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Phyllodes tumour with heterologous sarcomatous differentiation: Case series with literature review



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ABSTRACT

INTRODUCTION: Phyllodes tumours are rare fibroepithelial malignancies of the breast, accounting for less than 1% of malignant breast tumours. Further malignant differentiation of phyllodes tumours can occur, resulting in cases of extremely rare heterologous sarcomatous differentiation.

PRESENTATION OF CASE: Two females in their fifties were diagnosed with malignant phyllodes tumour associated with heterologous sarcomatous differentiation. The first patient, aged 50 had phyllodes tumour with chondrosarcoma, osteosarcoma and ductal carcinoma-in-situ. The second patient, aged 53 had phyllodes tumour with osteosarcoma and liposarcoma.

DISCUSSION: The association of phyllodes tumour and heterologous sarcomatous differentiation is rare, with only 4 previously reported cases in English literature. The paucity of evidence presents challenges in its management with uncertain prognosis and monitoring requirements for two aforementioned patients.

CONCLUSION: Further case series and long-term follow up is required for accurate characterisation of phyllodes tumours with heterologous sarcomatous differentiation.

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1. Introduction

Phyllodes tumours (PTs) are rare fibroepithelial malignancies of the breast and account for less than 1% of malignant breast tumours [1,2]. They are fast growing tumours that originate from peri-ductal stroma and are composed of both epithelial and stromal components [3]. PTs can be classified by histopathological features as benign, borderline or malignant, but all PTs have the potential to become malignant although behaviourally is relatively poorly predicted from histological appearances [4]

PTs are usually solitary tumours but can be associated with other malignancies of the breast [5,6]. In particular, malignant differentiation of both the epithelial and stromal components of PTs can occur with carcinomas, invasive and in situ, arising from the epithelial component sarcomas such as chondrosarcomas, osteosarcomas and liposarcomas, can be seen in association with the stromal component of a PT [6]. PTs can also co-exist with a distinctly separate malignant tumour in both the ipsilateral and/or contralateral breast

[3]. The association of PTs with heterologous sarcomatous differentiation is a rare occurrence with only 4 previously reported cases in English literature [5–8].

We present 2 cases of malignant PTs associated with multiple malignancies: the first patient had PT with chondrosarcomatous and osteosarcomatous differentiation and ductal carcinoma in situ (DCIS) in the ipsilateral breast, with lobular carcinoma and DCIS in the contralateral breast. The second patient had PT with osteosarcomatous and liposarcomatous differentiation.

2. Case series

2.1. Case 1

A 50 year old female presented with a 2 year history of a large palpable mass in her left breast. She had a sister who developed breast cancer at 45 years of age but had no other risk factors. A mammogram and ultrasound demonstrated a lesion of approximately 11 cm in the left breast, with a 10 mm impalpable lesion in her right breast (Fig. 1). Core biopsy of the left breast revealed a PT and a core biopsy of the right breast demonstrated atypical lobular neoplasia.

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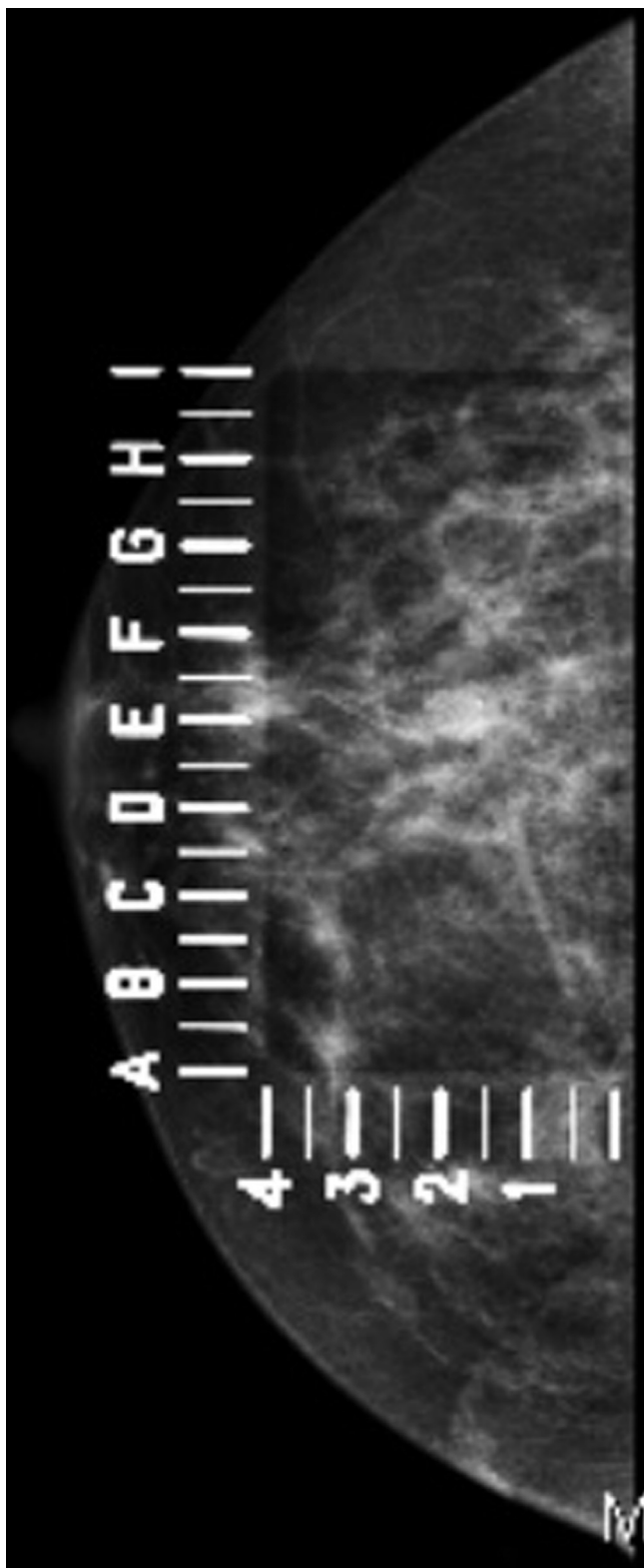


Fig. 1. Ultrasound imaging of right breast.

The patient underwent a left mastectomy and a hookwire localised excision of the right breast lesion, with no operative complications.

Pathology of the left mastectomy revealed a malignant PT characterised by a classical ‘leaf-like’ growth pattern showing marked stromal overgrowth containing malignant spindle cells with high mitotic rate up to 34 mitotic figures in 10 high power fields.

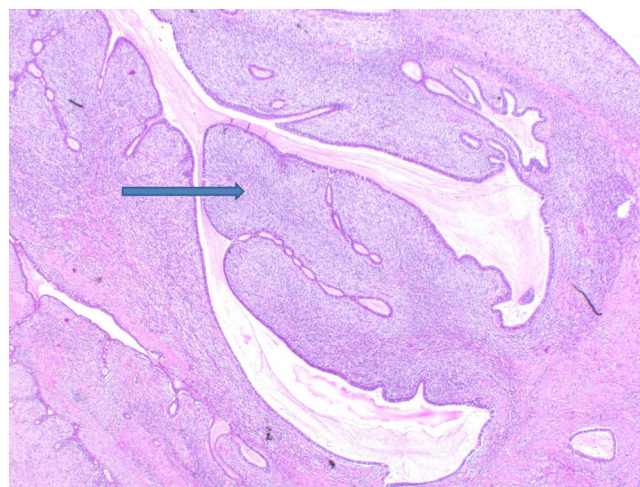


Fig. 2. (H&E) phyllodes tumour with leaf-shaped formation of ductal-carcinoma in situ.

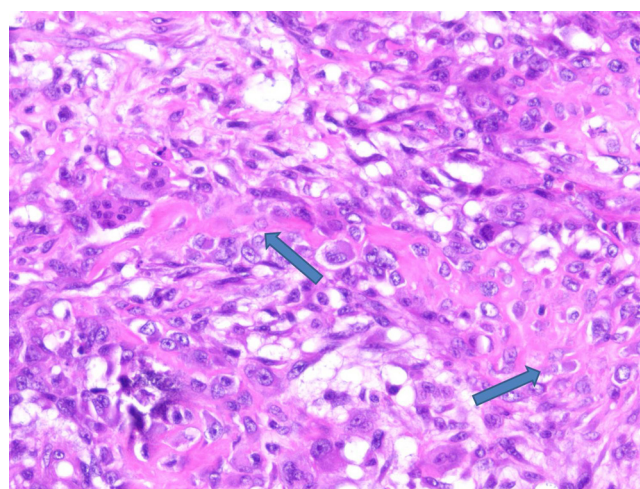


Fig. 3. (H&E) phyllodes tumour with malignant osteosarcoma.

Within the PT, elements of chondrosarcoma, osteosarcoma and DCIS (intermediate grade) were present. The DCIS was oestrogen and progesterone receptor positive. The pathology is demonstrated in Fig. 2–4.

The right hookwire localised excision demonstrated invasive lobular carcinoma (grade 1), which was oestrogen and progesterone receptor positive, HER2 negative. This excision was complete with clear margins. There was also a focus of DCIS (intermediate grade) within the excised sample.

On review of the pathology, the multidisciplinary team (MDT) recommended a right axillary sentinel lymph node biopsy due to the presence of mixed invasive lobular carcinoma and DCIS. The two sentinel lymph nodes biopsied demonstrated no evidence of malignancy.

Post-operatively, the patient received adjuvant radiotherapy to both breasts and adjuvant Tamoxifen 20 mg daily, in consideration of the hormone status on her lobular carcinoma of the right breast. At 2 years follow-up, the patient is well with no evidence of recurrence.

Table 1

Summary of previously reported cases of phyllodes tumours with heterogenic sarcomatous differentiation.

Authors	Year	Age	Site	Size (cm)	Treatment	Final pathology	Follow up
Tomas et al. [5]	2007	71	R	3.3	Mastectomy, axillary dissection and chemotherapy	Malignant phyllodes with osteo/chondro/liposarcomatous differentiation	1 year: disease free
Guerrero et al. [6]	2003	96	L	17 × 13 × 8	Wide local excision	Malignant phyllodes with lipo/fibro/rhabdo/leiomyosarcomatous differentiation	10 months: dead, due to pneumonia
Garcia et al. [8]	1999	51	L	5 × 4.5 × 3	Mastectomy, axillary dissection	Malignant phyllodes with chondro/osteosarcomatous and MFH differentiation	16 months: disease free
De Luca et al. [7]	1986	41	L	30 × 24 × 20	Mastectomy, chemotherapy	Malignant phyllodes with lipo/fibrosarcomatous, anaplastic and giant cell differentiation	4 months: dead with pulmonary metastases

2.2. Case 2

A 53 year old female presented with a painful, palpable lump in the upper outer quadrant of her left breast. She had a fibroadenoma excised from her left breast in 1995 and regularly attended breast screening for persisting breast cysts. On examination, there was a firm 3 cm mass in the upper outer quadrant of her left breast, just proximal to the scar that was made during the excision of her fibroadenoma. Ultrasound revealed a solid mass measuring 3.3 × 2.5 cm with a heterogeneous echo pattern, cystic spaces and well-defined margins.

A core biopsy demonstrated the lesion to be a PT and the patient underwent a wide local excision (WLE) of her left breast lesion. Pathology revealed a malignant PT measuring 2.5 × 3.3 cm with stromal cellularity varying from mild to sarcomatous, with both osteosarcoma and liposarcoma contained within the PT. In these areas, the mitotic rate was borderline (8 per 10 high power fields). The margins for PT were not clear at the anterior and inferior margins.

The patient considered a repeat WLE or a mastectomy and opted for the WLE. She underwent an upper outer quadrantectomy of her left breast, with no operative complications. The pathology from this excision demonstrated clear margins and she is currently being followed up 6 monthly. At 2 years follow-up, the patient is well with no evidence of recurrence.

3. Discussion

Phyllodes tumours, first described as *Cytosarcoma phyllodes* by Muller in 1838 [9], display a wide range of clinical, histological and cytological features [3,4]. Based on histological and cytological findings, PTs are classified as benign, borderline or malignant. This classification allows for the interpretation of PTs as a continuum of the spectrum of fibroepithelial neoplasms of breast tissue; benign PTs can be difficult to distinguish from fibroadenomas while malignant PTs can grow in size quickly and metastasise early [3].

Microscopically, PTs are characterised by a leaf-like appearance, created by projections of hypercellular stroma into epithelium-lined cystic spaces. The presence of dual population of both epithelial and stromal cells is necessary for the diagnosis of PT [9]. However, the characteristic histological features are related to the stroma [3] and PTs are differentiated from fibroadenomas by marked stromal overgrowth and hypercellularity [3].

There are numerous histological grading systems for PTs, with multiple revisions of the classification first described by Treves and Sutherland in 1951 [10]. Most grading systems are 3-tiered: “benign, borderline or malignant” or “low, intermediate or high grade” and use the same histological parameters (with varying cut-offs): margins characteristics, cellular atypia, stromal overgrowth, stromal cellularity, and mitotic rate [3].

A variety of associated malignancies can arise from PTs, with its dual population of cells [6]. The stromal cells can demonstrate sarcomatous differentiation while the epithelial component can become malignant with DCIS/LCIS or invasive carcinoma. There have also been case reports of two distinctly separate lesions of PT and primary sarcoma or PT and carcinoma [11,12].

The two cases discussed above demonstrate sarcomatous differentiation of the stromal cells in malignant PT, with further development of epithelial malignancy (DCIS) in the first case. The first case is also unique in that this was associated with a contralateral lobular carcinoma and DCIS. It is very unusual to note heterologous sarcomatous differentiation in PTs and Table 1 summarises the 4 previous cases of such heterogeneity in English literature, all of which arose out of malignant PTs.

There is a paucity of evidence regarding surgical and adjuvant therapy and rates of local control makes it difficult to recommend a specific treatment for patients [6,13]. In isolated PTs, wide local excision with margins of 1 cm is recommended with minimal evidence for chemotherapy or hormone therapy [4], and this was the treatment of choice of case 2, who continues to have close post-operative monitoring. However, some authors suggest the use of adjuvant therapy in PTs greater than 5 cm with more than 20 mitoses per 10 high power fields as these tumours may have a higher local recurrence rate [13], and hence adjuvant radiotherapy was offered in case 1.

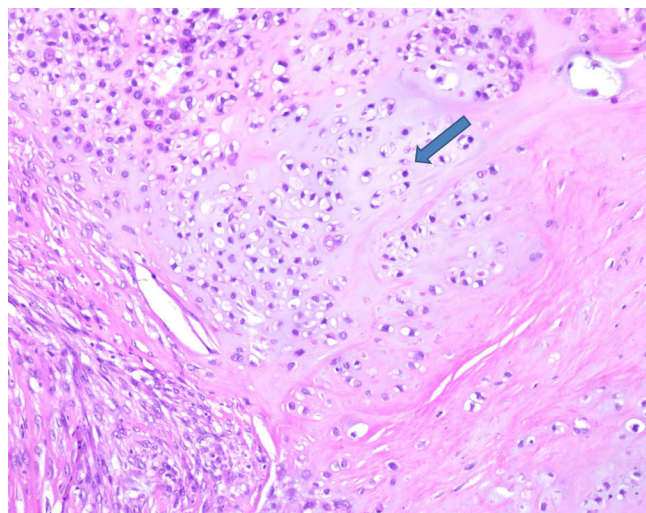


Fig. 4. (H&E): phyllodes tumour with malignant chondrosarcoma.

The prognosis of PTs is poorly defined, with local recurrence rates ranging from 10 to 40% (average 15%) and distant metastases occurring in 10% of all phyllodes tumours, and up to 20% of malignant phyllodes tumours [3]. Survival after metastatic disease is poor, with case series reporting median survival ranging from 4 to 17 months [4]. However, these figures vary from one case series to another, with Reinfuss et al. reporting 5 year disease-free survival rates of 96% in benign phyllodes tumours and 66% in malignant phyllodes tumours [14]. In the 4 case reports of malignant phyllodes tumours with heterologous sarcomatous differentiation, only 1 patient had disease-related death at 4 months [7], while another was disease-free at 16 months [8].

In summary, we present two extremely rare cases of malignant PT with heterologous sarcomatous differentiation, and note that further research is required to develop management guidelines for highly malignant PTs.

4. Learning points

1. Phyllodes tumours with heterologous sarcomatous differentiation are extremely rare.

2. There is limited literature to guide adjuvant therapy and prognosis for phyllodes tumours with heterologous sarcomatous differentiation.

5. Patient consent

Written informed consent was obtained from the patients 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.

Conflict of interest

All authors report no conflicts of interest.

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Consent

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Author contribution

A/Prof Sanjay Warrier and Dr Sang Hwang performed the literature review and wrote the manuscript.

Dr Keagan Gibbings contributed in data collection of the cases.

A/Prof Hugh Carmalt was the primary surgeon who performed the operations and Dr Sandra O'Toole was the pathologist who identified and characterised the pathology.

The latter 2 authors were also the senior authors, providing supervision through critical revision of the manuscript and approval of the final version for publication.

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