Although extremely rare, BC, either invasive or non-invasive, can be associated with PT: inside or outside of the PT; synchronously or metachronously; in the ipsilateral or other breast. Abdul Aziz et al. summarized 39 cases of the coexistence of PT and BC in 2010 [2], among which, coexisting PT and BC in distinct breasts occurred in only 7 cases and was even less common than being inside the PT (21 cases) or in the ipsilateral breast (16 cases; 5 cases were duplicated). Subsequently, we found three additional cases of the synchronous coexistence of PT and BC in distinct breasts [3–5]. Thus, overall only 10 cases have been reported in the English literature so far, and the current case is therefore extremely rare. All 11 cases of coexisting PT and BC in distinct breasts, including the current case, are summarized in the Table 1. Phyllodes tumor of the breast associated with BC in the contralateral breast tends to be malignant. Most previously reported cases had favorable prognoses, while only two patients, including the current case, had recurrence of PT and died.

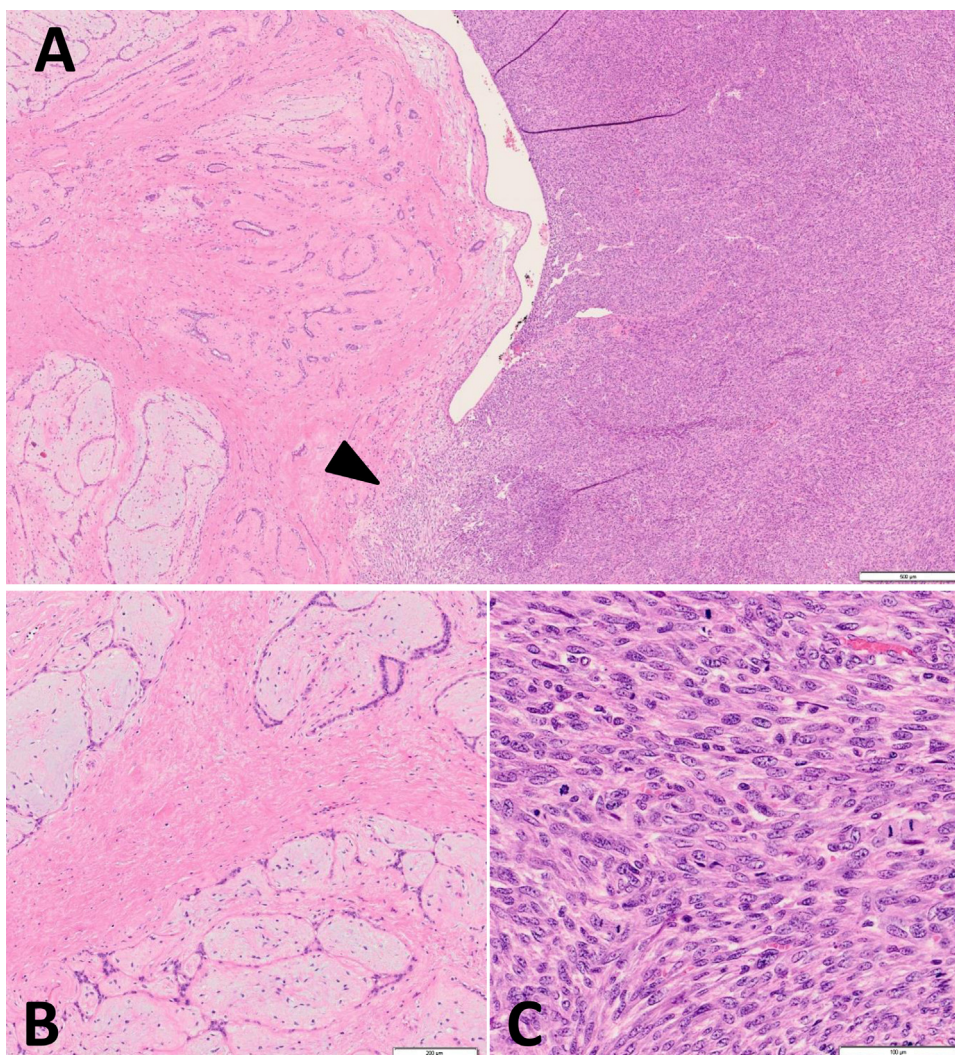
The etiology of the association between BC and PT is unknown. Genetic changes with intratumoral genetic heterogeneity have been reported [8] and might lead to malignant transformation of



**Fig. 5.** Macroscopic findings of the resected left breast tumor. The mass was 100 × 90 × 70 mm with massive hemorrhagic necrosis.

epithelial as well as stromal components, resulting in the development of benign to malignant PT and the association of BC inside the PT. However, their association in distinct breasts has not yet been explained. We speculate that this association was coincidental, as discussed by other authors [4].

In the current case, PT rapidly progressed during chemotherapy with taxane and anti-HER2 therapy. This treatment might have induced malignant transformation and accelerated its growth; however, there is no report of PT rapidly progressing during such treatment, and thus it might have been coincidental. Taxane can be used to treat various sarcomas [9], and therefore it is possible that the treatment might have affected part of the PT, resulting in necrosis and intratumoral hemorrhage, and finally, rapid enlargement of the tumor.



**Fig. 6.** Histology of the left breast tumor. A, Panoramic view shows benign, borderline and malignant parts of PT and their transition (arrowhead). B, Magnified view of the benign part of the PT. C, Magnified view of the malignant part of the PT. Dense atypical spindled mesenchymal cells with numerous mitoses (50 mitoses/10 high-power fields) can be seen.

**Table 1**  
Reported cases of coexisting phyllodes tumor and breast cancer in distinct breasts.

No	Author	Year	Age	PT	PT size (mm)	Timing	BC	Outcome
1	McCormick [3]	1977	45	Malignant	150	Synchronous	IDC	8 M alive
2	Stone-Tolin	1982	59	Benign	220	Metachronous	IDC	15 M alive
3	Morimoto	1993	49	Malignant	110	Synchronous	LCIS	132 M alive
4	Powell	1994	NS	Malignant	NS	Synchronous	LCIS	NS
5	Powell	1994	NS	Malignant	NS	Metachronous	IDC	Dead due to BC
6	Kasami	1997	47	Malignant	90	Synchronous	ILC	17 M dead due to PT
7	Gebirim	2000	58	Malignant	300	Synchronous	ILC	84 M alive
8	Merch	2006	NS	Malignant	50	Synchronous	IDC	32 M alive
9	Neto [4]	2012	66	Benign	90	Synchronous	IDC	NS
10	Jain [5]	2014	43	Borderline	150	Synchronous	IDC	6 M alive
11	Current case	2015	47	Malignant	55	Synchronous	IDC	9 M dead due to PT

Malignant PT rarely metastasizes to lymph nodes, and axillary lymphadenectomy should normally be avoided [1]. In the current case, preoperative diagnosis of the left breast mass could have been metaplastic carcinoma and an intraoperative frozen section of the sampled lymph node in the left axilla revealed involved cancer cells, resulting in unnecessary lymphadenectomy. We did not expect lymph node metastases from the contralateral BC which clinically disappeared after standard anti-HER2 chemotherapy.

Preoperative diagnosis of PT via imaging modalities and needle biopsies is often difficult. Using both modalities, differentiating between benign PT and FA is frequently challenging due to their morphological similarities [1,7,10]. Ward et al. reported that the sensitivity of core needle biopsy in diagnosing PT was 63% and imaging was 65% [7]; however, it was much lower for benign PT than for borderline or malignant PT [7]. In addition, intratumoral heterogeneity can exist, and therefore complete surgical excision is

usually required for final assessment to discriminate from FA [1]. In the current case, FA was initially diagnosed via core needle biopsy, probably because the tissue sampled was only from the benign part where significant cellularity or mitosis was absent.

Because large size is the one of the significant clinical findings suggesting PT rather than FA [10], the mass in the left breast should have been excised to confirm the histology at the first presentation in the current case. Surgical removal is the mainstay of PT treatment and usually leads to a favorable prognosis [6]. However, in the current case, the presence of unresectable, locally advanced BC in the contralateral breast precluded removal of the left breast mass until it had become massive, resulting in a negative outcome.

#### 4. Conclusion

Here we report an extremely rare case of the coexistence of locally advanced BC and malignant PT in distinct breasts. Only 10 cases of coexisting PT and BC in distinct breasts had been reported so far in the English literature. Phyllodes tumor which associates with BC in the contralateral breast is tend to be malignant. Even with a case of advanced or recurrent BC and during effective treatment, careful attention should also be paid to the contralateral breast for the possible association of a second malignancy such as PT.

#### Conflicts of interest

I have no conflicts of interest.

#### Funding

There are no sources of funding.

#### Ethical approval

This is not a research study.

#### Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

#### Competing interests

The authors declare that they have no competing interests.

#### Authors' contributions

TS was the physician in charge of this patient and made treatment decisions. IM participated in the operation and the management of this patient. TS was the pathologist responsible for the macroscopic and microscopic findings. All authors read and approved the final manuscript.

#### Guarantor

This is not a research study. All authors read and approved the final manuscript. Therefore, all authors are responsible for this report.

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