High-grade ductal carcinoma in-situ detected by microcalcification within borderline phyllodes tumour: A report of a case and literature review

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Case Report

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Abstract

Background

Phyllodes tumour is a rare biphasic neoplasm of the breast that mostly affects middle aged women. Ductal carcinoma in-situ and microcalcifications occurring within phyllodes tumours are documented but are rare findings. Primary surgical excision with adjuvant therapies remains the mainstay of treatment.

Case presentation

We report a case of a 42-year-old woman with high-grade ductal carcinoma in-situ within a borderline phyllodes tumour. Radiologically, clumps of microcalcification were detected within the lesion. Local excision followed by total mastectomy with axillary dissection was then performed. No tumour recurrence was detected up to a period of 8 years.

Conclusion

Presence of microcalcifications within a phyllodes tumour should alert clinicians and pathologists of possible coexisting carcinoma components. Stromal and epithelial components of these lesions should be evaluated separately when formulating a management plan.

Introduction

Phyllodes tumours (PTs) are rare tumours that constitute less than 1% of all breast neoplasms. PTs are subclassified into benign, borderline, and malignant based on histologic parameters regarding the stromal component. The parameters are tumour border, stromal cellularity, stromal atypia, mitotic activity, stromal overgrowth, and malignant heterologous elements. Of all PTs, the benign category constitutes 75%, borderline 16% and malignant 9% of the cases (1). Epithelial hyperplasia is a common finding that was seen in 74% of all PTs in one study (1). However, carcinoma within a PT remains rare and accounts for only 1–2% of all PTs (2, 3). Apart from carcinomas within PTs, they can also occur in breast tissues adjacent and ipsilateral to, or contralateral to a PT. In a previous literature review, which discussed PTs associated with carcinomas, carcinoma was more commonly seen within a benign PT whilst in malignant PTs they are more commonly found to be adjacent and ipsilateral to or contralateral to the PTs (4). We hereby report a case of high-grade ductal carcinoma in-situ (DCIS), with microcalcifications detected mammographically, within a PT in a 42-year-old Asian woman.

Case Presentation

A 42-year-old nulliparous Asian woman was referred for a non-tender right breast mass for one month. She enjoyed good past health and has no known family history of breast cancer. On physical examination, there was a 12 cm mass occupying the right lateral breast. No skin ulceration was noted. Mammography performed on the right breast showed a dumbbell-shaped mass with well-defined border and clumps of coarse punctate microcalcifications (Fig. 1). Ultrasonography of the index mass showed internal hyperechoic striations and occasional intramural cystic spaces. The overall features were those of BIRADS (Breast Imaging-Reporting and Data System) 4a. The left breast and bilateral axillae showed no significant radiological abnormality. Core biopsy of the index lesion showed findings consistent with fibroadenoma with no definite features of PTs. The patient subsequently underwent local excision of the mass. Gross examination of the excised specimen revealed a 6.5 x 4.5 x 4 cm well-circumscribed tumour showing lobulated growth and white cut surfaces. Necrosis was not observed.

Microscopic examination of the upper lateral tumour showed a well-circumscribed and encapsulated fibroepithelial tumour with pushing border. It consisted of biphasic epithelial and stromal proliferation, forming an extensive leaf-like architecture. The stroma was hypercellular with conspicuous subepithelial accentuation and stromal overgrowth was seen (Fig. 2). No heterologous element was noted. The stromal cells possessed moderate pleomorphism with prominent nucleolus. The mitotic count was 4 per mm^2. Adjacent fibroadenomatoid areas were also noted (Fig. 3). The DCIS component (measuring 2.7 cm across) consisted of epithelial cells with cribriform and micropapillary structures with foci of comedonecrosis and abundant luminal calcification (Fig. 4). The epithelial cells possessed enlarged hyperchromatic nuclei with occasional prominent nucleoli. Immunohistochemical study showed diffuse and strong oestrogen receptor staining and loss of CK5/6 staining. A diagnosis of borderline phyllodes tumour with high grade DCIS was therefore made. The resection margin was focally involved by both the phyllodes tumour and DCIS.

The patient subsequently underwent right modified radical mastectomy with axillary dissection of which pathological examination showed no residual tumour or lymph node metastasis. She remained disease free clinically and radiologically at her 8 years follow-up.

Discussion

To further investigate, a literature research was performed using PubMed database to look for published cases of carcinoma arising within a phyllode tumour. Including this case study, 47 published cases were analysed (Table 1) (2, 4–23, 23–41). All of them were female patients aged between 19 and 80 years old (mean age = 47.6 years old and median age = 49 years old). The size of the PTs ranged from 1.4 cm to 21 cm (mean = 7 cm, median = 5.4 cm). The most common carcinoma subtypes reported include DCIS (n = 22), followed by mixed in-situ and invasive carcinoma (n = 10) and invasive ductal carcinoma (IDC) (n = 7). There were 17 malignant PTs, 8 borderline PTs and 22 benign PTs. Invasive carcinomas were found in 7 (41%) cases of malignant PTs, 5 (63%) cases of borderline PTs and 8 (36%) cases of benign PTs. Of note, report of usual ductal hyperplasia within PTs is also most common in borderline PTs (83%), followed by benign PTs (74%) and malignant PTs (51%) (1).

Table 1
published data of carcinoma arising within a phyllodes tumour.

Case	First authors	Year	Age	Phyllodes tumour		Carcinoma component		Presences of microcalcifications (characteristics)	Management		
				Type	Size (cm)	Type	Size (cm)		Resection	Axillary dissection	Lymph node status
1	Leong *et al* (5)	1980	51	Benign	6.0	LCIS + ITC	Not available (N/A)	Yes (not available)	Mastectomy (MX)	Yes	Negativ
2	Cole-Beuglet *et al* (6)	1983	55	Benign	1.4	DCIS + LCIS	N/A	N/A	N/A	No	-
3	Cole-Beuglet *et al* (6)	1983	60	Benign	3.0	IDC	N/A	N/A	N/A	No	-
4	Grove *et al* (7)	1986	71	Benign	19.0	DCIS	N/A	No	MX	Yes	Negativ (0/11)
5	Ishida *et al* (8)	1984	41	Benign	5.6	IDC	Focal	No	MX	No	N/A
6	Kundsen *et al* (9)	1987	71	Benign	7.0	DCIS + LCIS	Multifocal	N/A	MX	Yes	Negativ
7	Yasumura *et al* (10)	1988	47	Benign	13.0	IDC	N/A	N/A	MX	Yes	Negativ (0/13)
8	Kodama *et al* (11)	2003	47	Benign	17.0	LCIS + ILC	N/A	No	MX	No	-
9	Parfitt *et al* (12)	2004	26	Benign	3.3	DCIS + IDC	Focal	N/A	Local excision (LoEx)	Yes	Positive (4/13)
10	Ramdass *et al* (13)	2006	59	Benign	N/A	Squamous cell carcinoma (SCC) + IDC	N/A	N/A	N/A	N/A	N/A
11	Yamaguchi *et al* (14)	2008	54	Benign	15.0	DCIS	Focal	No	MX	No	-
12	Nio *et al* (15)	2011	53	Benign	3.5	DCIS	0.5	N/A	LoEx	No	-
13	Shirah *et al* (16)	2011	49	Benign	4.8	LCIS + ILC	0.2 (ILC)	N/A	LoEx	No	-
14	Shin *et al* (17)	2013	42	Benign	1.8	DCIS	1.2	No	LoEx	No	-
15	Ghosh *et al* (18)	2014	42	Benign	2.2	DCIS	N/A	No	LoEx	No	-
16	Colakoglu *et al* (19)	2014	19	Benign	1.8	DCIS	0.8	N/A	LoEx	No	-
17	Chopra *et al* (20)	2016	23	Benign	5.0	DCIS	N/A	N/A	LoEx	No	-
18	Lui *et al* (21)	2017	19	Benign	5.1	DCIS	N/A	Yes (specks described as benign looking)	LoEx	Sentinel lymph node biopsy (SLNB)	Negativ (0/2)
19	Panko *et al* (22)	2017	70	Benign	2.3	DCIS + IDC	0.5 (IDC)	N/A	LoEx	SLNB	Negativ
20	Co *et al* (2)	2017	44	Benign	5	DCIS	Focal	No	Mx	No	-
21	Co *et al* (2)	2017	25	Benign	2.5	DCIS	Multifocal	No	LoEx	No	-
22	Sun *et al* (23)	2019	30	Benign	1.5	DCIS	0.35	No	LoEx	No	-
23	Deodhar *et al* (24)	1997	51	Borderline	14.0	DCIS	Focal	N/A	LoEx	N/A	N/A
24	Kuo *et al* (25)	2010	24	Borderline	10.0	DCIS + IDC	2.5	N/A	MX	SLNB	Isolated tumour cells (1/2)

Case	First authors	Year	Age	Phyllodes tumour		Carcinoma component		Presences of microcalcifications (characteristics)	Management		
				Type	Size (cm)	Type	Size (cm)		Resection	Axillary dissection	Lymph node status
25	Trabelsi *et al* (26)	2010	52	Borderline	15	DCIS + IDC	Foci	N/A	MX	No	-
26	Quinlan-Davidson *et al* (27)	2011	53	Borderline	6.5	LCIS + ITC	2.4	Yes (not available)	MX	SLNB	Negativ (0/3)
27	Wu *et al* (28)	2014	52	Borderline	3.0	IDC	Focal	N/A	MX	Yes	Positive (1/21)
28	Co *et al* (2)	2017	54	Borderline	9	DCIS	Focal	No	MX	No	-
29	Fischer *et al* (29)	2017	40	Borderline	4.2	LCIS + ILC	1.4 (ILC)	No	MX	Yes	Negativ
30	Present study	2020	42	Borderline	6.5	DCIS	x	Yes	MX	Yes	Negativ
31	Seemayer *et al* (30)	1975	27	Stromal sarcoma	6.0	DCIS	Focal	N/A	MX	No	-
32	Klausner *et al* (31)	1983	60	Malignant	4.0	IDC	Focal	N/A	MX	Yes	Negativ
33	Ward *et al* (32)	1986	55	Malignant	4.0	LCIS	N/A	N/A	MX	N/A	N/A
34	Padmanabhan *et al* (33)	1997	47	Malignant	7.5	LCIS	Focal	N/A	MX	Yes	Negativ (0/4)
35	Nishimura *et al* (34)	1997	80	Malignant	10.5	DCIS	N/A	N/A	MX	No	-
36	Lim *et al* (35)	2005	45	Malignant	12.0	DCIS	0.6	N/A	MX	No	-
37	Nomura *et al* (36)	2006	75	Malignant	3.5	DCIS	N/A	N/A	MX	Yes	Negativ
38	Sugie *et al* (37)	2007	54	Malignant	8.0	SCC	N/A	N/A	MX	Yes	Negativ
39	Korula *et al* (38)	2008	51	Malignant	21.0	DCIS	N/A	No	MX	Yes	Positive (2/12)
40	Macher-Goeppinger *et al* (39)	2010	70	Malignant	6.0	IDC	2.5	N/A	MX	Yes	Negativ
41	Abdul Aziz *et al* (4)	2010	43	Malignant	3.5	DCIS + ITC	0.2 (ITC)	Yes (not available)	LoEx	No	-
42	Choi *et al* (40)	2012	62	Malignant	10.0	Invasive cribriform carcinoma	6.0	N/A	MX	Yes	Negativ
43	Co *et al* (2)	2017	52	Malignant	10.0	DCIS	Focal	No	MX	No	-
44	Co *et al* (2)	2017	48	Malignant	5	DCIS	Focal	No	MX	No	-
45	Co *et al* (2)	2017	45	Malignant	4	IDC	Focal	Yes (not available)	Mx	SLNB	Negativ
46	Sun *et al* (23)	2019	30	Malignant	3.2	DCIS	1.5	Yes (punctated clusters, suspicious appearing)	LoEx	No	-
47	Kaur *et al* (41)	2019	26	Malignant	9	Neuroendocrine carcinoma	50%	N/A	LoEx	N/A	N/A

The significance of microcalcifications were only discussed in 21 cases, where they were present in both in-situ and invasive carcinomas. Fourteen of them were pure DCIS lesions, in which 5 cases had microcalcifications (33.3%). The other 7 cases were involved by invasive carcinomas, 4 of which reported microcalcifications (57.1%) including 2 cases of lobular carcinoma in-situ (LCIS) + invasive tubular carcinoma (ITC), 1 case of DCIS + ITC and a case of IDC; the remaining 3 cases with invasive carcinoma involvement did not have microcalcifications (two cases of LCIS + invasive lobular carcinoma and a case of IDC). Both benign looking specks (21) and suspicious coarse punctuated clusters of microcalcifications (23), such as those seen in this case, had been described in carcinomas.

There were 20 cases with axillary surgery performed. Thirteen cases of which involved invasive carcinoma and 3 of them had lymph node metastasis (23%); 6 cases were diagnosed with in-situ carcinoma and 1 of them had lymph node metastasis (14%). All the metastases were of ductal type. This frequency of

lymph node metastasis is comparable to that of ordinary invasive breast carcinoma not arising from a PT (42). None of the cases had sarcomatous lymph node involvement. The adjuvant modalities used to manage these patients were diverse. Two studies reported disease-related death as a result of distant metastasis of the sarcomatous component (34, 37). To date, no study has yet reported distant carcinomatous metastasis. Of the 32 cases with information on outcome and follow-up period available, there was no documented local recurrence (average follow-up period of 34.6 months).

Carcinoma, especially in-situ lesions, within a PT is often not suspected during the initial breast imaging (2). Thus, the carcinoma component is often only diagnosed incidentally on subsequent pathological examination of the core biopsy or excision specimen. The presence of microcalcifications, such as those seen in our case, is unusual for PTs and can alert the treating clinicians for the possibility of a carcinoma component within the PT. A targeted biopsy of the microcalcifications can therefore be performed.

The mainstay of treatment for these lesions is surgical excision followed by adjuvant therapies. The surgical approaches include local excision/lumpectomy (with margin of 1 cm advocated) (43–46) and mastectomy (47, 48). In contrast to true carcinosarcoma, it has been demonstrated that there is lack of clonality between the carcinoma and stromal neoplastic cells in carcinomas within PTs (39). Therefore, both the stromal and epithelial component of these lesions should be evaluated separately when formulating a management plan.

Conclusion

We have presented a rare case of pure high-grade DCIS, depicted by the presence of microcalcifications seen mammographically, found within a borderline phyllodes tumour. Clinicians and pathologists should be alert about the possibility of a carcinoma component when there are microcalcifications within a lesion with features of PTs. Both the stromal and epithelial components should be taken into account when formulating a management plan. Long-term follow-up with regular radiological surveillance is also important as prognostic data for this rare lesion is limited. Distant metastasis causing mortality has been reported but only in cases with malignant stromal component.

Abbreviations

BIRADS – Breast Imaging-Reporting and Data System

CT- Chemotherapy

DCIS – Ductal carcinoma in-situ

HT – Hormonal therapy

IDC – Invasive ductal carcinoma

ITC – Invasive tubular carcinoma

LCIS – Lobular carcinoma in-situ

MX – Mastectomy

N/A – Not available

PT(s) – Phyllodes tumour(s)

RT – Radiotherapy

SCC – Squamous cell carcinoma

SLNB – Sentinel lymph node biopsy

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Written informed consent was obtained from the patient for publication.

Availability of data and material – Data sharing is not applicable to this article as no dataset was generated or analysed in this study.

Competing interest – The authors declare that they have no competing interest.

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Authors' contributions – WNY drafted the manuscript and reviewed the slides and collected clinicopathological data. JJXL edited the manuscript and reviewed the slides. CMY collected and analysed clinical data. GMT conceived the idea of the study, reviewed the slides and critically revised the paper.

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Authors' information – Optional

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Figures

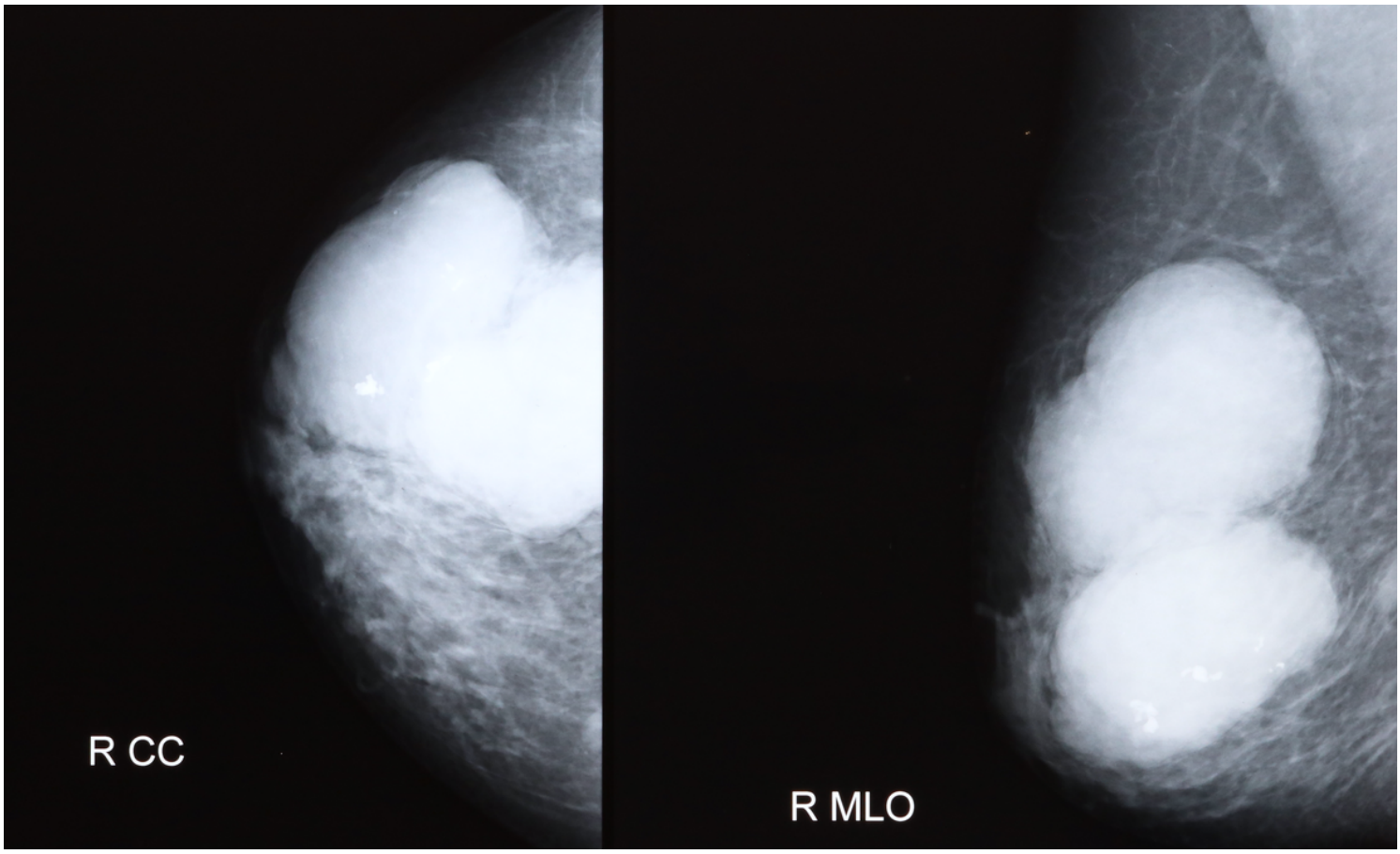

Figure 1

Mammogram in right craniocaudal (left) and right mediolateral oblique (right) views showing a dumbbell-shaped mass with a well-defined border and clumps of coarse amorphous microcalcifications.

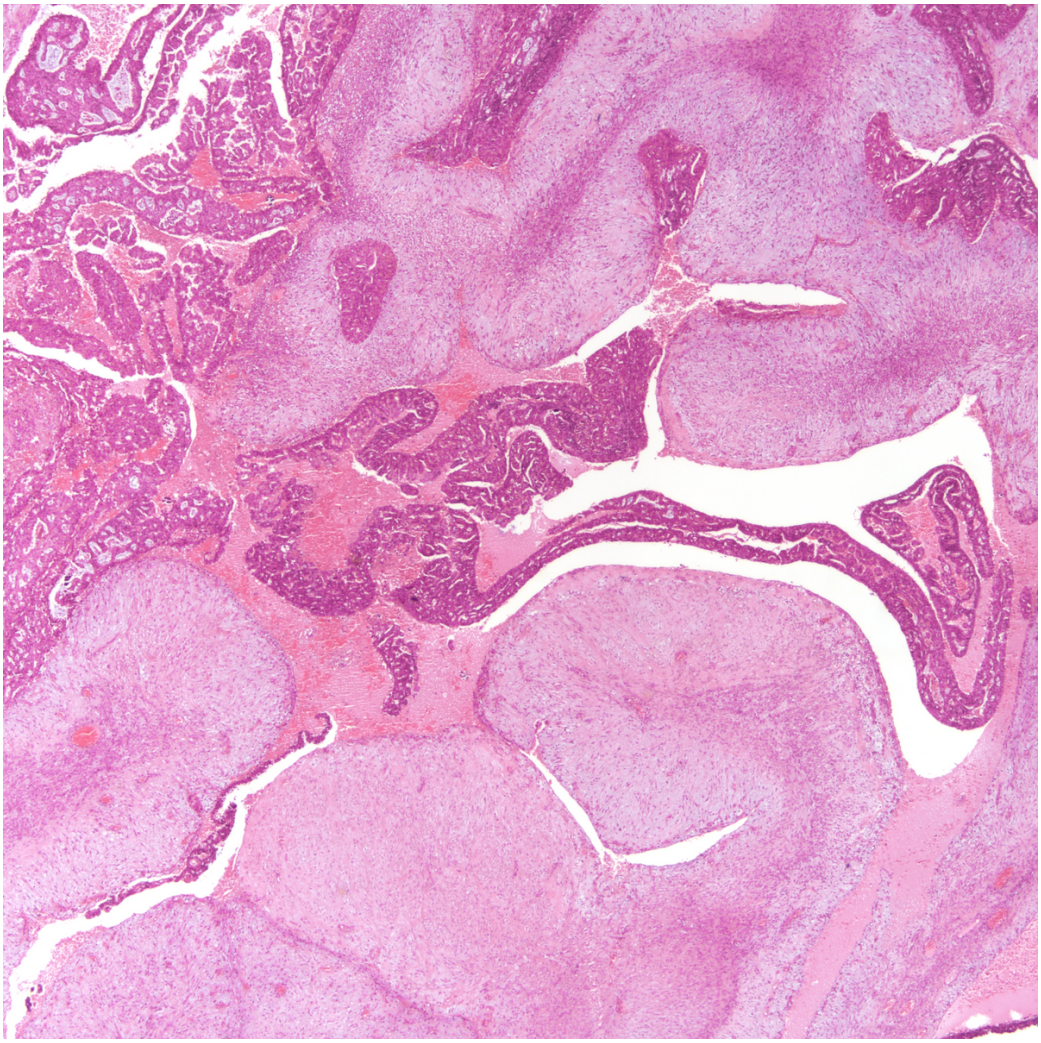

Figure 2

Borderline phyllodes tumour featuring hypercellular with conspicuous subepithelial accentuation and stromal overgrowth, 20x magnification.

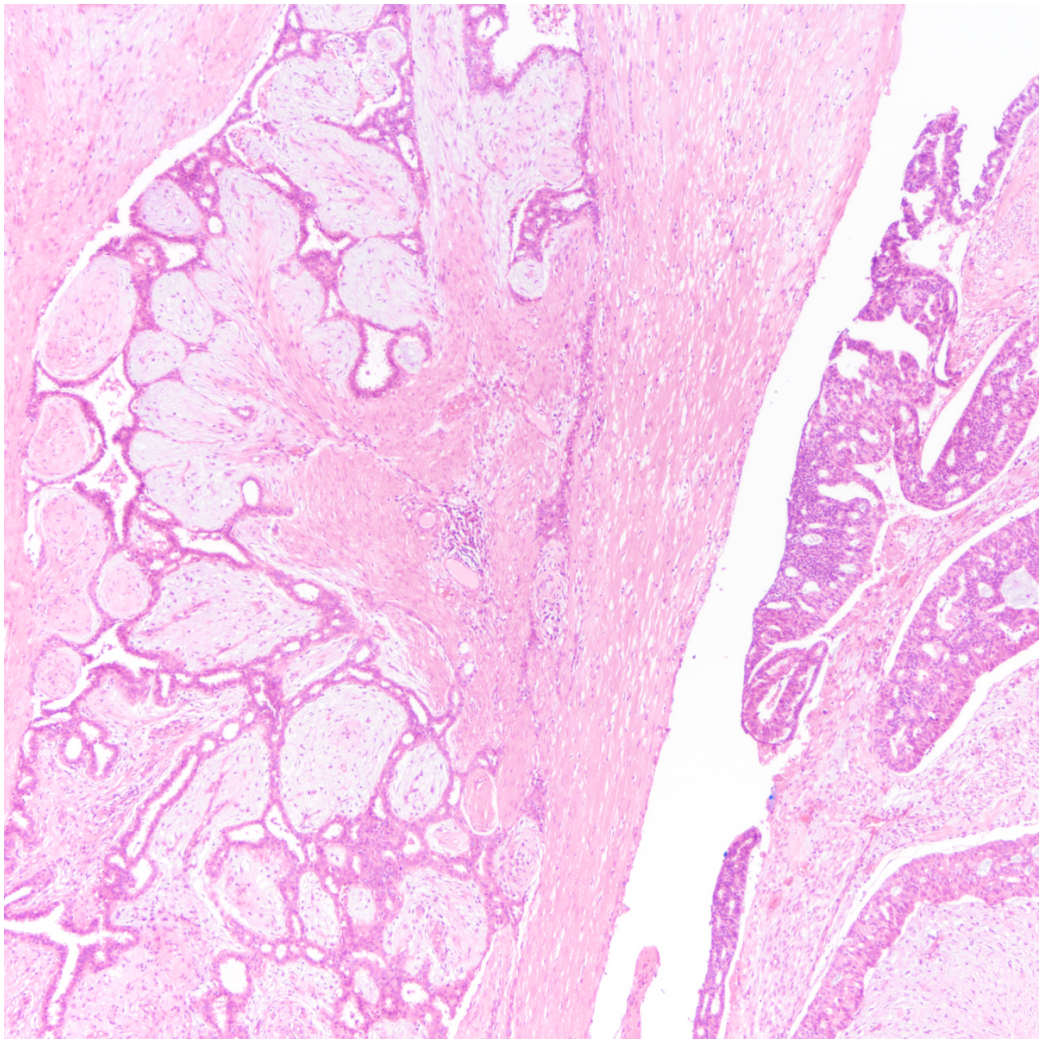

Figure 3

Fibroadenomatoid areas adjacent to borderline phyllodes tumour, 40x magnification.

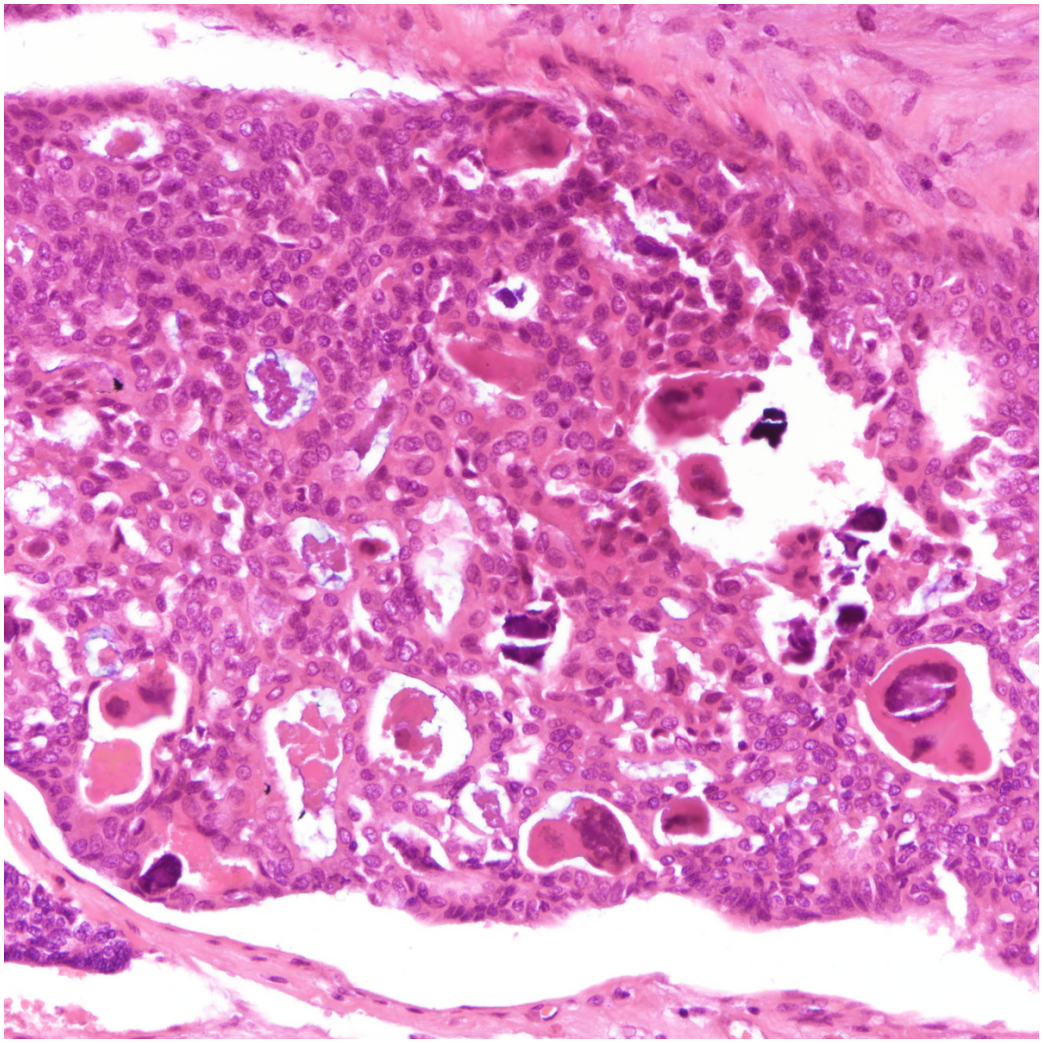

Figure 4

High-grade ductal carcinoma-in-situ with abundant luminal calcification, 200x magnification.

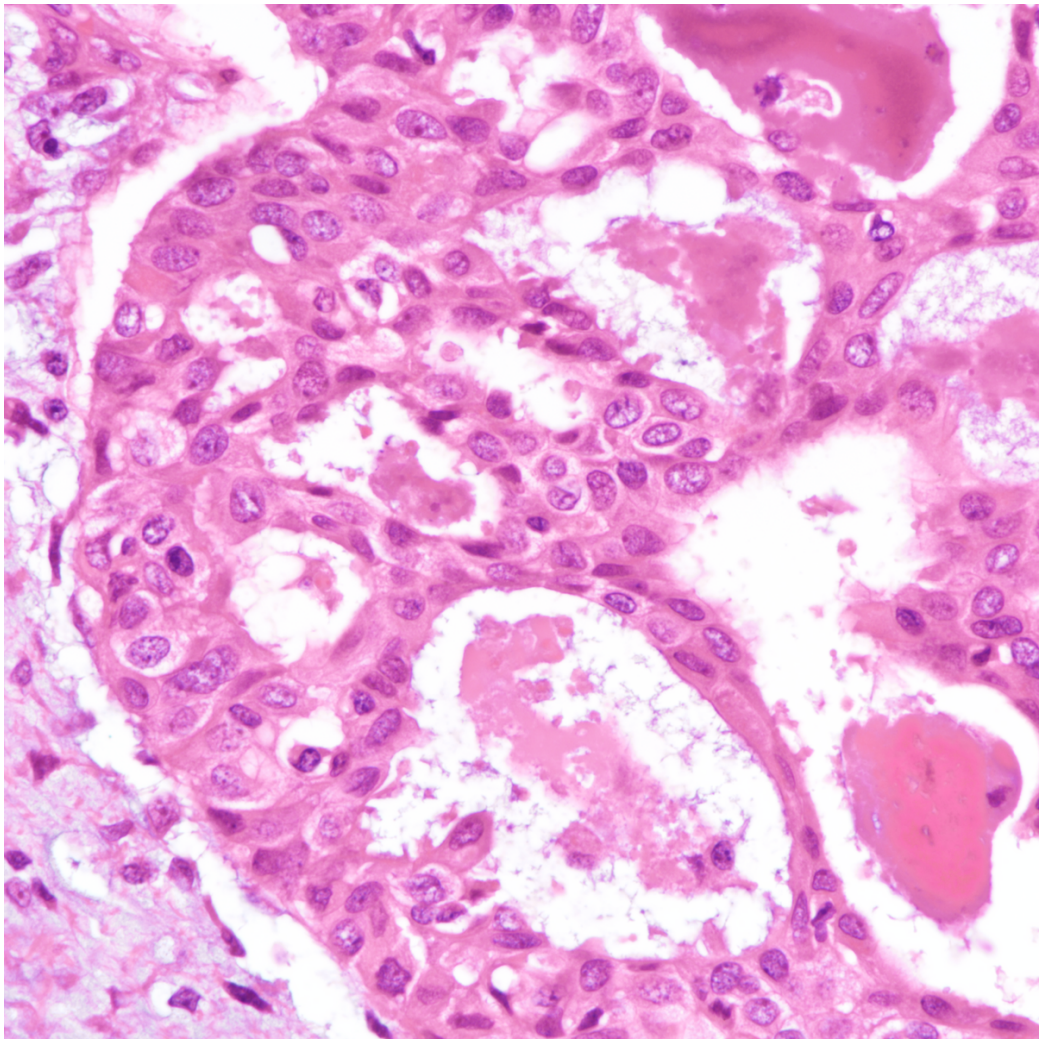

Figure 5

High-grade cytologic features including nuclear hyperchromasia and prominent nucleoli in high-grade ductal carcinoma-in-situ, 400x magnification.

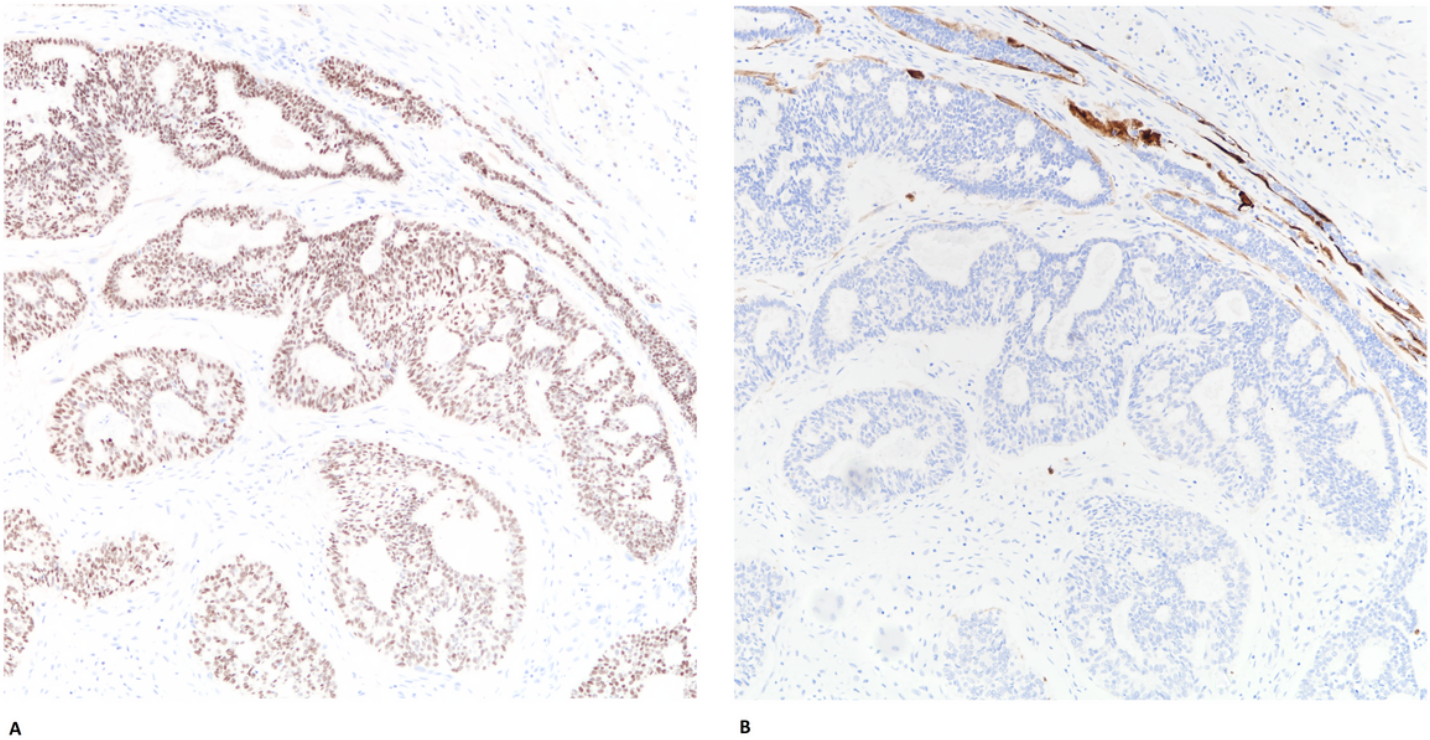

Figure 6

Immunohistochemistry – a) oestrogen receptor, 100x magnification; b) CK5/6, 100x magnification.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- CAREchecklist.pdf