



Case report

Invasive lobular carcinoma enclosed by a benign phyllodes tumor: A case report

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ABSTRACT

Introduction and importance: Phyllodes tumors (PT) account for approximately 1% of all breast tumors. The coexistence of phyllodes tumor and invasive lobular carcinoma in the ipsilateral breast is extremely rare with fewer than six cases reported worldwide in the last 20 years. We hereby present the first in Taiwan.

Case presentation: A 43-year-old female was presented with a protruding tumor with bleeding tendency over left breast in 2016. Breast sonography revealed highly suspected malignancy (ACR BI-RADS category 5). Computed tomography scan disclosed a protruding mass occupying the left breast. Core needle biopsy showed a fibroepithelial lesion favoring fibroadenoma. Considering clinicopathological discrepancy, a nipple-sparing mastectomy was conducted. Pathology report revealed a benign PT with an incidental finding of invasive lobular carcinoma (pT1cN0) within the tumor. Due to tumor recurrence, the patient received re-operation of total mastectomy in 2017, and is under regular adjuvant hormonal therapy without cancer recurrence to date.

Clinical discussion: Physicians could easily overlook carcinomas enclosed by PTs due to its occult property. However, when carcinomatous changes arise from within or along with the PT, the proposed therapeutical course may be altered. Moreover, invasive carcinoma components in PTs possess potential for lymph node metastasis. Multidisciplinary cooperation is key in detecting and managing PT with synchronous carcinomatosis.

Conclusion: Thorough examination of the excised tumor specimen and ensuring an adequate surgical margin is necessary. Sentinel lymph node biopsy (SLNB) should be considered whenever suspicious clinical features occur in PT patients. This may aid in the detection of microscopic invasive carcinomatous change.

1. Introduction and importance

Phyllodes tumor (PT) is a rare type of breast neoplasm, accounting for less than 1% [1] of all breast tumors. Carcinoma in situ or invasive carcinoma arising within or attached to the PT is extremely uncommon, with an incidence rate of only 1%–2% among all PTs [2]. Of all the literatures regarding coexistence of PT and other breast tumors, invasive lobular carcinoma (ILC) is far less frequently reported than lobular carcinoma in situ (LCIS), ductal carcinoma in situ (DCIS), or invasive ductal carcinoma (IDC) [3], with fewer than six cases reported in the last 20 years [4]. We present a case initially diagnosed as fibroadenoma through core needle biopsy (CNB), whom later underwent total

mastectomy, and in which PT was identified, with accidental finding of an ILC within the tumor. This case raises our concern for potentially overlooking ILC, as this finding could alter the therapeutical course. This case report has been reported in line with the SCARE 2020 criteria [5].

2. Case presentation

A 43-year-old woman suffered from a protruding mass with skin ulceration and bloody discharge over the left breast for months in 2016. This patient with regular menstrual period was nulliparous and had menarche at 12 years old. According to the patient, she had a maternal aunt who was diagnosed with breast tumor in her 50s.

Abbreviations: PT, phyllodes tumor; ILC, invasive lobular carcinoma; SLNB, sentinel lymph node biopsy; LCIS, lobular carcinoma in situ; DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma; CT, computed tomography; CNB, core needle biopsy; HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor; ALND, axillary lymph node dissection.

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The patient noticed a left palpable breast mass without tenderness for approximately 3 years and was taking self-administered Chinese herbal medicine for this problem. However, the progressive enlargement of this protruding mass with bleeding tendency led the patient to seek treatment at our breast clinic. The patient also provided photos, self-taken, to demonstrate the rapidity of the tumor's progression (Fig. 1a–d). Gross examination showed a >10 cm mass with skin ulceration (Fig. 1d).

Breast sonography confirmed highly suspected malignancy (ACR BI-RADS category 5) (Fig. 2). Chest computed tomography (CT) scan also revealed a protruding mass occupying the left breast (Fig. 3a) with level I, II axillary lymph node metastases (Fig. 3b–c). Core needle biopsy revealed a fibroepithelial lesion favoring fibroadenoma in the pathologic figure. Mammography modality was not performed due to the patient's refusal. However, considering the clinical presentations was incompatible with the pathological findings, nipple-sparing mastectomy was conducted in February 2016 by Dr. Shen-Liang Shih. The patient denied lymph node biopsy and further breast reconstruction due to personal reasons.

The pathology report revealed a benign PT measuring 12.0 cm × 8.5 cm × 4.5 cm with an incidental finding of a 1.8-cm × 0.9-cm mass of ILC (pT1cN0) within the tumor. The excised specimen grossly presented as a well-circumscribed, firm, grayish-white tumor with hemorrhage

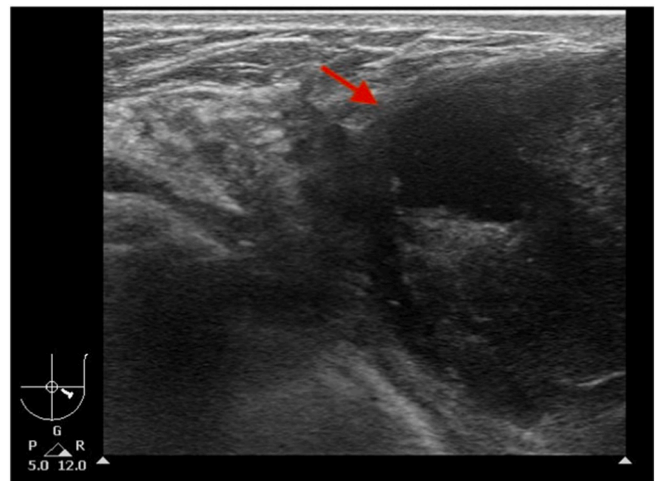


Fig. 2. Breast sonography revealing highly suspected malignancy (ACR BI-RADS category 5) (Arrow).



Fig. 1. a–d: Protruding mass progression; provided by the patient. e: 4 years post-total mastectomy follow up in November 2021.

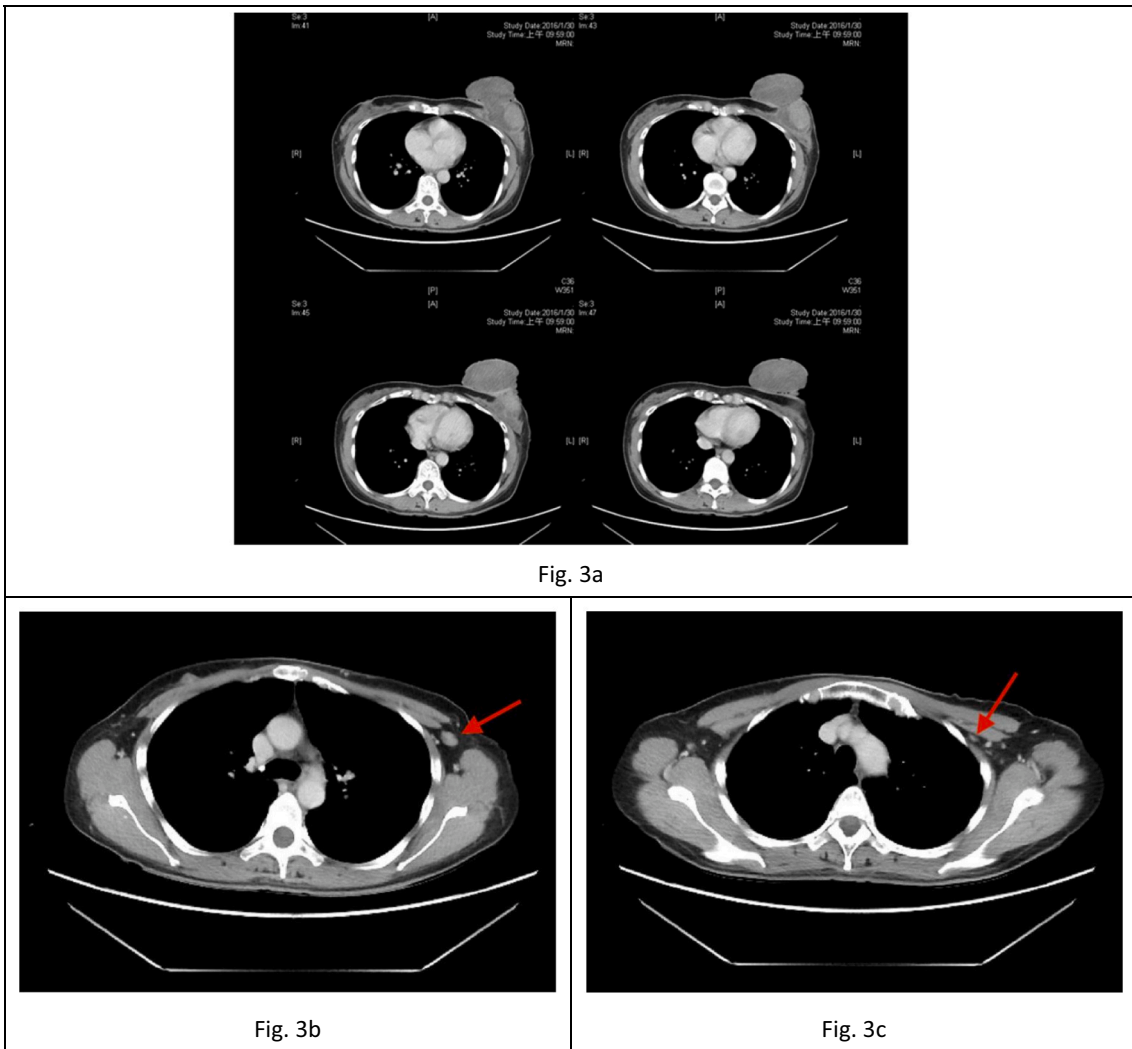


Fig. 3a

Fig. 3b

Fig. 3c

Fig. 3. a: Chest CT scan of protruding mass.
 b: Level I axillary lymph node (Arrow).
 c: Level II axillary lymph node (Arrow).



Fig. 4. Gross excised tumor specimen. A relatively well-circumscribed white and elastic tumor present in the specimen. No different component can be identified within the tumor.

(Fig. 4). The tumor was microscopically composed of a benign epithelial component and a cellular spindle cell stroma characterized by the formation of leaf-like processes protruding into cystic spaces (Fig. 5a, b). Incidentally, an ill-defined tumor composed of small, blue, round, discohesive, monomorphic cells in a single cell file arrangement was identified within the tumor (Fig. 5c, d). Immunohistochemical testing of the incidentally found tumor revealed E-cadherin negative and cyto-keratin positive results (Fig. 5e, f). The results for hormone receptors and the human epidermal growth factor receptor 2 (HER2) receptor were estrogen receptor (ER) 80% positive, progesterone receptor (PR) 90% positive, and HER2 negative. The Ki-67 labeling index value was 10%.

After the operation, the patient did not adhere to further managements, and lost follow up for about one year until recurrent protruding tumor was noticed in August 2017. The patient revisited our clinic, where CNB was performed and showed ILC. Subsequently, the patient received 4 cycles of neo-adjuvant chemotherapy followed by total mastectomy and axillary lymph node dissection (ALND) without breast reconstruction in December of 2017 (Fig. 1e), with 4 more cycles of adjuvant chemotherapy afterwards. Regarding the axillary lymph node status, 3 out of the 13 excised nodes were found involved. Since then, the patient is under hormonal therapy with tamoxifen and has been followed up regularly for more than 4 years without cancer recurrence.

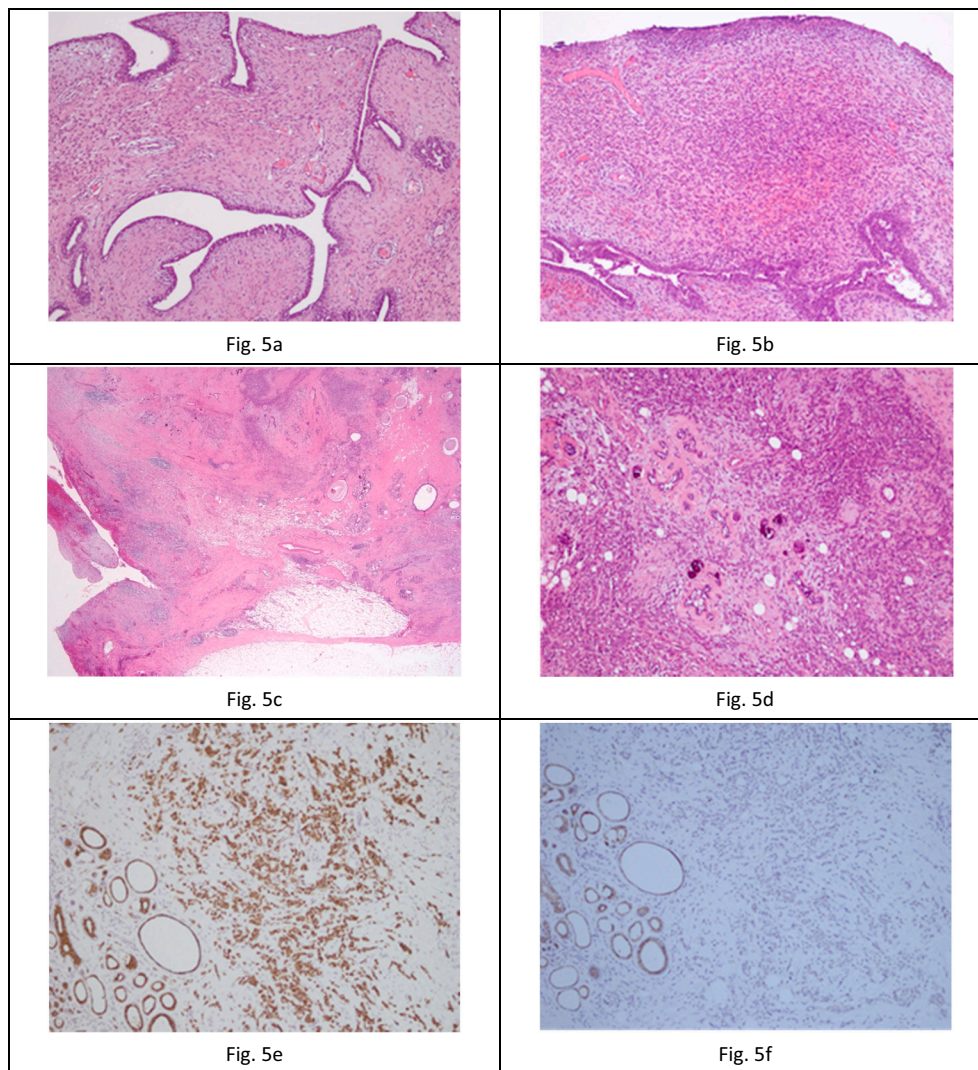


Fig. 5. a–f: Microscopic examination of the tumor.

Benign phyllodes tumor illustrating expansion of the stroma into leaf-like structures (Fig. 5a) with focal hypercellular stroma (Fig. 5b).

Typical phyllodes tumor present in the left side, lobular carcinoma in stromal overgrowth area in the middle upper area (Fig. 5c).

A different component incidentally found within the tumor displaying discohesive small cells arranged in single-file linear cords (Fig. 5d).

Cytokeratin immunohistochemically confirms epithelial phenotype of invasive lobular carcinoma component (Fig. 5e) and E-cadherin reveals an absence of membranous staining in tumor cells (Fig. 5f).

3. Clinical discussion

PT is a rare type of fibroepithelial tumor that accounts for approximately 1% of all breast neoplasms [1]. It can be classified into benign, borderline, and malignant subtypes. Benign PTs have sonographic and mammographic features similar to fibroadenomas [6]; both possess smooth, well-defined, and polylobulated characteristics. However, PTs can be distinguished from fibroadenomas by its rapid growth tendency and relatively large size. To more clearly differentiate suspected PT from fibroadenomas, a large-sized CNB is required. An excisional biopsy may also be considered when clinical figures does not correlate with pathological findings.

Coexistence of PT and other breast carcinomas is extremely rare.

Although most studies have reported the incidence rate of this type of coexistence to be approximately 1% [1], one case series by Widya et al. reported the prevalence of malignant epithelial transformation in PTs to be 6% [7]. The numbers ranging from 1%–6% implies a dispute over the incidence of synchronous PT and other breast carcinomas. This is possibly due to the scarcity of cases encountered and the occult nature of this condition. Furthermore, only five cases of synchronous PT and ILC have been reported in the last 20 years (Table 1) [1,4,8–10]. We hereby report another case of coexistence of PT and ILC, and is the first reported in Taiwan.

Regarding PT management, according to the National Comprehensive Cancer Network (NCCN) guidelines for phyllodes tumor [6], excisional biopsy should be performed if clinical suspicion of PT, and wide excision with tumor-free margin of at least 1 cm is suggested for borderline or malignant PTs. Since PTs are typically hematogenous spread rather than lymphatic, routine axillary dissection is not warranted. Although there are no prospective randomized data supporting the use of radiotherapy for PT, it may still be considered in some cases, whereas chemotherapy and hormone therapy are not indicated in all PT subtypes. In contrast, according to the NCCN guidelines for invasive breast cancer, when invasive carcinomas are discovered, patients should receive adjuvant radiotherapy and are subjected to further chemotherapy if necessary [6]. Hormone therapy and target therapy may also be warranted based on the patient's immunohistochemistry results. This

Table 1

Case of synchronous PT and ILC reported in the last 20 years.

Author	Type of PT/ILC coexistence	Age	Size of PT/invasive carcinoma	Management
Kodama et al., 2003 [1]	ILC + LCIS within benign PT	47	17 cm/NA	Right subcutaneous mastectomy
Shirah et al., 2011 [8]	ILC + LCIS within benign PT	49	4.8 cm/2 mm	Excisional biopsy
Potdevin et al., 2016 [9]	ILC + LCIS on margin of borderline PT	63	4.2 cm/1.5 mm	Excisional biopsy
Fischer et al., 2017 [10]	ILC + LCIS within borderline PT	40	4.2 cm/1.4 cm	Total mastectomy + SLNB
To et al., 2018 [4]	ILC + LCIS separated from malignant PT on ipsilateral side	48	6.5 cm/2.0 cm	Total mastectomy + SLNB
Our case	ILC within benign PT	43	12 cm/1.8 cm	Total mastectomy + ALND

PT: phyllodes tumor, LCIS: lobular carcinoma in situ, ILC: invasive lobular carcinoma, SLNB: sentinel lymph node biopsy, NA: not applicable, ALND: axillary lymph node dissection.

contradiction in managing PTs and invasive carcinomas highlights the possibility that patients could be treated as a case of simple PT without other malignancies, bearing the risk of occult carcinomatous changes being neglected. Therefore, when carcinomatous changes arise from within or along with the PT, the proposed therapeutical course may be altered, and treatment plans must be tailored to the individual due to the lack of universal consensus on managing the coexistence of invasive carcinoma and PT.

The presence of carcinomatous components within PTs is difficult for clinicians to detect because of its occult properties and the low chance of encounter. Since it is difficult to locate preoperatively, pathologists must examine excised tumor specimens thoroughly to reveal possible enclosed cancerous lesions. The current consensus does not recommend routine axillary dissection for simple PTs. However, our case report highlights the menace of hidden invasive carcinoma inside PTs. Hence, we suggest surgeons to perform sentinel lymph node biopsy (SLNB) when clinical presentations contradict pathological findings in PT cases. The evidence of lymph node involvement can serve as an indicator for pathologists to ensure a more accurate diagnosis of invasive or in situ carcinoma arising in PTs.

4. Conclusion

The discovery of ILC developing within PT could impact a case's entire clinical course and managing principles. Thorough clinical inspection, comprehensive imaging of the neoplasm, and ensuring adequate surgical margin (>1 cm) are required before providing patients with individualized treatments. We suggest SLNB to be performed whenever suspicious clinical features occur in PT patients, this may aid in the detection of microscopic invasive carcinomatous change. To sum up, multidisciplinary cooperation is crucial in instances of detecting and managing PT with potential synchronous malignancies.

Consent

Written informed consent was obtained from the patient for 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 on request.

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Registration of research studies

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Guarantor

Shen-Liang Shih, M.D., Msc.

CRediT authorship contribution statement

Yu-Hsuan Chen:

1. Conceptualization of the case report
2. Writing - Original Draft
3. Preparation for publication

Yu-Ling Tu:

1. Writing - Review & Editing
2. Preparation for publication

Han-Ku Chen:

1. Writing - Review & Editing
2. Curation and analyzation of the patient's pathological findings

Shen-Liang Shih:

1. Verification of the manuscript
2. Provision of study materials, photographs, images and pathology specimens
3. Obtaining the informed consent of the patient
4. Supervision
5. Guarantor

Declaration of competing interest

The authors declare no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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