

# Malignant phyllodes tumour with intraductal and invasive carcinoma and lymph node metastasis

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## ABSTRACT

Phyllodes tumours constitute 2–3 percent of fibroepithelial breast tumours, with a 1–2 percent rate of malignancy. Metastasis is usually haematogeneous, and axillary lymph node dissection is not routinely performed. Carcinoma in a phyllodes tumour is distinctly uncommon, but has been known to occur in benign phyllodes tumours. We describe a 51-year-old woman with a malignant phyllodes tumour with foci of intraductal carcinoma within the tumour and adjacent breast tissue. Though the carcinoma was found to be invasive based on the presence of carcinomatous lymph node metastasis, extensive sampling did not yield an invasive component within the breast, probably because of the marked stromal overgrowth of the phyllodes. A malignant phyllodes tumour with foci of intraductal carcinoma and axillary lymph node metastases was diagnosed rather than carcinosarcoma. Chemotherapy and irradiation were included in the postoperative management. Coexistence of phyllodes tumour and carcinoma is rare, and extensive sampling may be necessary to find the foci of carcinoma within an extensive and obviously malignant stromal overgrowth. There is little consensus on the treatment and prognosis in these cases, and it is recommended that treatment be tailored to individual patients, based on the presence of invasion, lymph node metastasis and/or distant metastasis.

**Keywords:** breast carcinoma, breast tumour, cystosarcoma phyllodes, phyllodes tumour, intraductal carcinoma, lymph node metastasis, malignant phyllodes tumour

*Singapore Med J 2008; 49(11):e318-e321*

## INTRODUCTION

Phyllodes tumours (PT) constitute 2%–3% of fibroepithelial breast tumours. The median age group in which these tumours occur (45 years) is about 15 years older than the age group for fibroadenomas. PTs vary greatly in size and larger tumours are more likely



Fig. 1 Operative photograph shows a large fleshy tumour occupying almost the entire breast.

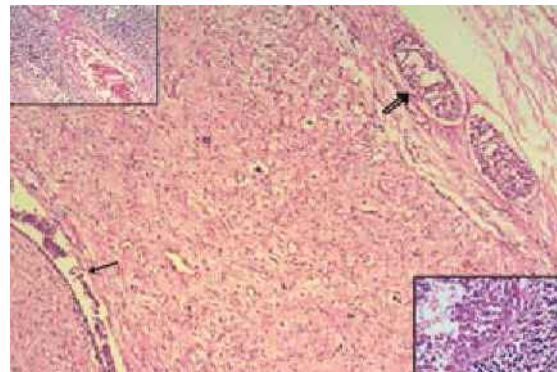


Fig. 2 Photomicrograph of the malignant phyllodes tumour shows benign ducts (black arrow) and foci of intraductal carcinoma at the edge (hollow arrow) (Haematoxylin & eosin,  $\times 100$ ). Insets: Upper left: Foci of intraductal carcinoma within the malignant phyllodes (Haematoxylin & eosin,  $\times 200$ ). Lower right: Intraductal carcinoma of low nuclear grade (Haematoxylin & eosin,  $\times 400$ ).

to be malignant, but there are many exceptions, and histological characteristics remain the basis for diagnosis and subclassification into benign, borderline (low-grade malignant) and malignant (high-grade malignant). The extent of surgery is guided by the fundamental principle of prevention of local recurrence, and mastectomy may be required if a malignant phyllodes cannot be adequately excised. Metastasis is usually haematogeneous and axillary lymph node dissection is not routinely performed. The ductal component of PTs may show varying degrees of epithelial hyperplasia, but intraductal or invasive carcinoma in these tumours is uncommon. Malignant

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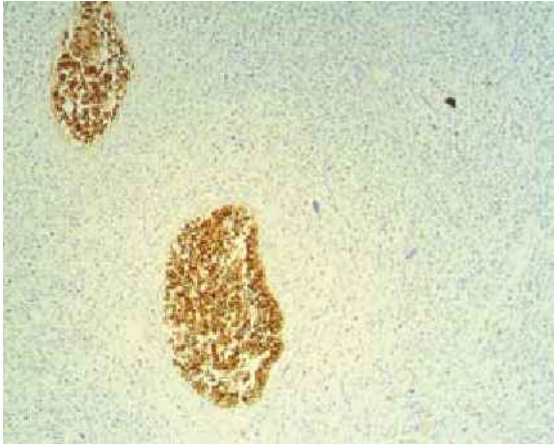
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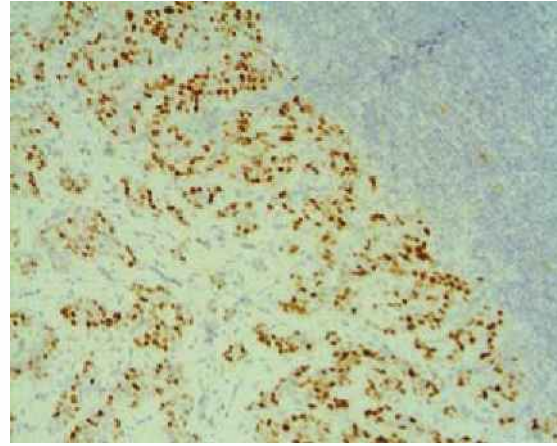
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**Fig. 3** Photomicrograph of the carcinomatous foci shows positive immunostaining with EMA, while background sarcomatous stroma is negative (Avidin-Biotin peroxidase,  $\times 100$ ).



**Fig. 4** Photomicrograph of the carcinomatous lymph node metastases with tumour cells show nuclear positivity for oestrogen receptors (Avidin Biotin peroxidase,  $\times 200$ ).

PT with coexisting carcinoma showing lymph node metastases is extremely rare, and there are no standard treatment protocols for these cases.

#### CASE REPORT

A 51-year-old woman presented with a nine-month history of a left breast mass. The mass was fixed to the pectoralis fascia, and there were multiple palpable hard nodes in the left axilla. The clinical diagnosis was cystosarcoma phyllodes, and a trucut biopsy of the mass showed a malignant spindle cell tumour. Malignant PT and metaplastic carcinoma were offered as differential diagnoses. A left mastectomy and axillary node clearance was performed. Grossly, there was a large tumour replacing almost the whole of the breast measuring 16 cm  $\times$  13 cm  $\times$  21 cm, extending to 1 mm from the deep resection margin. The tumour had a fleshy, tan cut surface with foci of necrosis, haemorrhage and cystic change, with a gritty feel in the foci (Fig. 1). The lymph nodes in the axilla formed a matted mass, and a total of 12 nodes were dissected.

18 representative sections taken from the tumour revealed a circumscribed biphasic neoplasm, consisting predominantly of a stromal overgrowth with cells showing marked nuclear atypia, including bizarre tumour cells, frequent mitoses ( $> 10/10$  HPF) and necrosis, with many compressed ducts. There was no invasion of the underlying skeletal muscle. The features were consistent with a malignant PT. Within the tumour were foci of intraductal carcinoma of low nuclear grade (Fig. 2). The adjacent breast tissue also showed foci of intraductal carcinoma. Several lymphovascular tumour emboli were seen within the PT; however, despite extensive sampling, an invasive component could not be found. Two out of the 12 lymph nodes showed metastatic carcinoma.

Thus, though the carcinoma presumably had an invasive component (in view of lymph node metastases), this could not be demonstrated, probably due to the extensive nature of the stromal component of the PT. The presence of intraductal carcinoma within the adjacent breast tissue may indicate that the carcinoma was almost completely over-run by the malignant PT, leaving only foci of intraductal tumour, along with lymph node metastases.

Immunohistochemistry was performed on representative sections by the Avidin-Biotin peroxidase method, using monoclonal mouse anti-human antibodies (DakoCytomation, Denmark). Antigen retrieval was done using trypsin for cytokeratin and vimentin, EDTA for desmin, myogenin, oestrogen receptor (ER) and progesterone receptor (PR), and citrate for CD31. No antigen retrieval was done for epithelial membrane antigen (EMA). Antibody dilutions were as follows: cytoK 1:100, EMA 1:20, vimentin 1:50, desmin 1:50, myogenin 1:10, CD31 1:20, ER 1:50 and PR 1:100. Immunohistochemistry for ER and PR was performed on sections from an involved lymph node. The intraductal carcinoma stained with cytokeratin and EMA (Fig. 3). The sarcomatous component of the PT stained for vimentin, and focally for desmin and myogenin, while epithelial markers (cytokeratin and EMA) and S100 were negative. Immunostaining with CD31 highlighted the lymphatic channels with tumour emboli. The carcinomatous lymph node metastasis showed strong diffuse nuclear positivity for oestrogen (Fig. 4) and progesterone receptors. The patient received four cycles of chemotherapy (adriamycin and cyclophosphamide), and local irradiation, following which she was put on tamoxifen. At the last visit 11 months postsurgery, she was clinically free of disease. Mammography and ultrasonography showed no evidence of local recurrence.

## DISCUSSION

PTs, also called cystosarcoma phyllodes, are classified as benign, borderline and malignant. The term, cystosarcoma phyllodes, may be misleading, as this term implies a diagnosis of sarcoma even for the benign subtype. There are no reliable clinical criteria that can differentiate a fibroadenoma, a benign PT and a malignant PT.<sup>(1)</sup> Subclassification is based on microscopic findings, and features suggestive of a malignant PT include stromal hypercellularity and pleomorphism, high mitotic rate (> 5/10 hpf), necrosis and infiltrative tumour edge. The distinction between a benign and malignant PT is important because malignant tumours show higher rates of recurrence, and can show distal metastases. A wide local excision with a margin of more than 1 cm is considered adequate in all subtypes of PTs, and a mastectomy is done only if breast conservative surgery is not possible.<sup>(2)</sup> Metastasis in a PT is almost always haematogenous, and though lymph node metastasis been documented,<sup>(1,3,4)</sup> the incidence is not frequent enough to warrant a routine lymph node dissection.

The ductal component of a PT is usually benign, and though ductal elements may occur in local recurrences, metastatic lesions consist of only the sarcomatous component.<sup>(5)</sup> Kracht et al reported an exceptional case of metastatic PT in the lungs with glandular elements.<sup>(6)</sup> Ductal epithelium in a PT (or a fibroadenoma) may show squamous metaplasia and varying degrees of epithelial hyperplasia, ranging from mild to florid,<sup>(7)</sup> but very rarely warrants the diagnosis of intraductal carcinoma. The subtypes reported include *in situ* and invasive lobular carcinoma, tubular carcinoma, squamous carcinoma and ductal carcinoma (NOS). Carcinomatous lymph node metastases are extremely rare in these tumours, even in invasive carcinomas. In a series of 105 cases of carcinoma arising within fibroadenomas, there were no cases with lymph node metastases.<sup>(8)</sup> There has been only one case reported of invasive carcinoma with lymph node metastases arising in a benign PT.<sup>(9)</sup>

PTs that harbour carcinoma are usually benign,<sup>(10-15)</sup> and it has been stated that when malignant PT contains carcinoma, it becomes, by definition, a carcinosarcoma or metaplastic carcinoma<sup>(15)</sup> – as the tumour is composed of carcinomatous and sarcomatous elements. Non-invasive ductal carcinoma coexisting with a malignant PT is extremely rare, and has been described in only two cases, neither of which showed nodal metastases.<sup>(16,17)</sup> Nishimura et al described a case with intraductal papillary carcinoma, and a stromal component showing fibrosarcoma with foci of osteosarcoma and rhabdomyosarcoma. They speculated that a PT may be one of the origins of true carcinosarcoma.<sup>(16)</sup> In the case described by Nomura et al, non-invasive ductal carcinoma was seen within a malignant PT.<sup>(17)</sup> The sarcomatous areas were negative for the epithelial markers, and a

diagnosis of malignant PT with a non-invasive ductal carcinoma was made, rather than true carcinosarcoma of the breast. In agreement with Nomura et al, it is our opinion that when a tumour shows the distinctive morphology of a PT with coexistent foci of carcinoma, it should not be classified as a carcinosarcoma, and the two components present should be reported as separate entities.

Malignant PT with intraductal/invasive carcinoma differs in behaviour, treatment and prognosis from a carcinosarcoma. The latter, also known as metaplastic carcinoma, is a highly aggressive carcinoma with sarcomatoid features, and shows frequent metastasis (lymphatic and blood-borne) with a high mortality rate.<sup>(18)</sup> Malignant PTs, on the other hand, have a high rate of recurrence, and metastasis, which is less common, is almost exclusively haematogenous.<sup>(19)</sup>

Metaplastic carcinomas are almost always negative for hormone receptors.<sup>(20,21)</sup> Foci of intraductal/invasive carcinoma in a PT will show variable ER/PR expression, based on nuclear grade. Tumours (both intraductal and invasive) of a low nuclear grade are usually ER/PR positive, and those of a high nuclear grade are usually negative.<sup>(22)</sup> Both metaplastic carcinomas and malignant PTs with carcinomatous foci are rare, but it is important to distinguish between them as their treatment and prognosis varies.

Diaz et al advocated wide local excision as adequate treatment for patients with invasive carcinoma arising within a fibroadenoma, as they found no lymph node metastases in their series.<sup>(8)</sup> In the case described by Nomura et al, there was no recurrence in spite of the patient receiving neither chemotherapy nor irradiation.<sup>(17)</sup> Merck et al described a rare case of infiltrating duct carcinoma in one breast and synchronous PT arising in the other breast, and advocated treating each component individually, with no change from individual treatment regimes.<sup>(23)</sup> In the case described here, the presence of metastatic tumour in the lymph node suggests that axillary lymph node dissection should be performed in cases where lymph nodes are clinically involved.

The outcome in cases of carcinoma within a benign PTs is generally favourable,<sup>(12,13)</sup> however in a malignant PT the prognosis may be more guarded. Axillary lymph node dissection is not part of the standard treatment for PTs, but is required when there is coexistent invasive carcinoma. Conversely, in a PT where lymph nodes are clinically enlarged, extensive sampling of the tumour is important, to rule out foci of intraductal and/or invasive carcinoma. As these cases are extremely rare, treatment and follow-up of these cases are not standardised. It is recommended that treatment be customised in each case based on the presence of an invasive component, lymph node and distant metastases, and the carcinomatous component be treated independently of the PT.

## REFERENCES

1. Cohn-Cedermark G, Rutqvist LE, Rosendahl I, Silfversw ard C. Prognostic factors in cystosarcoma phyllodes. A clinicopathologic study of 77 patients. *Cancer* 1991; 68:2017-22.
2. Fou A, Schnabel FR, Hamel-Bena D, et al. Long-term outcomes of malignant phyllodes tumors patients: an institutional experience. *Am J Surg* 2006; 192:492-5.
3. Harada S, Fujiwara H, Hisatsugu T, Sugihara H. Malignant cystosarcoma phyllodes with lymph node metastasis--a case report. *Jpn J Surg* 1987; 17:174-7.
4. Minowitz S, Zeichner M, Di Maio V, Nicastri AD. Cystosarcoma phyllodes: a unique case with multiple unilateral lesions and ipsilateral axillary metastase. *J Pathol Bacteriol* 1968; 96:514-7.
5. Rosen PP. Fibroepithelial neoplasms. In: Rosen's Breast Pathology. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2001:190.
6. Kracht J, Sapino A, Bussolati G. Malignant phyllodes tumor of breast with lung metastases mimicking the primary. *Am J Surg Pathol* 1998; 22:1284-90.
7. Grimes MM. Cystosarcoma phyllodes of the breast: histologic features, flow cytometric analysis, and clinical correlations. *Mod Pathol* 1992; 5:232-9.
8. Diaz NM, Palmer JO, McDivitt RW. Carcinoma arising within fibroadenomas of the breast. A clinicopathologic study of 105 patients. *Am J Clin Pathol* 1991; 95:614-22.
9. Parfitt JR, Armstrong C, O'Malley. In-situ and invasive carcinoma within a phyllodes tumor associated with lymph node metastases. *World J Surg Oncol* 2004; 15:46.
10. Ramdass MJ, Dindyal S. Phyllodes breast tumour showing invasive squamous-cell carcinoma with invasive ductal, clear-cell, secretory and squamous components. *Lancet Oncol* 2006; 7:880.
11. Lim SM, Tan PH. Ductal carcinoma in situ within phyllodes tumour: a rare occurrence. *Pathology* 2005; 37:393-6.
12. Yasumura T, Matsui S, Hamajima T, et al. Infiltrating ductal carcinoma developing within cystosarcoma phyllodes--a case report. *Jpn J Surg* 1988; 18:326-9.
13. Ishida T, Izuo M, Kawai T. Breast carcinoma arising in cystosarcoma phyllodes: report of a case with a review of the literature. *Jpn J Clin Oncol* 1984; 14:99-106.
14. Christensen L, Nielsen M, Madsen PM. Cystosarcoma phyllodes. A review of 19 cases with emphasis on the occurrence of associated breast carcinoma. *Acta Pathol Microbiol Immunol Scand [A]* 1986; 94:35-41.
15. Rosen PP. Unusual clinical presentations of carcinoma. In: Rosen's Breast Pathology. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2001:660.
16. Nishimura R, Takahiro H, Imoto S, Mukai K. Malignant phyllodes tumor with a noninvasive ductal carcinoma component. *Virchows Arch* 1998; 432:89-93.
17. Nomura M, Inoue Y, Fujita S. A case of noninvasive ductal carcinoma arising in malignant phyllodes tumor. *Breast Cancer* 2006; 13:89-94.
18. Luini A, Aguilar M, Gatti G, et al. Metaplastic carcinoma of the breast, an unusual disease with worse prognosis: the experience of the European Institute of Oncology and review of the literature. *Breast Cancer Res Treat* 2007; 101:349-53.
19. Lenhard MS, Kahlert S, Hims I, et al. Phyllodes tumour of the breast: clinical follow-up of 33 cases of this rare disease. *Eur J Obstet Gynecol Reprod Biol* 2007; 138:217-21.
20. Tse GM, Tan PH, Putti TC, et al. Metaplastic carcinoma of the breast: a clinicopathological review. *J Clin Pathol* 2006; 59:1079-83.
21. Beatty JD, Atwood M, Tickman R, Reiner M. Metaplastic breast cancer: clinical significance. *Am J Surg* 2006; 191:657-64.
22. Tang P, Wang X, Schiffhauer L, et al. Expression patterns of ER-alpha, PR, HER-2/neu, and EGFR in different cell origin subtypes of high grade and non-high grade ductal carcinoma in situ. *Ann Clin Lab Sci* 2006; 36:137-43.
23. Merck B, Cansado Martinez P, Peres Ramos M. Infiltrating ductal carcinoma and synchronous malignant phyllodes tumour. Diagnostic and therapeutic approaches. *Clin Transl Oncol* 2006; 8:830-2.