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Case Report and Review of the Literature

Benign Phyllodes Tumor and Ductal Carcinoma *in situ* Coexist in the Same Breast Tumor: A Case Report and Review of the Literature

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ARTICLE INFO

Article history:
Received: 24 October, 2022
Accepted: 15 November, 2022
Published: 25 November, 2022

Keywords:
Phyllodes tumor
ductal carcinoma in situ
breast cancer
mastectomy

ABSTRACT

Background: Breast phyllodes tumor (PT), the rare fibroepithelial mammary tumor is composed by mesenchymal and epithelial components, only 1%~2% of which were accompanied by epithelial breast cancer. The incidence of non-invasive ductal carcinoma (DCIS) arising in benign PTs is even rarer. There is no certain treatment for it currently because of the low incidence of PT with DCIS.

Case Description: Here, we report a 57-year-old female patient who was diagnosed with ductal carcinoma *in situ* arising in a benign phyllodes tumor of the breast. Mastectomy and sentinel lymph nodes biopsy were performed, and endocrine therapy was administrated to the patient. No recurrence was noted during follow-up.

Conclusion: Since PTs are prone to recurrence, adjuvant therapy should be considered comprehensively by the histopathological results after surgical treatment. In addition, regular follow-up is recommended.

Introduction

Breast phyllodes tumor (PT) is a rare fibroepithelial neoplasm of the breast, accounting for 0.3%-1% of all breast tumors [1, 2]. PTs can be classified as benign, borderline and malignant [3]. For their diverse histologic features, such as stromal cellularity, nuclear atypia, mitotic activity, stromal overgrowth and tumor margin appearance, these tumors carry risk of local recurrence or metastasis [4]. It has been reported that carcinoma occurred in only 1%~2% of all PTs, most of which are invasive ductal carcinoma (IDC) and lobular carcinoma *in situ* (LCIS) [5]. The incidence of noninvasive ductal carcinoma (DCIS) arising in benign PTs is even rarer [6]. Because of the rare incidence, there was no standard treatment consensus. Thus, it is critical to summarize the experience from clinical cases. In the present study, we report a 57-year-old female patient who was diagnosed with ductal carcinoma *in situ* arising in a benign phyllodes tumor of the breast. Meanwhile, we further discuss the diagnosis and treatment of DCIS within benign PT based on our case and the previous literature, which may deepen the understanding of such rare disease.

Case Presentation

On July 14, 2021, a 57-year-old female patient visited the First Affiliated Hospital of Jinan University, as she noticed a round painless mass in her left breast for above half a year. Under our physical examination, a visible mass was in the upper outer quadrant of her left breast. The tough mass was about 2.5cm away from the left nipple, measuring about 5cm × 6cm. Besides, the mass was nonadherent to the skin and there were no palpable lymph nodes in the axilla or supraclavicular fossa on physical examination.

Next, ultrasound was performed and showed a regular hypoechoic nodule in her left breast, measuring about 30mm × 56mm × 52mm with circumscribed margins. There are also some scattered microcalcifications in it (Figure 1). The final imaging classification of the mass is BI-RADS 4B. As for her right breast, ultrasound showed a

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http://dx.doi.org/10.31487/j.SCR.2022.11.05

nonhomogeneous hypoechoic nodule with a clear boundary on the upper outer quadrant, measuring about 5mm × 9mm and without blood flow signal. Besides, there is no obvious swollen lymph node echo. The classification of the mass is BI-RADS 3 according to the ultrasound.

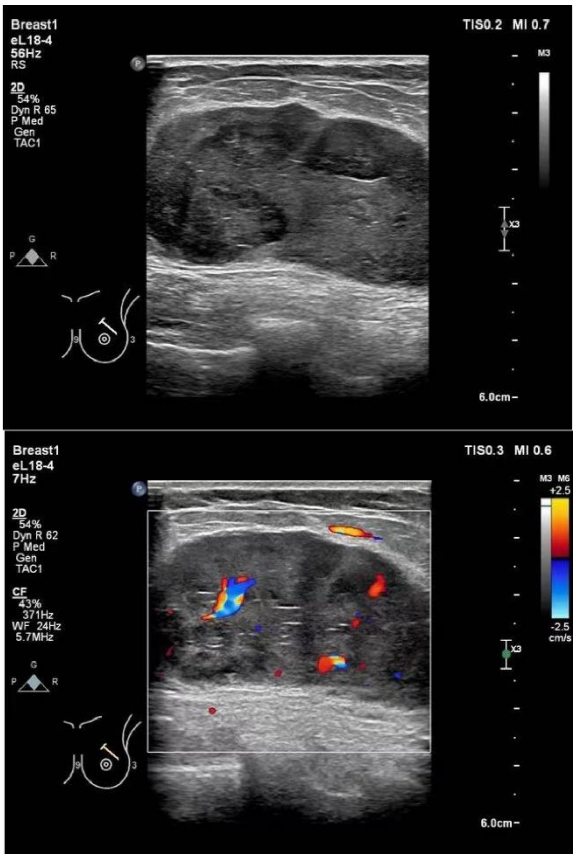

Figure 1: Ultrasound image of left breast.

Her mammogram also showed a round-shaped mass in the upper outer quadrant of her left breast. With its ill-defined margins and scattered microcalcifications in it, the radiologic classification of the mass is BI-RADS 4B and considered it to be a malignant lesion (Figure 2). As for the mass in her right breast, it was reported to be a hyperplastic nodule. Therefore, minimally invasive breast surgery using vacuum assisted breast biopsy system (VABB) was performed to remove the mass of right breast and core needle biopsy (CNB) was performed on the mass of left breast under the guidance of ultrasound. According to the pathologic reports, the mass of her right breast was diagnosed as fibroadenosis and the mass of her left breast was a fibroadenoma. (Figure 3). Therefore, lumpectomy was performed to remove the large but benign mass in her left breast. However, the final pathological report demonstrated that the mass not only a benign phyllodes tumor but combined with low-grade ductal carcinoma *in situ*. The analysis of immunohistochemistry was ER (+), CK5/6 (-), CerbB2 (+), Ki-67 5% (+) (Figure 4). After serious discussion, a mastectomy and ipsilateral axillary lymph node dissection was performed. Intraoperative frozen section and post operative histopathologic results suggest no involvement of axillary lymph nodes. After surgical treatment, the patient takes tamoxifen as endocrine therapy and follow up twice a year. At present, her condition is stable.

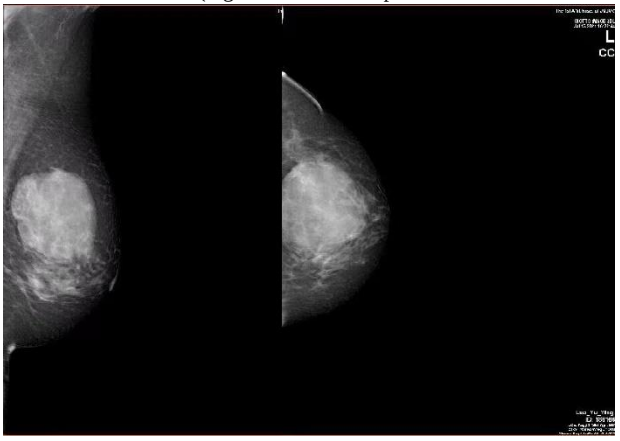

Figure 2: Mammogram of the left breast. Lump in the upper outer quadrant of the left breast with scattered microcalcifications.

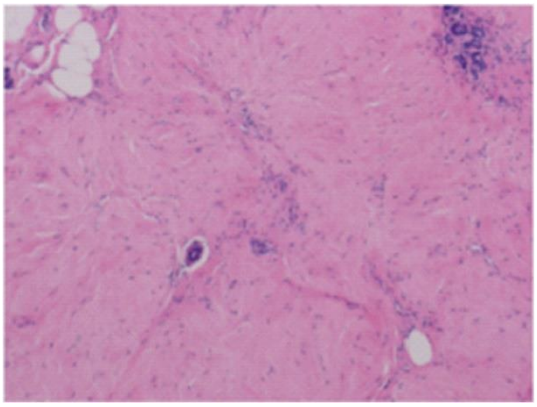

Figure 3: Pathological biopsy of the left breast tumor with a core needle (H&E, original magnification 20x).

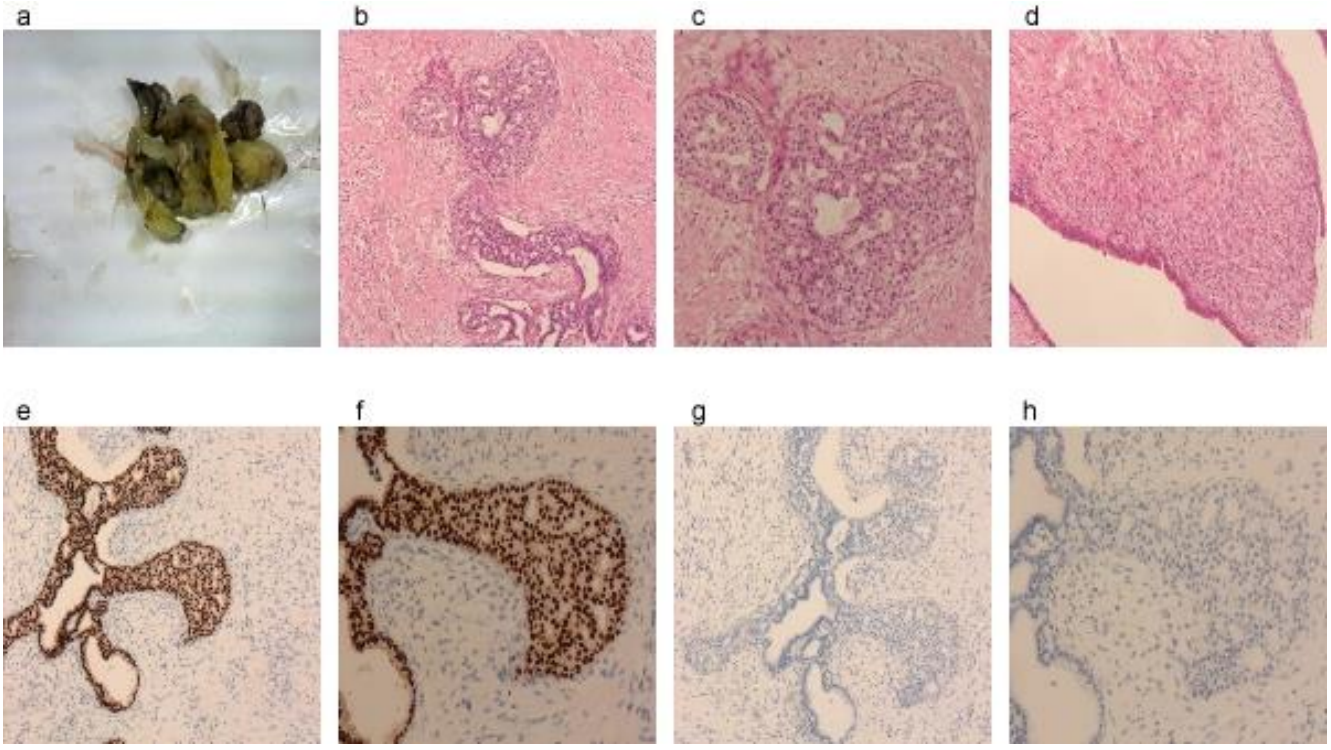

Figure 4: Pathology after left breast segment resection：**a)** Gross specimen； **b)** (left breast segment) benign phyllodes tumor combined with low-grade intraductal carcinoma (H&E, original magnification 20x)；**c)** benign phyllodes tumor (H&E, original magnification 50x)；**d)** benign phyllodes tumor (H&E, original magnification 100x); **e)** ER(+) (H&E, original magnification 50x); **f)** ER(+) (H&E, original magnification 100x); **g)** CK5/6 (-) (H&E, original magnification 50x); **h)** CK5/6 (-) (H&E, original magnification 100x).

Differential Diagnosis

I Phyllodes Tumors with Hyperplasia of Epithelial Components

The phyllodes tumors with hyperplasia of epithelial tissue is common. However, the hyperplasia lack of consistency but present the feature of usual ductal hyperplasia (UDH), which can be distinguished from DCIS.

II Carcinoma Within Fibroadenoma

Carcinoma within fibroadenoma, whose cancer tissue is within the fibroadenoma or just invading the surrounding breast tissue, is the cancerous change of fibroadenoma. As phyllodes tumors are generally larger and most of the hyperplasia are mesenchymal, the tumor size and the features of hyperplasia can help distinguish the fibroadenoma and DCIS within PT.

III Metaplastic Carcinoma

Metaplastic carcinoma, which including several differentiation, encompasses a group of neoplasms characterized by the neoplastic epithelium into squamous cells and/or mesenchymal-looking elements [7]. Spindle cell carcinoma as a rare variant of metaplastic carcinoma, can be confused with the PT with malignant epithelial tissue easily. However, metaplastic carcinoma cannot present the structure like foliose or fissure as PT, and their estrogen receptors (ER), progesterone receptors (PR) and human epidermal growth factor receptor 2 (HER2) are negative in usual [8].

IV Carcinosarcoma

This tumor including both carcinomatous component and malignant non-epithelial component of mesenchymal origin, without evidence of a transition zone between the two elements, while the epithelial component of PT is transformed into cancer, showing a histologically defined transition zone [9]. Most carcinosarcoma of the breast reveal that ER, PR and HER2 are all negative [10].

Discussion

Phyllodes tumors are biphasic tumors with intratumoral morphologic and genetic heterogeneity, which may contribute to their unpredictable clinical behaviour and the difficulty in classifying them histologically. Benign PT comprises 50% to 70% of all PTs. Invasive breast carcinomas and DCIS can occur in only about 1% of patients with PTs. Sawyer *et al*. suggested that both the epithelial and stromal components of PTs may participate in the neoplastic process, but the etiology of carcinoma arising in PT remains largely unknown [11].

As it is a very rare presentation, it poses several challenges in regard to both diagnosis and management. In this case, core needle biopsy revealed a fibroadenoma, but after breast lumpectomy, pathological report showed the mass as benign phyllodes tumor combined with DCIS. It is difficult to distinguish benign PT from fibroadenoma because histologic heterogeneity in stromal cellularity and structure in benign PT on core biopsy. Removal of the tumor for pathological examination is recommended to confirm the diagnosis.

Reviewing the relevant cases since 1984, we found that there were only 9 cases of pure DCIS arising in patients with benign PTs including our case (Table 1) [12-18]. Another 2 cases had concomitant DCIS and invasive ductal carcinoma components. All 9 patients were female, with ages ranging from 19 to 77 years old and the median age were 46. The size of PTs ranged from 2.2~19cm and the average size was 7.0 cm. Four cases underwent wide local excision while the other 3 cases underwent total mastectomy. Different surgical choices may depend on tumor size. If the tumor size is less than 5cm, wide local excision is feasible with negative margins. If the tumor size is larger than 5cm, or even 10cm, total mastectomy should be performed. In our case, total mastectomy was performed since the tumor size was larger than 5cm. In our opinion, breast reconstruction surgery may also be considered since the recurrence rate of both benign PT and DCIS is low. In addition, the patients' will also need to be considered.

Table 1: Clinical and pathological data of 9 cases of breast benign PTs combined with DCIS reported in literatures since 1984.

First author	Year	Breast Tumor location	Age（y/o）	Size(cm)	Epithelial component	Operation	lymph node dissection	Endocrine therapy	radiation therapy	Follow-up （month）
S-A Lui [12]	2017	Right	19	5.1	DCIS (low to intermediate)	Wide local excision	none	tamoxifen	none	Unspecified
Çolakoğlu MK [13]	2014	Right	19	2.3	DCIS	Wide local excision	none	tamoxifen	accepted	36, no relapse
Ghosh P [14]	2014	Right	42	2.2	DCIS (medium-grade)	Wide local excision	none	none	none	Unspecified
Chopra S [15]	2016	Right	23	5	DCIS (high-grade)	Wide local excision	none	none	none	Unspecified
Nio Y [16]	2011	Left	53	3.5	DCIS	Wide local excision	none	none	none	24, no relapse
Yamaguchi R [5]	2008	Right	54	15	DCIS	Simple mastectomy	none	tamoxifen	none	12, no relapse
De Rosa [17]	1989	Left	77	5	DCIS	Simple mastectomy	accepted	none	none	10, no relapse
Grove A [18]	1984	Right	71	19	DCIS	Simple mastectomy	accepted	none	none	4, no relapse
Present case	2021	Left	57	5.6	DCIS (low-grade)	Simple mastectomy	accepted	tamoxifen	none	6, no relapse

Whether benign PTs or DCIS needs no axillary sampling or dissection. Previous reported cases indicated that patients with pure DCIS arising in benign PTs had negative lymph node involvement or did not undergo axillary lymph node biopsy or dissection [19]. However, since DCIS is often mixed with invasive components and the concomitant rate increased with tumor size, axillary lymph node biopsy should be recommended especially when the tumor is larger than 5cm. Although nodal metastases were reported in rare cases, we performed axillary lymph node biopsy in case the presence of invasive components and involvement of axillary lymph nodes in our case [17].

For the rarity of DCIS arising in benign PTs, a variety of post-surgical therapies were applied to the various cases. Therefore, patient age, tumor size, surgical management, epithelial component, hormone receptor status, HER-2 status as well as the involvement of lymph nodes should be comprehensively considered [20]. Although there was no standard adjuvant treatment, previous reported cases suggested that radiotherapy, chemotherapy or endocrine therapy should be indicated for patients accordingly. Treatment strategies should be made on the more aggressive tumor components. For benign PTs, surgical management alone is acceptable. While for DCIS arising from benign PTs, DCIS components have to be considered [20].

Çolakoğlu reported a 19-year-old patient received radiation therapy (RT) after local excision [13]. In another case, Ghosh reported a 42-year-old patient treated without RT after local excision [14]. In our opinion, Van Nuys Prognositic Index (VNPI) is helpful to determine whether radiation therapy is needed for patients who underwent local excision [12]. For those underwent mastectomy, radiation therapy can be omitted. Systematic therapies, chemotherapy and endocrine therapy, may be administrated depending on pathological type and hormone receptor status. Chemotherapy is not recommended for patients with pure DCIS in benign PTs without no invasive components. Endocrine therapy is recommended if the combined DCIS was ER and PR positive. TAM was preferred in previous cases. However, there was no evidence comparing selective estrogen receptor modulators (SERMs) with aromatase inhibitors (AIs) due to the rarity. In our opinion, SERMs may be indicated for premenopausal patients, either SERMs or AIs is optional for postmenopausal patients. Since the high mutation rate of CYP2D6 enzyme in the Chinese population, the patient in our case received toremifene as endocrine therapy and her condition is stable [21].

Conclusion

In conclusion, a rare case of a DCIS arising in benign PT is presented and the diagnosis and treatment is discussed. The etiology of carcinoma arising in PT has yet to be elucidated. Therefore, the etiology needs to be explored and adjuvant therapy needs to be further investigated. Different case reports may enhance our treatment experience.

Informed Consent and Ethical Approval

We should state that subjects have given their written informed consent to publish their case (including publication of images). This study protocol was reviewed and approved by committee of the first affiliated hospital of Jinan university. Written informed consent was obtained from the patient for publication of the details of their medical case and accompanying images.

Funding Sources

This work was supported by grants from the National Natural Science Foundation of China, No. 81702598; the Science Foundation of Guangdong Province, No. 2017A030313803; the Science and Technology Program of Guangzhou, No. 201804010011 and the Flagship specialty construction project- General surgery, No. 711003.

Conflicts of Interest

None.

Author Contributions

Chiseng Lei, Jiamei Hu, Yuan Li and Shaohua Qu contributed to manuscript drafting; Yude Xie, Jie Zhang and Ningxia Wang provided patient information and collected the data; Shaohua Qu was responsible for the revision of the manuscript; all authors contributed to the article and approved the final manuscript.

Data Availability

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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