Ductal carcinoma *in situ* arising within a benign phyllodes tumor: A case report with a review of the literature

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Abstract. Phyllodes tumor (PT) is a rare type of breast tumor that rarely occurs with breast carcinoma. This study evaluated a 53-year-old female patient with a benign PT with ductal carcinoma *in situ* (DCIS) within the tumor. A firm, painless, well-demarcated tumor measuring 4-5 cm was noted in the left breast. Over the course of the previous 14 years, the patient underwent excision of a breast tumor four times at the same site in the left breast. The pathological diagnosis of the first tumor was a fibroadenoma (FA), and those of the following three were benign PTs. The tumor was the 5th one noted over the course of the previous 14 years, following the previously recorded surgeries. A firm tumor with a diameter of 3.5 cm was located beneath the scar from the previous surgery, just above the nipple of the left breast. Mammography revealed a high-density irregularly shaped mass with a clear margin. An ultrasound showed low but heterogeneous echogenicity. A computed tomography scan revealed a well-defined enhanced tumor. These image examinations were compatible with recurrent PT. Fine-needle aspiration cytology revealed that the tumor was likely a benign FA. The patient underwent a partial mastectomy with a 1.0 cm margin from the tumor edge, and the firm, attached scar tissue was also resected. Macroscopic examination showed a hard elastic mass, which was encapsulated by thin fibrous tissue and which adhered firmly to the adjacent scar tissue. Microscopic examination showed a 5 mm in diameter DCIS of the cribiform type in a section of the PT epithelial component with an apparently benign stroma. The DCIS cells were strongly positive for estrogen and progesterone receptors, but HER2 expression was negative (score 0). The patient received local irradiation following surgery and no evidence of recurrence or metastasis was detected in the 2 years following surgery. This was a noteworthy case of a DCIS arising in benign PT. To the best of our knowledge, a total of 28 breast carcinomas were previously reported to arise in PT. In this case report, a female patient who presented with a PT was evaluated. A review of the literature is also discussed.

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Abbreviations: BC, breast carcinoma; IDC, invasive ductal carcinoma; SCC, squamous cell carcinoma; PT, phyllodes tumor; CIS, carcinoma *in situ*; MX, mastectomy; LoEx, local excision; LNI, lymph node involvement; AxDx, axillary dissection; DCIS, ductal carcinoma *in situ*; LCIS, lobular carcinoma *in situ*

Key words: phyllodes tumor, ductal carcinoma *in situ*

Introduction

Phyllodes tumor (PT) is a rare type of breast tumor, accounting for less than 1% of benign and malignant breast tumors (1). PT is classified as benign, borderline or malignant, with approximately 10% of PT being malignant. Malignant transformation of PT usually occurs in the stromal component, and is rare in the epithelial component. The occurrence of PT and BC involves a twofold pattern: a separate coexistence within an ipsilateral or contralateral breast, and BC occurring in PT. The incidence of breast carcinoma (BC) in PT is thought to be only 1-2% of all PTs (2,3). To the best of our knowledge, 27 PT cases with 28 BCs have been reported in the literature, and 15 out of the 28 BCs were reported to be carcinoma *in situ* (CIS) (4-29).

A 53-year-old female with a benign PT with a ductal carcinoma *in situ* (DCIS) within the tumor was evaluated. The literature available was also reviewed.

Materials and methods

Patient. A firm, painless, well-demarcated tumor in the left breast, measuring 4-5 cm, was found in a 53-year-old female patient. Over the course the previous 14 years, she underwent excision of a breast tumor four times at the same site in the left breast. The pathological diagnosis of the first tumor was a fibroadenoma (FA), and those of the following three tumors were benign PTs. The tumor was the 5th one noted in the 14 years following the previously recorded surgeries.

A firm tumor with a diameter of 3.5 cm was located beneath the scar from the previous surgery, just above the nipple of the left breast. Mammography revealed a high-density irregularly-shaped mass with a clear margin (Fig. 1), and an ultrasound showed low but heterogeneous echogenicity (Fig. 1). A computed tomography (CT) scan displayed a well-defined enhanced tumor (Fig. 1). The image examinations were compatible with recurrent PT. Fine-needle aspiration (FNA) cytology revealed that the tumor was likely a benign FA.

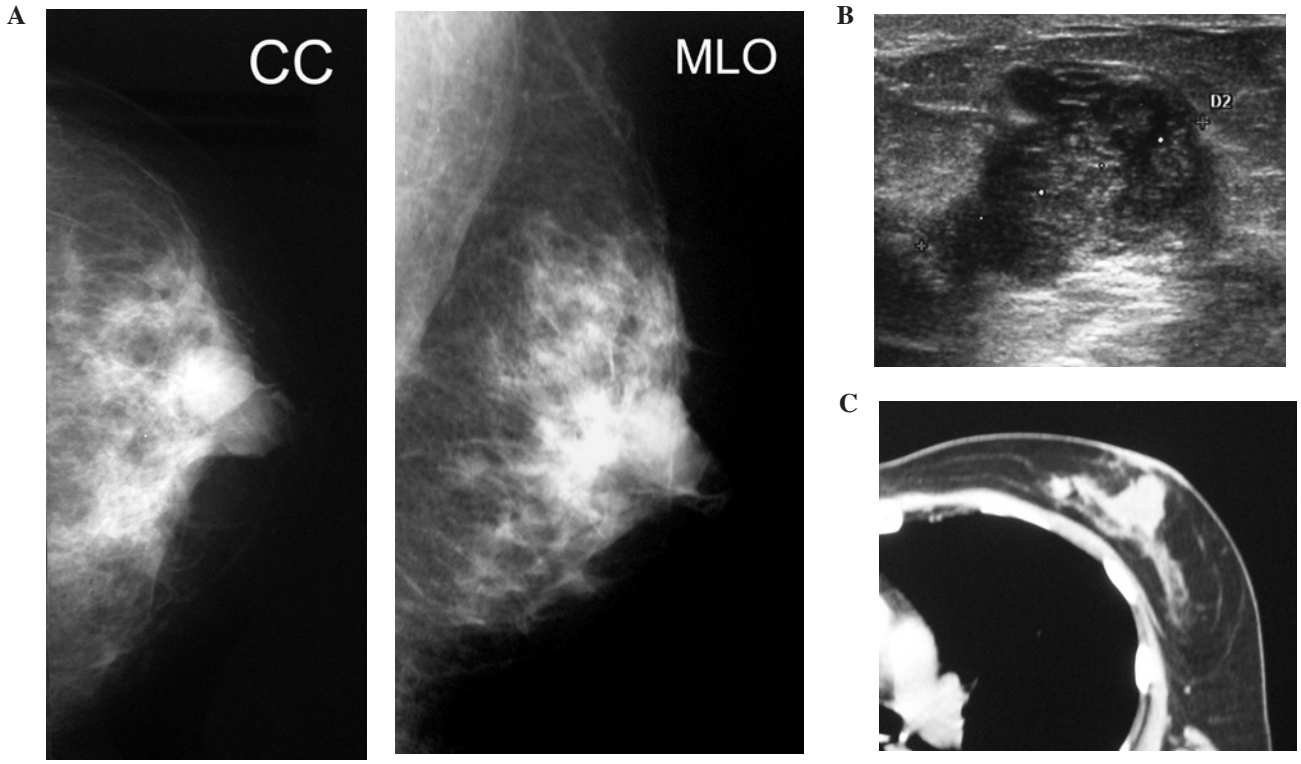

Figure 1. (A) Mammography shows a well-defined lobular tumor mass beneath the nipple. (B) Ultrasonography shows a hypoechoic, heterogeneous, lobular mass with a regular border. (C) A computed tomography scan shows a well-defined mass. CC, craniocaudal view; MLO, mediolateral oblique view.

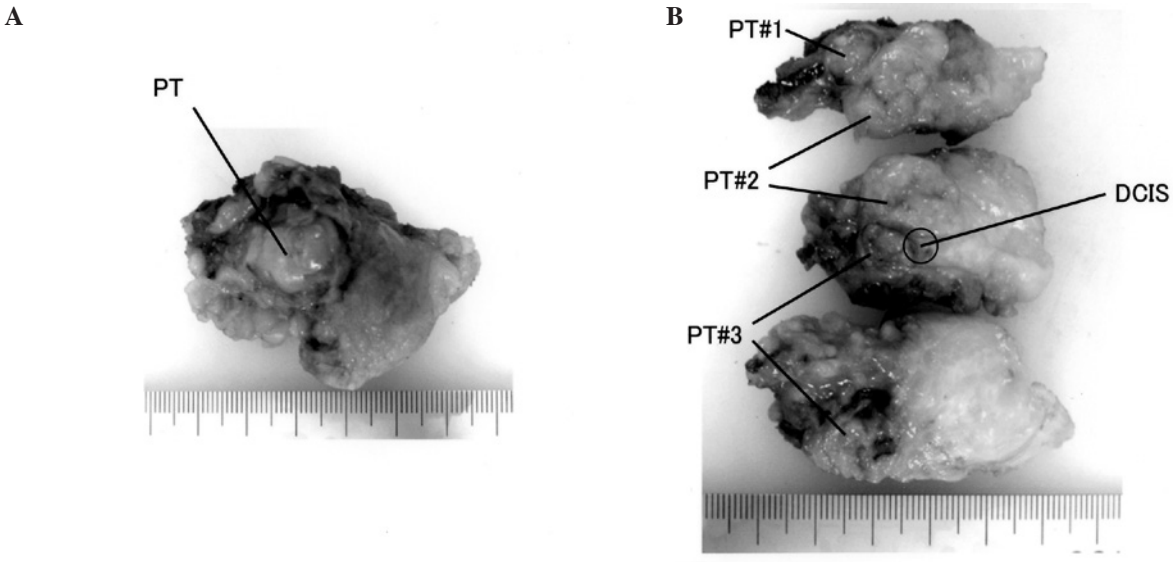

Figure 2. (A) Macroscopic findings of the resected specimen. (B) Macroscopic findings of the cut surfaces of 3 slices: The PT comprised 3 different tumors, PT#1, PT#2 and PT#3. The DCIS lesion is visible in the stroma between tumors PT#2 and PT#3. The PT was 3.5x3.0x2.7 cm, and the DCIS lesion was 5 mm. PT, phyllodes tumor; DCIS, ductal carcinoma *in situ*.

Surgery. The patient underwent local excision (LoEx) with a 1.0 cm margin from the tumor edge. The firm, attached scar tissue was also resected.

Results

Macroscopic findings. The macroscopic examination revealed a hard elastic mass, which was encapsulated by thin fibrous tissue and which adhered firmly to the adjacent scar tissue. The tumor comprised 3 discrete PT nodules (Fig. 2). The overall size of the PT was 3.5x3.0x2.7 cm.

Microscopic findings. A histopathological examination showed that the tumor had two components; epithelium and stroma. The stroma consisted of monotonous, uniform and spindle-shaped tumor cells without atypia or mitosis, indicating that the

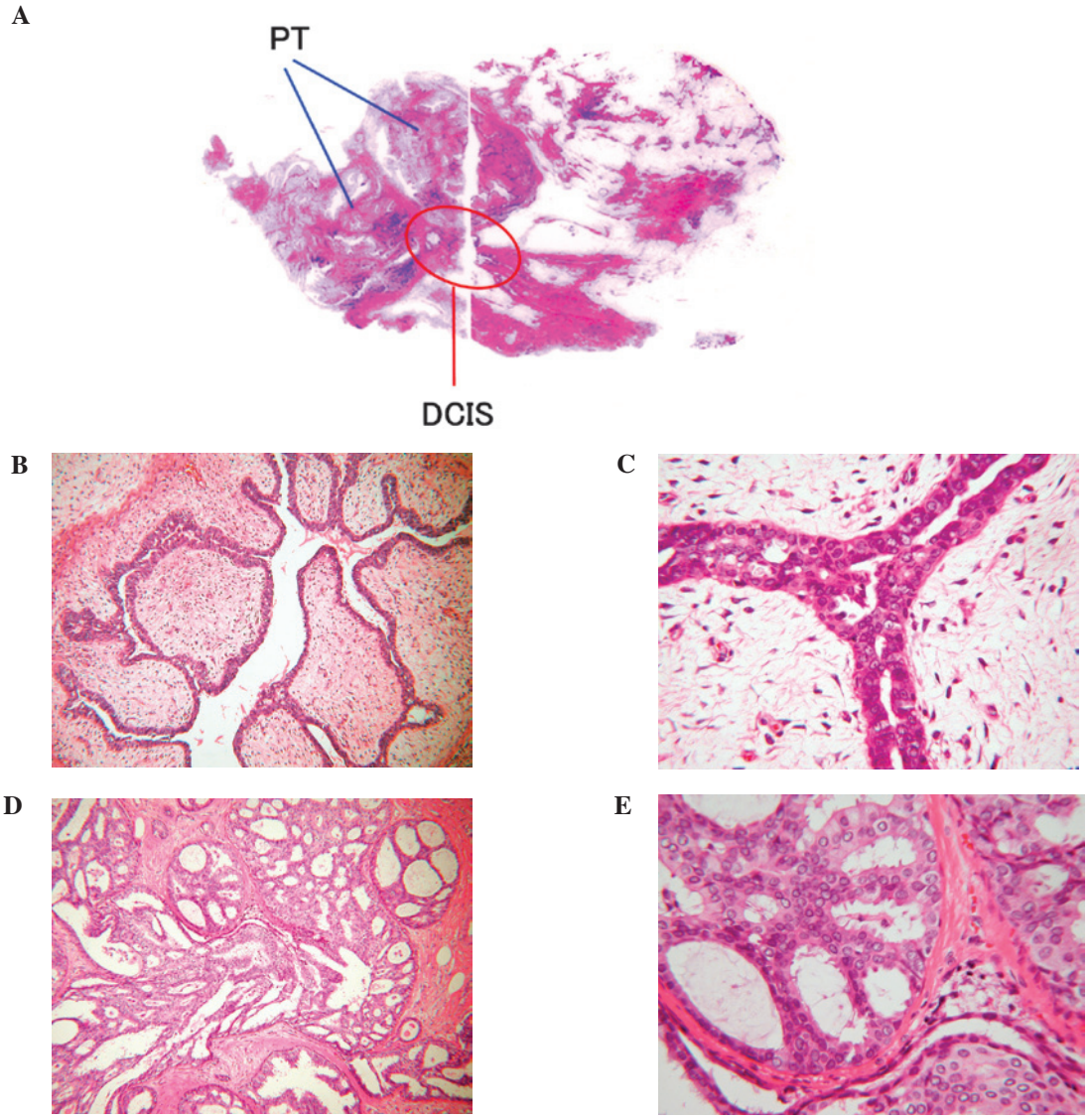

Figure 3. (A) Panoramic view of the microscopic features. (B) PT lesion; the benign stromal component consisted of monotonous, uniform and spindle-shaped tumor cells without atypia or mitosis. H&E stain, magnification, x 100. (C) PT, the epithelial component lining the ductal structure shows benign features in the majority of areas of PT lesions. H&E stain, magnification, x 400. (D) DCIS lesion with a cribiform pattern of 5 mm in diameter. H&E stain; magnification, x 100. (E) DCIS lesion. H&E stain, magnification, x 400. PT, phyllodes tumor; DCIS, ductal carcinoma *in situ*.

tumor was benign (Fig. 3). The epithelium lined the elongated ductal structures or leaf-like processes protruding into dilated ducts formed by the overgrowth of the stromal component. The epithelium lining the ducts also exhibited benign features in the majority of areas, but, in part, showed significant nuclear atypia and a prominent proliferation in a cribiform pattern, definite features of low to intermediate grade DCIS. The DCIS was ~5 mm in diameter (Fig. 3).

Fig. 4 shows the results of immunohistochemical staining. The DCIS cells were strongly positive for estrogen (ER) and progesterone receptors (PgR), but HER2 expression was negative (score 0).

Post-surgical course. The patient received local irradiation (50 Gy) following surgery and no evidence of recurrence or metastasis was detected in the 2 years following surgery.

The previous cases are shown in Table I. A total of 1 patient had 2 BCs in 2 PTs. The first BC was a DCIS and the second one was a tubular carcinoma (5). The patient ages ranged between 26 and 80 years (average 52.7). Of the 28 PTs, 12 cases were identified as malignant and 14 as benign, with 1 borderline case. The diameters of the tumors ranged between 2.0 and 21 cm (average 8.0). The combined BCs included 15 CISs, 12 invasive BCs, and 1 patient had recurrent PTs twice in combination with a lobular carcinoma *in situ* (LCIS) at the first recurrence and a tubular carcinoma at the second recurrence. A total of 15 CISs included 10 DCISs and 3 LCISs, and 2 cases presented with both DCIS and LCIS. The CIS sizes were not described in 7 cases, but the majority of the remaining CISs were focal, and the largest CIS was 2.0 cm in diameter. On the other hand, 13 invasive BCs included 7 invasive ductal carcinomas (IDCs), 4 squamous cell carcinomas (SCCs), 1 invasive lobular carcinoma (ILC) and 1 tubular carcinoma. The tumor size was not described in 12 BC cases, and in 1 case the diameter was 2.5 cm. Axillary lymph nodes (AxLNs) were involved in 2 of 7 invasive BC cases reported,

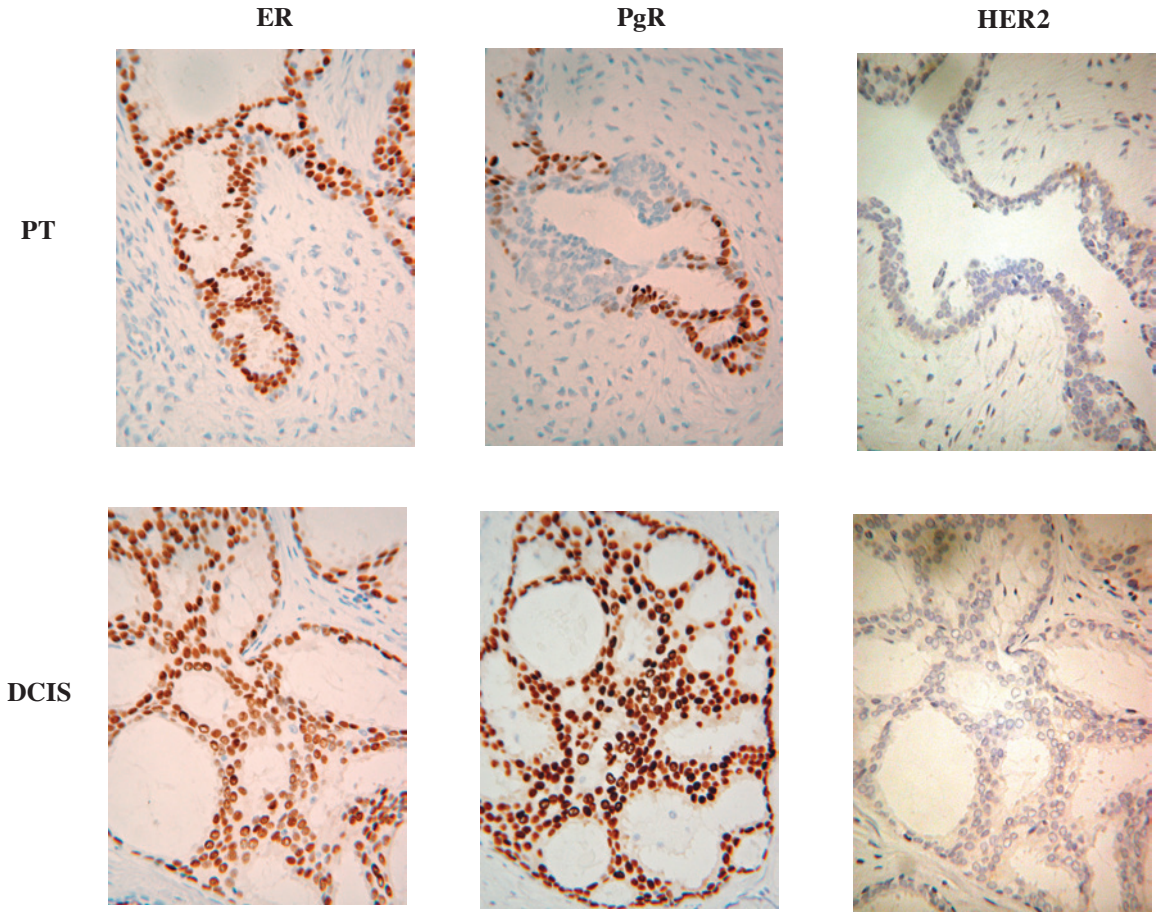

Figure 4. Ductal carcinoma *in situ* and benign ductal epithelial cells in the phyllodes tumor were strongly positive for estrogen and progesterone receptors, but HER2 expression was negative (score 0).

but no lymph nodes (LNs) were involved in any of the 7 CIS cases described. The LN involvement noted was metastasized from BCs, but not from PTs.

Discussion

The coexistence of PT and BC includes two patterns; a separate coexistence within an ipsilateral or contralateral breast, and a BC arising within PT. The present case was the latter type, a DCIS arising in a benign PT. To the best of our knowledge, the literature shows a total of 28 BCs arising in PT in 27 patients.

A variety of therapies were applied to the various cases. The present case received a LoEx with a margin of 1 cm from the tumor edge, and local irradiation at a total dose of 50 Gy since the PT tumors locally recurred four times at the same site. Two years have elapsed since the previous surgery and the patient remains disease-free. The additional surgeries included 5 LoExs, 21 mastectomies (MXs), 3 no descriptions, AxLNs were dissected in 10 cases, 12 patients received no Ax dissection (Dx) and 6 were not described. It appears that MX or LoEx was selected according to the size of the PT. MX with AxDx was applied for large PTs, but LoEx was applied for small PTs. Overall, 4 cases received LoEx first and then MX again according to the pathological diagnosis of malignancy or combination with invasive BC (10,12,20,23). AxDx was also applied for large PTs, but no LNs involving PTs were noted in the 10 cases described. AxDx may thus be restricted to patients suspected of having LN involvement by image diagnosis.

Post-surgical radiotherapy (RT), chemotherapy and/or endocrine therapy were applied for large PTs or those with combined invasive BCs. Overall, 1 patient with a 15.5 cm malignant PT with SCC of the breast received chemotherapy with cyclophosphamide, methotrexate and 5-fluorouracil (CMF) following surgery (22), and 1 patient with a benign PT with a diameter of 15 cm received chemotherapy with oral Tegafur for 2 years following surgery. This second patient has been disease-free for 5 years (23). A patient with a 3.3 cm benign PT with AxLN involving a combined invasive BC received chemotherapy with cyclophosphamide, epirubicin and 5-fluorouracil (CEF) and local RT following surgery, followed by tamoxifen (TAM), and was disease-free for 3 years (25). A patient with a 21 cm malignant PT with LN involving combined BC received chemotherapy with 4-cycle adriamycin and cyclophosphamide (AC), local RT and TAM, and was disease-free for 11 months (28). A patient with a 12 cm benign PT received TAM alone since the combined DCIS was ER- and PgR-positive, and remained disease-free for 1 year (18). A patient with a recurring benign PT combined with an invasive BC received local RT at 5500 rad following surgery, similar to the present case, and this patient was disease-free for 21 months (5). Notably, a patient was diagnosed with SCC

Table I. Non-invasive carcinoma within phyllodes tumor.

No.	Author	Year	Age	Surgery	AxDx	PT			CIS			Refs.
						Type	Size (cm)	LNI	Type	Size (cm)	LNI	
1	Seemayer *et al*	1975	27	MX	(-)	Malignant	6.0		DCIS	Focal		4
2	Leong *et al*	1980	49	LoEx	(-)	Benign	6.0		LCIS	-		5
3	Cole-Beuglet *et al*	1983	55	LoEx	(-)	Benign	3.5		DCIS+LCIS	-		6
4	Grove *et al*	1986	71	MX	(+)	Benign	19.0	(-)	DCIS	2.0	(-)	7
5	Ward *et al*	1986	55	MX	-	Benign	4.0		LCIS	Focal		8
6	Knudsen *et al*	1987	71	MX	(+)	Benign	7.0	(-)	DCIS+LCIS	Multi-focal	(-)	9
7	De Rosa *et al*	1989	77	MX	(+)	Benign	5.0	(-)	DCIS	0.3	(-)	10
8	Schwickerath *et al*	1992	47	MX	(+)	Malignant	2.0	(-)	DCIS	-	(-)	11
9	Padmanabhan *et al*	1997	47	MX	(+)	Malignant	7.5	(-)	LCIS	Focal	(-)	12
10	Naresh	1997	51	LoEx	(-)	Borderline	14.0		DCIS	Focal		13
11	Nishimura *et al*	1998	80	LoEx	(-)	Malignant	10.5		DCIS	-		14
12	Alo *et al*	2001	39	MX	-	Malignant	9.0		DCIS			15
13	Lim *et al*	2005	45	MX	(-)	Malignant	12.0		DCIS	0.6		16
14	Nomura *et al*	2006	75	MX	(-)	Malignant	3.5		DCIS	-		17
15	Yamaguchi *et al*	2008	54	MX	(-)	Benign	15.0		DCIS	Focal		18
16	Present case	-	53	LoEx	(-)	Benign	3.5		DCIS	0.5		-

PT, phyllodes tumor; MX, mastectomy; LNI, lymph node involvement; DCIS, ductal carcinoma *in situ*; CIS, carcinoma *in situ*; LoEx, local excision; AxDx, axillary dissection; LCIS, lobular carcinoma *in situ*.

Table II. Invasive ductal carcinoma within phyllodes tumor.

No.	Author	Year	Age	Surgery	AxDx	PT			CIS			Refs.
						Type	Size (cm)	LNI	Type	Size (cm)	LNI	
1	Bassermann *et al*	1980	-	-	-	-	-	-	SCC	-	-	19
2	Leong *et al*	1980	51	MX	(+)	Benign	4.0		IDC	-	(-)	5
3	Cole-Beuglet *et al*	1983	60	LoEx	(-)	Benign	3.0		IDC	-		6
4	Klausner *et al*	1983	60	MX	(+)	Malignant	4.0	(-)	IDC	Focal	(-)	20
5	Ishida *et al*	1984	41	MX	(-)	Benign	5.6	(-)	IDC	Focal	(-)	21
6	Hunger *et al*	1984	57	MX	(+)	Malignant	15.5	-	SCC	-	-	22
7	Yasumura *et al*	1988	47	MX	(+)	Benign	13.0	-	IDC	-	(-)	23
8	Kodama *et al*	2003	47	MX	(-)	Benign	17.0	(-)	ILC	Focal	-	24
9	Parfitt *et al*	2004	26	LoEX	(+)	Benign	3.3	-	DCIS+IDC	-	(+) 4/13	25
10	Ramdass *et al*	2006	69	-	-	Benign	-	-	SCC	-	-	26
11	Sugie *et al*	2007	54	MX	(+)	Malignant	8.0	(-)	SCC	-	(-)	27
12	Korula *et al*	2008	51	-	-	Malignant	21.0	-	DCIS+IDC	-	(+) 2/12	28
13	Macher-Goeppinger *et al*	2010	70	MX	(+)	Malignant	6.0	(-)	IDC	2.5	(-)	29

PT, phyllodes tumor; MX, mastectomy; BC, breast carcinoma; LoEx, local excision; AxDx, axillary dissection; IDC, invasive ductal carcinoma; LNI, lymph node involvement; DCIS, ductal carcinoma *in situ*; SCC, squamous cell carcinoma.

of the breast by FNA biopsy, and post-surgical pathology showed an SCC arising in malignant PT. The patient received preoperative chemotherapy with FEC followed by PTX. However, no post-surgical chemotherapy was administered, and the patient succumbed to PT lung metastasis 40 months following surgery (27). Since no standard therapy for PT has been established, a variety of combinations of surgery, chemotherapy, endocrine therapy and/or RT are applied.

The patient outcomes were described in 12 cases, and the majority of these patients were followed for a number of months or years. A total of 2 patients survived for 5 years following surgery (16,23). A total of 2 patients succumbed to the disease,

1 is mentioned above (27) and 1 developed lung metastasis and succumbed 10 months following surgery (14).

In conclusion, a rare case of a DCIS arising in benign PT is reported. Various types of carcinoma have been reported to arise in PT, such as IDC, ILC, DCIS, LCIS, SCC and tubular carcinoma. The etiological relationship between PT and carcinoma has yet to be elucidated. This type of combination therefore remains to be investigated.

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