Incidental finding of invasive lobular carcinoma within a borderline phyllodes tumour of the breast: a case report

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Background: Phyllodes tumours (PTs) are rare neoplasms of the breast with similar clinical and radiological features to fibroadenomas. The presence of invasive carcinoma within a PT occurs in less than 1% of cases. Furthermore, the presence of invasive lobular carcinoma (ILC) within a borderline PT has only been reported once before in a female under the peak incidence age of 45 years, making the case presented here exceedingly rare. The incidental finding of ILC highlights the importance of the multidisciplinary team's (MDT) collaborative expertise and rigorous investigative work-up where inconsistencies in the breast triple assessment are identified.

Case Presentation: A 40-year-old female presented with a 2-month history of core biopsy proven fibroadenoma. An excisional biopsy was performed due to radiological concerns raised in the MDT meeting for a PT, despite the histological outcome of the biopsy. Postoperatively, microscopic examination of the 37 mm lobulated specimen showed typical phyllodes leaf-like architecture containing a 6 mm focus of triple negative ILC. The resulting axillary sentinel lymph node biopsy was negative, leading to an overall staging of pT1b pN0. 2 months post-biopsy, the patient is well with 6 monthly ultrasonography and annual mammography for 2 years in the breast clinic planned. A referral to oncology for radiotherapy and endocrine therapy was also made.

Conclusions: This case adds significantly to the minimal literature describing the co-existence of PT and ILC. This case also highlights the crucial role of MDT discussion where discordances in the triple assessment are identified. Without this, surgical intervention may not have been considered, resulting in inadequate management and poorer outcomes. Continually, this case emphasises the need for adequate tissue sampling at biopsy to avoid missing small foci of invasive disease. Adequate resection, post-operative surveillance and patient education all continue to be key in the ongoing management of PTs. Owing to the rarity of synchronous invasive carcinoma and PT and the resulting paucity of literature, such cases should continue to be managed on a case-by-case basis by an experienced MDT.

Keywords: Phyllodes tumour (PT); invasive lobular carcinoma (ILC); case report; multidisciplinary team; breast surgery

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Introduction

Phyllodes tumours (PTs), also known as cystosarcoma phyllodes, are rare neoplasms of the breast and comprise less than 1% of all breast neoplasms (1). Morphologically they represent a continuum and can be classified as 'benign', 'borderline' or 'malignant' based on several histological features (2,3). Around 10% of PTs are 'malignant' with these tumours showing a propensity for haematogenous rather than lymphatic spread (4,5). Whilst PTs are clinically and radiologically similar to fibroadenomas, they tend to occur more frequently in older women with a peak incidence at 45–49 years of age (6,7). The presence of invasive carcinoma within a PT is exceedingly rare, occurring in less than 1% of PTs (8,9). Where invasive carcinomas and PTs occur synchronously, invasive lobular carcinoma (ILC), rather than invasive ductal carcinoma (IDC), is rarer still (10).

We report a case of a woman in her early 40's who underwent an excisional biopsy of a fibroadenoma where post-operative histology showed an incidental finding of a triple negative grade 2 ILC within a borderline PT. In addition to the importance of corroborating the scarce existing literature on the simultaneous presence of PTs and ILC, this case report crucially highlights the importance of rigorous investigative work-up and management under an experienced breast multidisciplinary team (MDT) to avoid missed diagnoses of breast cancers in seemingly benign breast lumps. We present the following case in accordance with the CARE reporting checklist (available at https://amj.amegroups.com/article/view/10.21037/amj-22-52/rc).

Highlight box

Key findings

- The incidental finding of an invasive lobular carcinoma within a phyllodes tumour.

What is known and what is new?

- There is limited existing knowledge surrounding the coexistence of invasive carcinomas and Phyllodes Tumours.
- When these pathologies co-exist, the phyllodes tumours are typically of the malignant subtype and the carcinomas are DCIS, LCIS or IDC; not ILC as reported here.
- This case report characterizes the rare coexistence of invasive lobular carcinoma within a borderline phyllodes tumour.

What is the implication, and what should change now?

- The rarity of these two pathologies highlights the importance of management by an experienced multidisciplinary team on a case-by-case basis.
- This case seeks to emphasize the importance of thoroughly investigating breast lumps with discordant triple assessment findings under multidisciplinary team guidance.

Case presentation

A 40-year-old woman presented to the one-stop breast clinic with a 2-month history of a lump in the right breast. This was associated with a 1-week history of associated discomfort and tightness which encouraged a visit to the General Practitioner where an urgent referral to the breast unit for specialist input was made. She had a past medical history of type 2 diabetes mellitus for which she was taking oral hypoglycaemics (metformin). She had no family history of breast or ovarian cancer. She was pre-menopausal with a regular menstrual cycle and was para 1.

On clinical examination, there was tender nodularity in the upper outer quadrant of the right breast as well as multiple suspected sebaceous cysts in the mid chest (P2/3). Based on these clinical findings she underwent an ultrasound scan of the right breast and a bilateral mammogram.

Mammography (*Figure 1*) showed dense fibroglandular appearances with lobulated densities (see arrows) in the upper outer quadrant of the right breast, possibly cysts, with few scattered microcalcifications suggestive of fibrocystic changes (RM3). Ultrasonography (*Figure 2*) of the symptomatic lump confirmed a lobulated hypoechoic nodule measuring 45 mm × 17 mm × 20 mm in the upper outer breast in keeping with a fibroadenoma (U3). Ultrasound-guided core biopsy of the lump was performed which reported histological features consistent with fibroadenoma (B2) and further immunohistochemistry with CK5 showed a benign staining pattern and no evidence of *in situ* or invasive malignancy.

This case was discussed in the Breast MDT meeting and, due to radiological findings suggestive of a PT and discordance on triple assessment, the consensus was to proceed with excisional biopsy of the lump.

At this stage, a diagnosis of probable fibroadenoma was made due to the clinical findings, core biopsy and ultrasonographic features of a lobulated hypoechoic mass. A PT was included in the differential diagnosis due to its known similarity in clinical and radiological features to fibroadenoma. The presence of microcalcifications on the mammogram also raised concerns as these features are not typically associated with a fibroadenoma.

Excisional biopsy of right breast lump was performed

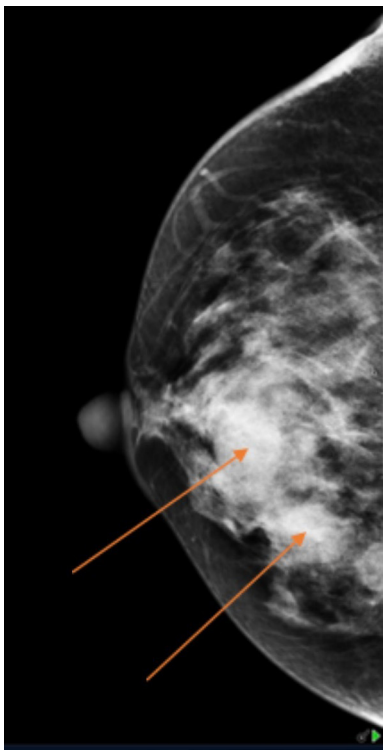

Figure 1 Mammogram of the right breast (CC view) with arrows showing lobulated densities in the upper outer quadrant with scattered microcalcifications suggestive of fibrocystic change. CC, craniocaudal.

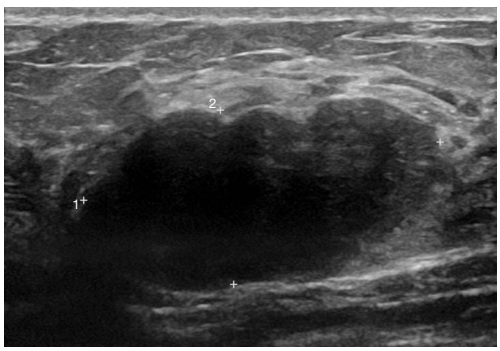

Figure 2 Ultrasound scan of the right breast showing a lobulated hypoechoic nodule measuring 45 mm × 17 mm × 20 mm.

under general anaesthesia and post-operative histology revealed an incidental ILC arising in a fibroepithelial lesion composed of both an ordinary fibroadenoma and a 'borderline' PT. The invasive component measured 6 mm with features consistent of a classical grade 2 ILC. The tumour was completely excised, all resection margins were

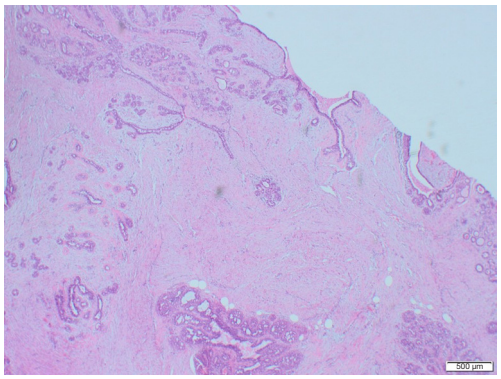

Figure 3 This histological slide shows typical phyllodes leaf-like architecture, with moderate stromal cellularity and periductal condensation pattern. Staining: haematoxylin and eosin.

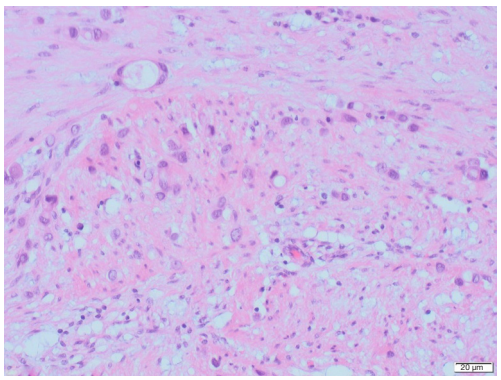

Figure 4 This histological image shows a 6 mm area of atypical cells displaying nuclear pleomorphism and prominent nucleoli. This confirms the presence of invasive lobular carcinoma. Staining: haematoxylin and eosin.

clear by at least 4 mm and no lymphovascular invasion was seen. The tumour was considered triple negative with oestrogen receptor score 4/8, progesterone receptor score 0/8 and human epidermal growth factor receptor 2 (HER2). The Ki67 proliferation index was 3–5%. Microscopic appearance is shown in *Figures 3*-7.

Following further discussion in the post-operative Breast MDT meeting, she then had a sentinel lymph node biopsy to assess for regional nodal status which was negative. The tumour's final histological staging was reported as pT1b pN0. Regarding prognosis and risk of recurrence, it is difficult to make evidence-based predictions owing to the rarity of ILCs and PTs co-existing. However, the recurrence risk of non-metastatic low grade breast cancers (pT1a/b pN0, pM0), such as the ILC reported here, has

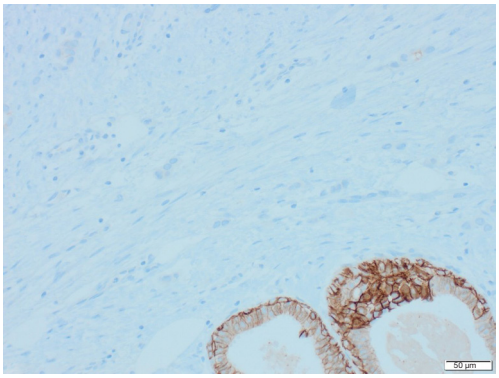

Figure 5 Immunohistochemistry revealed atypical cells to be negative for e-cadherin staining.

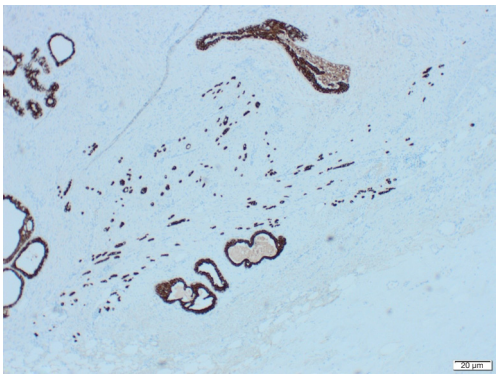

Figure 6 Immunohistochemistry revealed strong positive diffuse staining of neoplastic invasive lobular carcinoma cells on cytokeratin AE1/AE3 staining.

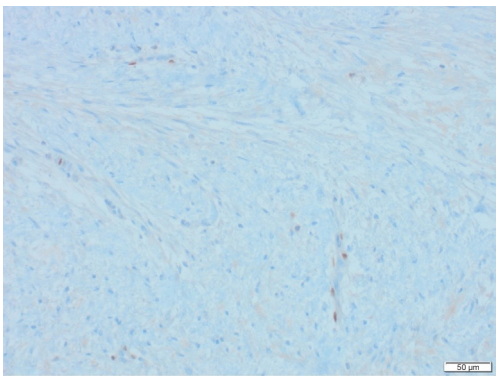

Figure 7 Using the Allred scoring system, ER expression within tumour cells was graded at 4/8. Staining: e-cadherin. ER, estrogen receptor.

been previously characterised, with overall survival and recurrence-free survival rates of 98.4% and 97.1% at 5-year follow up (11). Similarly, whilst previous studies have estimated the recurrence rate of borderline PTs to be 13% (12), the chance of recurrence in this specific instance is hard to predict owing to the rarity of PTs containing invasive carcinoma.

At 2 months following axillary surgery, the patient was well with fully healed wounds in the breast and axilla; no post-operative complications. She had had regular contact with the breast care nurses for support and advice. She was also referred to oncology for adjuvant radiotherapy to the breast and endocrine therapy. Six monthly ultrasonography surveillance and annual mammography for 2 years with follow-up in the breast clinic was also planned. To date, all surveillance imaging has shown no evidence of recurrent disease.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). 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 editorial office of this journal.

Discussion

PTs are a rare breast neoplasm comprising less than 1% of all breast tumours (1). They are classified as either 'benign', 'borderline' or 'malignant', with around 10% of cases being classified as malignant (2,3,5). PTs can be difficult to differentiate from fibroadenomas. Clinically, PTs present as a palpable lump and patients may report rapid growth (13). Ultrasound alone may not be sufficient to distinguish PT from fibroadenoma owing to the substantial overlap in sonographic characteristics (14). The presence clefts or round cysts within a solid mass is suggestive of a PT (15). Histological features typical of PT, rather than fibroadenoma, include: leaf-like architecture, increased stromal cellularity, stromal overgrowth, fragmentation and the presence of adipose tissue within the lesion (16). In this case, the crucial identification of radiological inconsistencies with the working diagnosis of fibroadenoma and an awareness of the possible confirmation bias conferred by the

Table 1 Reported cases in literature of phyllodes tumour containing invasive lobular carcinoma and/or lobular carcinoma *in situ*

Study	Age (years)	Duration of symptoms	Pathology	Surgical management
Chen *et al.* 2022 (17)	43	3 years	ILC within benign PT	Nipple sparing mastectomy follow by total mastectomy with ANC
Shirah *et al.* 2011 (18)	49	Asymptomatic	ILC and LCIS within benign PT	Wide local excision followed by re-excision of margins and SLNB
Kodama *et al.* 2003 (19)	47	10 years	ILC and LCIS within benign PT	Skin sparing mastectomy
Fischer *et al.* 2018 (20)	40	Unknown	ILC and LCIS within borderline PT	Lumpectomy with sentinel node biopsy followed by bilateral total mastectomy
Potdevin *et al.* 2016 (21)	63	Detected on routine clinical examination	ILC and LCIS within borderline PT	Excisional biopsy followed by Nipple sparing mastectomy
Current case	40	2 months	ILC within borderline PT	Excisional biopsy followed by SLNB

ILC, invasive lobular carcinoma; PT, phyllodes tumour; LCIS, lobular carcinoma in situ; ANC, axillary node clearance; SLNB, sentinel lymph node biopsy.

core-biopsy result enabled the experienced MDT to dictate the need for an excision biopsy to confirm a diagnosis of PT and ILC and therefore suggest further management (15).

The coexistence of PTs and invasive breast carcinoma or *in situ* carcinoma is rare, featuring in less than 1% of PTs (8,9). Where invasive carcinoma and PTs exist synchronously, ILC occurs less often than IDC (10). Only 5 other cases have been reported over the last 20 years to describe the presence of ILC within a PT (*Table 1*). Of this, only 2 feature 'borderline' type of PT and both of these contain invasive and *in situ* lobular carcinoma. Our case is the first to report the presence of exclusively ILC within a 'borderline' type PT.

On comparing the clinical presentation with the 5 other reported cases, 2 were asymptomatic and discovered on routine examination or via breast screening and 3 were long-standing breast lumps (3, 10 and 10 years). For the latter 3 cases, it was suggested that the long growth period of the PT may have contributed to the development of the concomitant ILC (17-19). Our case conflicts this theory with only a 2-month history of a breast lump and an even shorter 1-week history of symptoms (discomfort and tightness). This perhaps suggests the possibility of simultaneous PT and ILC growth. Any theorised relationship between ILC and PT growth is ultimately speculative and a definitive link between the two conditions is not likely to be determined owing to the rarity of their coexistence.

The National Institute for Health and Care Excellence (NICE) guidelines dictate that patients aged over 30 with an unexplained breast lump, or patients over 50 with concerning unilateral nipple changes, are referred for specialist assessment within 2 weeks (22). This assessment comprises of the triple assessment (clinical examination, imaging and tissue biopsy) which informs diagnosis and management. In the case of PTs, no clear guidelines exist to define the optimal management and follow-up. Whilst mastectomy has historically been the treatment of choice, breast conserving surgery (BCS) with tumour free margins is now the generally accepted approach regardless of PT stage (23). In our case, excisional biopsy was performed as opposed to BCS or mastectomy as there was no definite pre-operative diagnosis of PT or invasive disease, and core biopsy had shown features in keeping with a fibroadenoma. As the tumour was fully excised with clear resection margins of a minimum of 4mm, no further excision of breast tissue was required. Second stage sentinel lymph node biopsy only was carried out to assess for nodal spread to the axilla.

Local recurrence of breast cancer is heavily influenced by the status of the resection margins (positive or negative). Despite this, systematic review by Lu *et al.* has shown that local recurrence is not significantly affected by margin status when the PT is 'benign' or 'borderline' (12). A resection margin of 1 cm is recommended by some studies, though others have suggested a margin of 1mm may be more appropriate, especially for 'benign' PT (12,24,25). The National Comprehensive Cancer Network recommends wide local excision with resection margins of

1 cm or greater for the surgical management of borderline/malignant PTs (26). This is considerably larger than the 1 mm minimum resection margin that is recommended by the National Institute for Health and Care Excellence for invasive or *in situ* breast cancer (27). The need for such a considerable resection margin of ≥h cm has been argued by some studies though a meta-analysis study by Thind *et al.* concluded that current available evidence suggests margins of less than 1 cm are adequate for the management of borderline or malignant PTs (28). This smaller resection margin also offers the benefit of better cosmetic outcomes especially in those with a smaller breast-to-tumour volume ratio.

Histological factors thought to predict local recurrence of PT include: stromal atypia, stromal mitoses, stromal overgrowth and stromal cellularity as well as tumour features such as tumour necrosis and tumour borders (12,29). Overall, systematic review and meta-analysis has suggested a local recurrence rate of 8% for benign PT, 13% for borderline PT and 18% for malignant PT (12). This highlights the importance of close follow up and surveillance regardless of the surgical management, tumour stage or resection margin (12).

Conclusions

This case raises awareness and acts as a reminder of the potential of invasive carcinoma to present in seemingly benign breast lumps. This case also emphasises the crucial role of the MDT and the attention paid to discordances in the triple assessment findings. It highlights why it is important not to succumb to confirmation biases when presented with a breast lump that has been shown to be a benign fibroadenoma on core biopsy despite radiological concerns for alternative diagnoses, such as a PT. Without the thorough and unbiased MDT discussion that took place, the decision to further investigate the seemingly benign breast lump in the form of a surgical excisional biopsy would have otherwise been overlooked, resulting in inadequate management and poorer outcomes. Due to the rarity of this case, the available literature on the topic is limited and there is scope for further research in this area. From the available literature, it seems that patient outcomes are better when PTs are 'benign' rather than 'malignant', irrespective of the presence of an invasive carcinoma or an *in situ* carcinoma (21). Ultimately, the niche nature of these coexisting diagnoses means that cases are, and must continue to be, managed by an experienced MDT on a case-by-case basis and seemingly benign breast lumps with discordant triple assessment findings must always undergo thorough MDT-led assessment.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://amj.amegroups.com/article/view/10.21037/amj-22-52/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://amj.amegroups.com/article/view/10.21037/amj-22-52/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). 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 editorial office of this journal.

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