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CASE REPORT

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# Malignant phyllodes tumour with a noninvasive ductal carcinoma component

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**Abstract** A malignant phyllodes tumour with a noninvasive ductal carcinoma component is reported. The patient was an 80-year-old Japanese woman with a breast tumour detected by routine physical examination. A simple mastectomy was performed. The excised tumour was 10.5×9.4×5.4 cm in size and bulged into the skin with ulceration. The macroscopic appearance was that of a phyllodes tumour. Histologically the tumour consisted mainly of stromal components with a leaf-like structure lined by atypical ductal epithelium. The epithelial component showed gradual evolution to intraductal papillary carcinoma in a few areas. The stromal component was composed mainly of fibrosarcoma with areas of osteosarcoma and rhabdomyosarcoma. Neither stromal invasion of intraductal carcinoma nor transition between the stromal and epithelial elements was seen. Three months after the operation, death occurred, with multiple pulmonary and subcutaneous metastases. This case probably represents malignant change in both the stromal and the epithelial components of a phyllodes tumour. Since the two elements were independent, the possibility that a phyllodes tumour may be one of the origins of true carcinosarcoma is raised.

**Key words** Breast · Malignant phyllodes tumour · Noninvasive ductal carcinoma · Carcinosarcoma

## Introduction

Breast tumours with macroscopical features of a phyllodes tumour, consisting of malignant stromal and epithelial components, are extremely rare. Only three such cases have been reported in the English literature [3, 6]. These cases are considered to be carcinoma arising from a malignant phyllodes tumour.

We now describe a case highly suggestive of noninvasive ductal carcinoma arising from a malignant phyllodes tumour.

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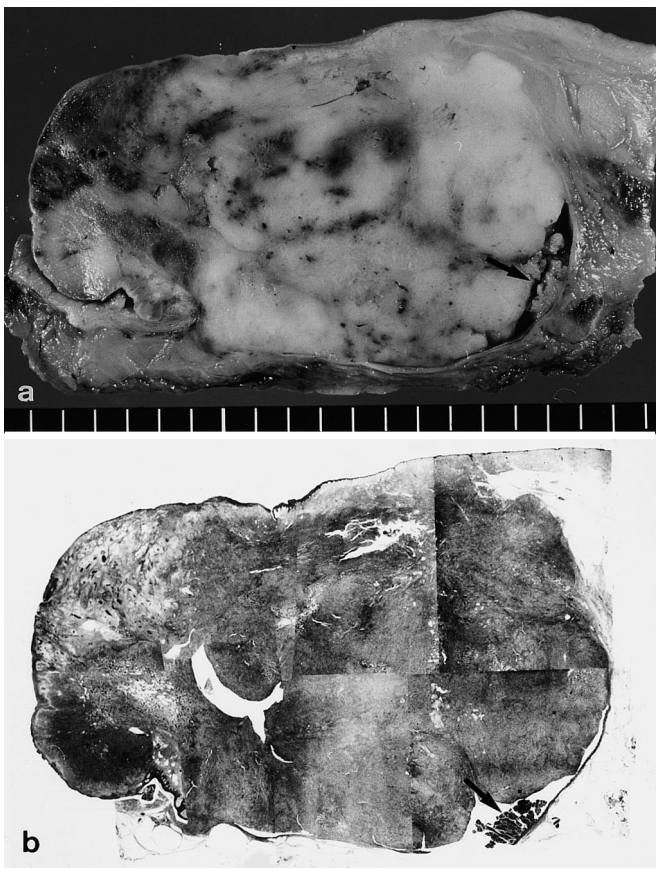


**Fig. 1a, b** Cut surface of the breast tumour. **a** Macroscopically, the cut surface is greyish white and lobulated. A cleft with intraluminal epithelial papillary projections is seen (*arrow*). **b** Panoramic view of the microscopic features. A cleft with papillary projections is indicated by the *arrow*. The stromal component is predominant

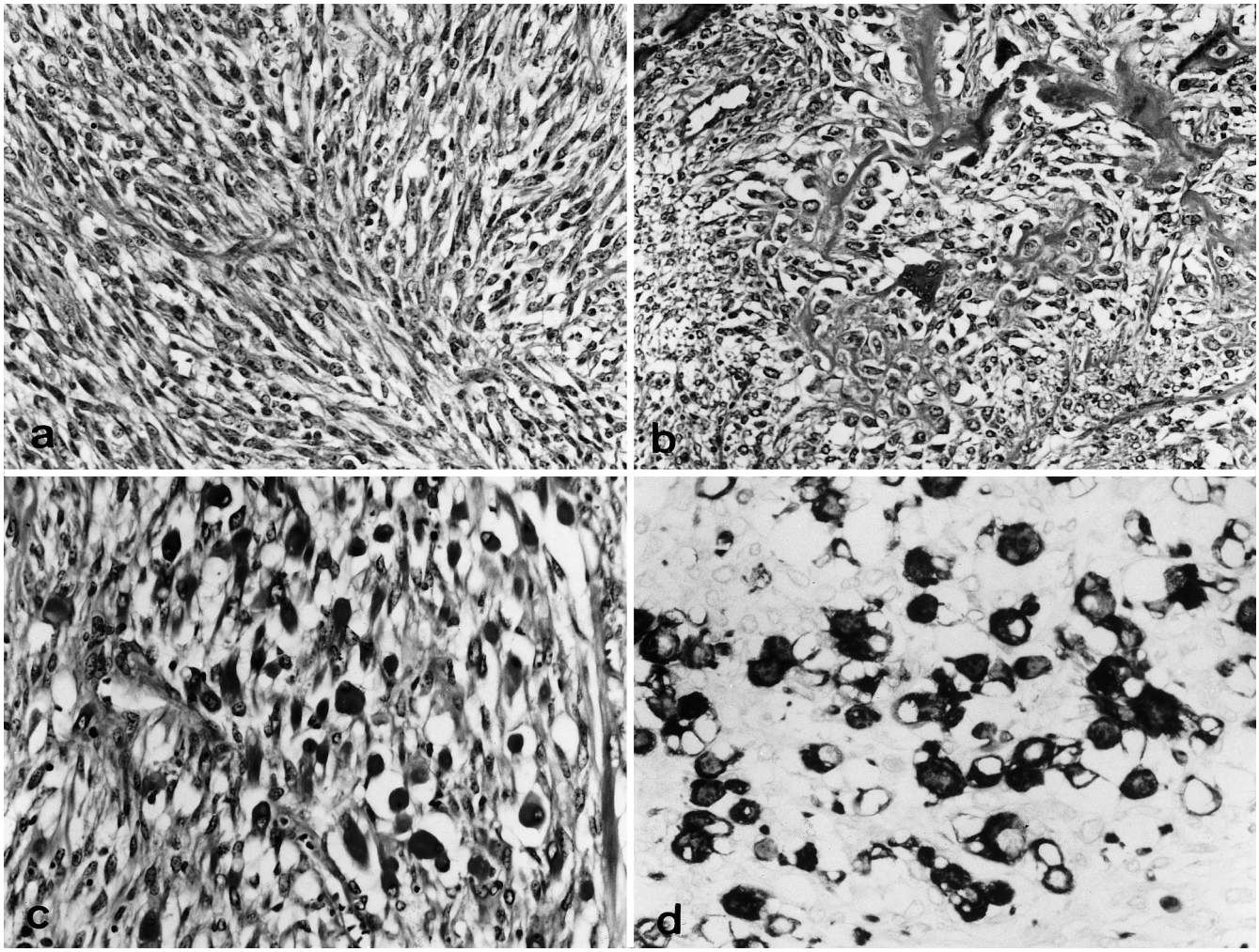


**Fig. 2a–d** The stromal component of the tumour. **a** Fibrosarcomatous area consisting of atypical spindle-shaped tumour cells arranged in an irregular fashion with a storiform appearance. H&E, X160. **b** Osteosarcoma. The irregularly-shaped osteoids and woven bone are shown. H&E, X160. **c** Rhabdomyosarcoma. The tumour cells have abundant eosinophilic cytoplasm with striation. H&E, X160. **d** Positive cytoplasmic staining for desmin is observed in the tumour cells with rhabdomyoblastic features. X320

## Clinical history

In December, 1995, an 80-year-old Japanese woman was admitted to the National Cancer Centre Hospital East, because of a lump in her right breast detected by routine physical examination at another hospital. Physical examination on admission revealed a firm tumour, 3.4×2.5 cm in size, in the lower half of the right breast. The mass invaded the skin, but was not fixed to the chest wall. The axillary lymph nodes were not palpable. On the basis of aspiration cytology, ultrasound and mammography, primary breast cancer was suspected. Initially, she was treated with anti-oestrogen therapy because of her past history of secondary Parkinsonism and her advanced age. However, the tumour grew rapidly despite this therapy, causing ulceration of the overlying skin. To achieve symptom palliation, a simple mastectomy was performed. Two months after the operation, multiple metastases to the lung and generalized subcutaneous tissue metastases were observed. Biopsy of the lung confirmed metastasis of the breast tumour. In October, 1996, the patient died at another hospital. Autopsy was not performed.

## Pathological findings

The tumour was 10.5×9.4×5.4 cm in size, and the upper portion bulged into the skin with ulceration. Its cut surface was greyish white with some haemorrhagic and fragile-appearing areas (Fig. 1a). The cut surface showed lobulation with clefts having intraluminal papillary projections (Fig. 1b). The tumour showed expansive growth into the extramammary adipose tissue, but did not invade the thoracic muscle.

Microscopically, the tumour consisted of both stromal and epithelial components. The stromal element predominated and was composed of fibrosarcomatous, osteosarcomatous, and rhabdomyosarcomatous components. In addition, synovial sarcoma-like areas with gland-like formation and areas of epithelioid cells were present. Most prominent were areas of fibrosarcoma consisting of markedly atypical spindle cells arranged in an irregular fashion (Fig. 2a). In osteosarcomatous areas the stroma showed the formation of irregularly shaped osteoid or woven bone, surrounded by proliferation of atypical osteoblasts (Fig. 2b). In rhabdomyosarcomatous components, tumour cells with abundant eosinophilic cytoplasm with striation were seen (Fig. 2c).

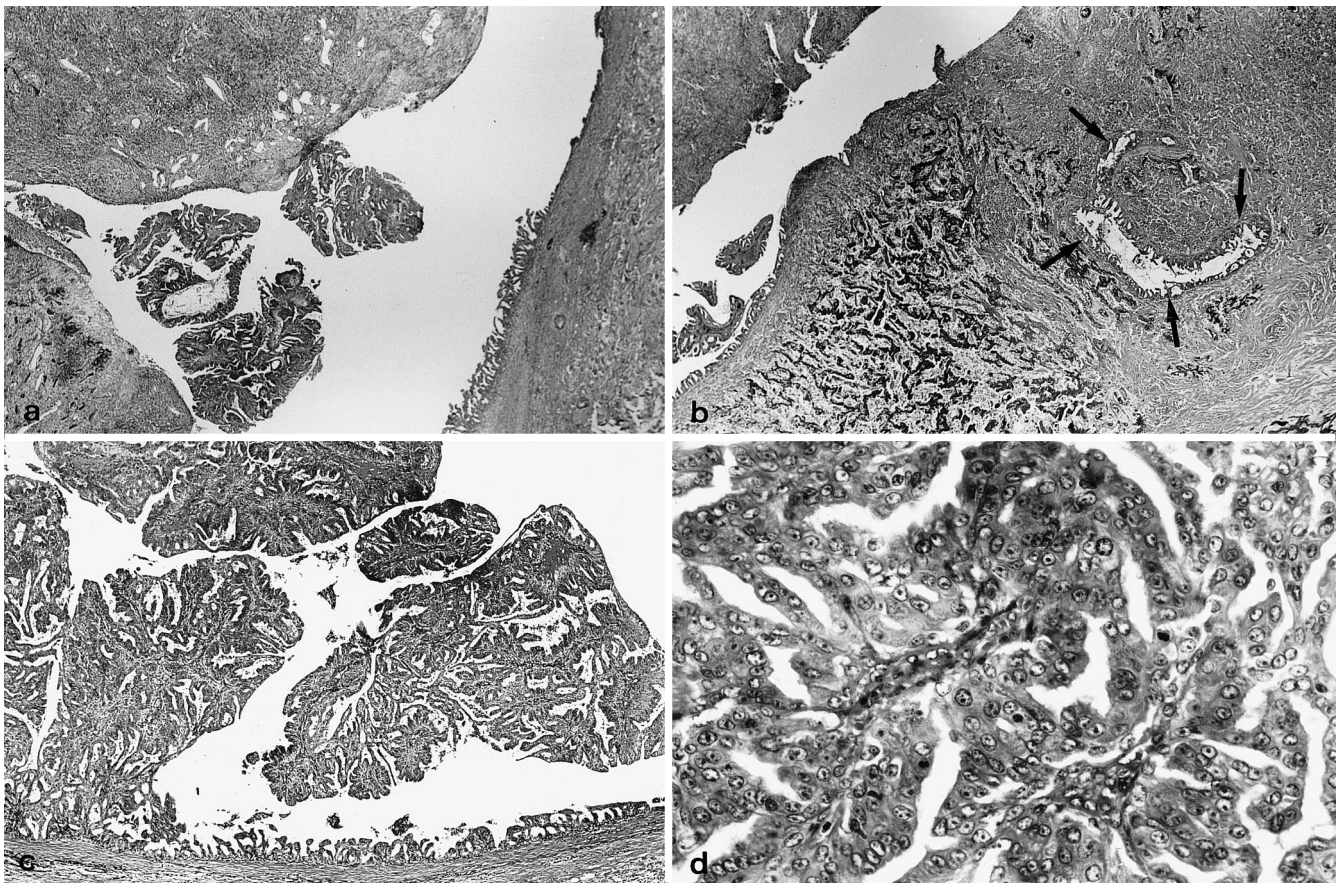


**Fig. 3a–d** Epithelial component of the tumour. H&E. **a** A cleft, lined with atypical ductal epithelium, shows papillary feature. X16. **b** A tubular duct, lined with atypical epithelium, is seen adjacent to the cleft (*arrows*). X16. **c** Atypical ductal epithelium is seen to gradually evolve into a markedly atypical papillary lesion. X32. **d** High-power magnification of the atypical papillary lesion. The epithelial cells have markedly atypical nuclei with prominent nucleoli. There are no myoepithelial cells in the lesion. On the basis of these features, the lesion was diagnosed as an intraductal carcinoma. X320

The epithelial element consisted of slit-like ducts compressed by stromal elements, which resembled the epithelial element of a phyllodes tumour (Fig. 3a). Adjacent to the slit-like ducts, there were tubular ducts lined by atypical epithelium without papillary features (Fig. 3b, arrows). The epithelial cells lining the slit-like ducts gradually changed from a single layer of low-grade atypical cells to highly atypical cells with papillary features (Fig. 3c). Atypical cells showing papillary features had markedly atypical nuclei with prominent nucleoli, indicative of malignancy of the noninvasive ductal carcinoma papillary type (Fig. 3d). There was no clear-cut boundary between the atypical epithelium and the definite carcinoma, nor was there evidence of stromal invasion by the carcinoma component. However, in some areas there was a suggestion of transition between the stromal elements and the epithelial elements with high-grade atypia (Fig. 4a).

The lung biopsy specimen obtained at another hospital showed proliferation of neoplastic spindle cells, resembling the stromal element of the primary breast tumour; this observation allowed the stromal elements to be interpreted as metastasis from the breast tumour.

Paraffin sections of formalin-fixed tumor tissue were used for immunohistochemical staining by the streptavidin–biotin-peroxidase complex (sABC) method [4]. Antibodies used in this study are listed in Table 1. All stromal elements showed diffuse positive staining for vimentin, but were negative for cytokeratin, EMA, and CEA (Table 2). Strongly positive cytoplasmic staining for desmin and sarcomeric actin was observed only in the rhabdomyosarcomatous element (Fig. 2d, Table 2). The “glands” in the synovial sarcoma-like element were negative for cytokeratin and EMA. Therefore, the possibility of synovial sarcoma was excluded. The epithelioid element was negative for cytokeratin, desmin, actins, and S-100, and thus did not support a diagnosis of epithelioid sarcoma, epithelioid leiomyosarcoma or epithelioid schwannoma, as initially suggested by haematoxylin and eosin staining (Table 2). Thus, the immunohistochemical results suggested that the stromal component of this tumour consisted mainly of fibrosarcoma with variable histological features, as well as a few areas indicative of osteosarcoma and rhabdomyosarcoma.

In the area suggestive of a transition between the stromal and epithelial elements, the latter stained positively for cytokeratin and EMA, whereas the former was negative for both (Fig. 4b). In addition, there was distinct linear staining of laminin and type IV collagen between the

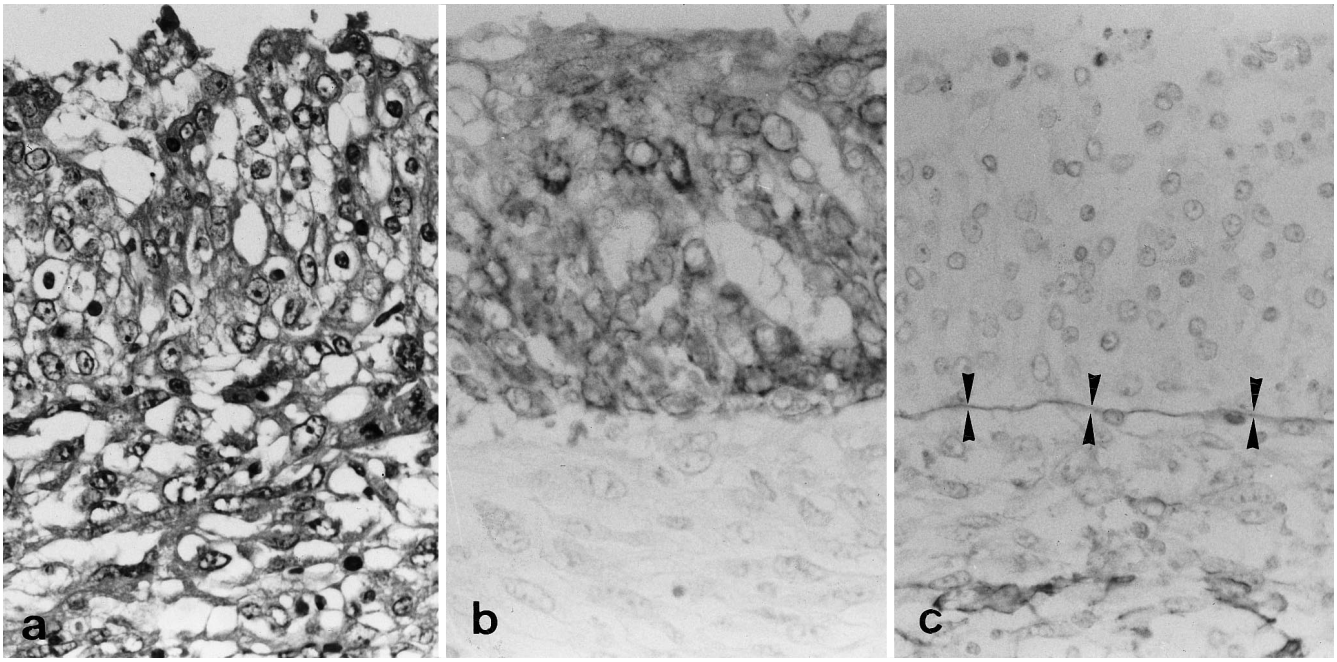


**Fig. 4a–c** An area suggestive of transition between the stromal and epithelial elements. X320. **a** The border between the epithelial and stromal components is indistinct. H&E. **b** The epithelial component is clearly demarcated from the stromal component by positive cytokeratin staining (AE1/3). **c** The basement membrane forming the border between the epithelial and stromal components is clearly demonstrated by positive staining for type IV collagen (*arrowheads*)

**Table 1** Primary antibodies used (*EMA* epithelial membrane antigen, *CEA* carcinoembryonic antigen, *Sr-Actin* sarcomeric actin, *Sm-Actin* alpha-smooth muscle actin, *S-100* S-100 protein, *ER* oestrogen receptor, *PgR* progesterone receptor, *P* polyclonal, *M* monoclonal)

| Antibody to | Source | Clonality | Dilution |
|---|---|---|---|
| Cytokeratins | | | |
| AE1/3[a] | Immunon, Pittsburgh, Pa. USA | M | ×100 |
| MNF116 | Dako, Glostrup, Denmark | M | ×100 |
| EMA | Dako | M | ×100 |
| CEA | Takara, Shiga, Japan | M | ×200 |
| Vimentin | Dako | M | ×50 |
| Desmin | Bio-Science, Emmenbrücke, Switzerland | P | ×250 |
| Sr-Actin | Dako | M | ×50 |
| Sm-Actin | Dako | M | ×500 |
| Myoglobin | Dako | P | ×200 |
| S-100 | Dako | M | ×1000 |
| ER | Novocastra, Newcastle-upon-Tyne, UK | M | ×50 |
| PgR | Novocastra | M | ×40 |
| Type IV collagen | Dako | M | ×100 |
| Laminin | E-Y Laboratories, San Mateo, Calif., USA | P | ×50 |

[a] Equivalent mixture of AE1 and 3

epithelial and stromal elements, indicating a basement membrane separating the stromal and epithelial elements (Fig. 4c, arrowheads).

There were no oestrogen or progesterone receptors in either the stromal or the epithelial elements.

## Discussion

Breast tumours showing both carcinomatous and sarcomatous components are divided into two categories. The first is carcinoma with metaplasia, especially of the heterologous or pseudosarcomatous type [5, 8]. The second is true carcinosarcoma [1, 3]. Carcinoma with metaplasia shows a transition between carcinoma and sarcomatous components, whereas the true carcinosarcoma does not.

In the present case, the tumour demonstrated histological features consistent with carcinoma with metaplasia, because there was a zone suggestive of transition between the stromal and epithelial elements. However, the immunohistochemical study clearly demonstrated the presence of a basement membrane between the two, and the stromal element was negative for cytokeratin and EMA. It was therefore concluded that the tumour was not a carcinoma with metaplasia.

True carcinosarcoma of the breast is defined as a tumour consisting of two distinct components, carcinoma and sarcoma, without evidence of transition between the two [1, 2]. According to this definition, the tumour in

**Table 2** Immunohistochemical staining of stromal and epithelial elements (*Stromal* stromal component, *FS* fibrosarcoma-like component, *OS* osteosarcoma-like component, *SS* synovial sarcoma-like component, *E* presenting epithelioid features, *RS* rhabdomyosarcoma-like component, *Epithelial*, epithelial component, ++ strongly positive, + positive, – negative)

| Antibody to | Tumour | | | | | |
|---|---|---|---|---|---|---|
| | Stromal | | | | | Epithelial |
| | FS | OS | SS | E | RS | |
| Cytokeratins | | | | | | |
| AE1/3[a] | – | – | – | – | – | ++ |
| MNF116 | – | – | – | – | – | ++ |
| EMA | – | – | – | – | – | ++ |
| CEA | – | – | – | – | – | + |
| Vimentin | ++ | ++ | ++ | + | ++ | – |
| Desmin | – | – | – | – | + | – |
| Sr-Actin | – | – | – | – | + | – |
| Sm-Actin | – | – | – | – | – | – |
| Myoglobin | – | – | – | – | – | – |
| S-100 | – | – | – | – | – | – |
| ER | – | – | – | – | – | – |
| PgR | – | – | – | – | – | – |

[a] Equivalent mixture of AE1 and 3

our present case can be classified as true carcinosarcoma. However, the macroscopic appearance of the cut surface of the tumour demonstrated a lobulated pattern with leaf-like features resembling those of a phyllodes tumour. In addition, the present case clearly demonstrated that some of the slit-like structures were composed of elongated ducts, compressed by the stromal element and lined with atypical ductal epithelium. The lining epithelium showed a transition from low- to high-grade atypical epithelium, and finally, definite carcinoma of the papillary type. On the basis of these observations, the tumour was diagnosed as a malignant phyllodes tumour with a component of noninvasive ductal carcinoma rather than a true carcinosarcoma.

Only three cases of malignant phyllodes tumour of the breast with a carcinomatous component have been reported [3, 4]. In the earlier reports, the macroscopic appearance of the tumours was not described in detail. In addition, immunohistochemical study to rule out a transition between the sarcomatous and epithelial elements was not performed. These cases may have been carcinomas with metaplasia.

The prognosis of a tumour such as that of our case is thought to be similar to that of a malignant phyllodes tumour without a carcinomatous component, because in this case the latter component was noninvasive. Malignant phyllodes tumour with an osteosarcomatous component have been recognized as highly aggressive and as producing systemic metastasis [7], as in our patient.

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