INTRODUCTION

Phyllodes tumor (PT) of the breast is a rare biphasic fibroepithelial neoplasm that accounts for less than 1% [1] of primary breast neoplasms. PT usually presents as a rapidly growing and clinically benign breast lump in females within the fourth or fifth decade of life [2,3]. PT typically exhibits an enhanced intracanalicular growth pattern with leaf-like projections into dilated lumens. Malignant PTs are more readily characterized by stromal pleomorphism and overgrowth, frequent mitoses and infiltrative borders [4]. In case of large growing malignant PTs with stromal predominance, it is difficult to distinguish between a pure sarcoma and malignant PT. It is important to thoroughly examine multiple sections from the view point of residual epithelial structure in morphological diagnosis.

CASE REPORT

A 57-year-old woman presented with a 20-year history of swelling of the right breast. She was referred to another hospital due to a painful and swollen right breast with bleeding. Physical examination revealed a massively enlarged right breast over 20 cm in maximum diameter. Core-needle biopsy was suspicious for low-grade myofibroblastic sarcoma (LGMS). The subsequent total mastectomy with partial resection of the pectoral muscles showed predominance of stromal hypercellularity without an epithelial component. However, we diagnosed this as a malignant PT because focal areas showed a leaf-like pattern. In the case of large malignant PTs that exhibit stromal predominance, it can be difficult to distinguish between a pure sarcoma and malignant PT. It is important to thoroughly examine multiple sections from the view point of residual epithelial structure in morphological diagnosis.

Summary: We present a case of a 57-year-old woman with a giant malignant phyllodes tumor (PT) in her right breast, with maximum diameter of 20 cm. The core-needle and excisional biopsy specimens were diagnosed as suspicious for low-grade myofibroblastic sarcoma (LGMS). The subsequent total mastectomy with partial resection of the pectoral muscles showed predominance of stromal hypercellularity without an epithelial component. However, we diagnosed this as a malignant PT because focal areas showed a leaf-like pattern. In the case of large malignant PTs that exhibit stromal predominance, it can be difficult to distinguish between a pure sarcoma and malignant PT. It is important to thoroughly examine multiple sections from the view point of residual epithelial structure in morphological diagnosis.

Key words giant phyllodes tumor, phyllodes tumor, phyllodes tumor malignant type
Mammographic and ultrasonographic examinations could not be carried out because of the pain caused by the huge tumor. Computed tomography (CT) showed a $20 \times 14 \times 9.7$ cm heterogeneous breast mass with diffuse enhancement that was suspicious for chest wall invasion (Fig. 2a). T2 weighted magnetic resonance imaging (MRI) study revealed a heterogeneous pattern with high signal intensity (Fig. 2b). Axillary lymph nodes were not detected in MRI.

We performed an excisional biopsy of the tumor, which showed marked stromal hypercellularity without an epithelial component. By immunohistochemistry staining, the stromal cells were positive diffusely for alpha smooth muscle actin, Calponin, HHF35, CD10 and vimentin. But they were negative for desmin, S-100, CD34, epithelial membrane antigen and AE1/AE3. Reactivity with MIB-1 and p53 was seen in 20.6% and 24.7% of the cells, respectively. Histopathological diagnosis of the excisional specimen was the same as the prior core-needle biopsy: “suspicious for LGMS”.

Her hemoglobin improved from 6.9 g/dl to 11.0 g/dl by preoperative blood transfusion. Furthermore we performed transcatheter arterial embolization of the breast tumor in order to reduce blood loss during the operation and applied Mohs’ paste, which is often used for hemorrhagic tumors to reduce the amount of exudate, bleeding and foul smell. Administration of internal oxycodone hydrochlorides relieved the severe breast pain.

She underwent a modified radical mastectomy with sufficient surgical margin, and partial resection of the pectoral muscles. The tumor had no invasion into the rib, but axillary lymph nodes were swollen. The wound was able to close primarily, without skin grafting (Figs. 3), and the total blood loss was 985 cc.
The resected tumor specimen measured $21.5 \times 16 \times 9$ cm and weighed 2120 g, and appeared as a white, soft and mucoid homogenous mass with focal hemorrhage. Microscopic findings showed a highly cellular stromal tumor composed of spindled cells with marked atypia and brisk mitotic activity (mean: 30/10HPFs) (Figs 4a,b). Immunohistochemically, MIB-1 and p53 was seen in 50.5% and 41.3% of the cells, respectively.

**Figs. 3(a,b,c).** Operative findings: A modified radical mastectomy and partial resection of pectoral muscles were performed.

**Figs. 4(a,b,c,d).** Histopathological findings: The tumor is highly cellular with stromal overgrowth. They are spindled in shape with marked atypia and brisk mitotic activity (HE stain, a: $\times 100$, b: $\times 400$ magnification). Immunohistochemically, MIB-1(c) and p53 (d) was seen in 50.5% and 41.3% of the cells, respectively (c, d: $\times 400$ magnification).
TAKENAKA ET AL.

Kurume Medical Journal Vol. 58, No. 2, 2011

(Figs. 4c,d). Some stromal cells showed lipoblast-like differentiation. However, further careful examination of additional sections revealed an epithelial component with a leaf-like pattern (Figs. 5). The final histopathological diagnosis was PT, malignant type. The margin of the resected tumor showed partially infiltrative growth into skin, but no invasion into muscles or lymphovas. There were no axillary lymph node metastases.

She recovered well, and there was no evidence of local recurrence or distant metastasis 17 months after surgery without adjuvant chemotherapy.

DISCUSSION

PT of the breast is a rare biphasic fibroepithelial neoplasm that accounts for about 1% [1] of primary breast tumors. The disease occurs predominantly in middle-aged women, with the average age of presentation at 40 years old [5-8]. They often present clinically as a painless mass with an average size of 4-5 cm [9,10]. The first treatment of choice is surgical resection. Axillary lymph node metastasis is rare, and lymph node dissection is not required. The role of adjuvant therapy for PT with chemotherapy and/or radiation therapy has not been clearly defined by prospective studies [6,11].

Although local recurrence is common (21% for benign types, 46% for borderline types, and 65% for malignant types [12]), prognosis is generally good, with 5-year survival rates of 91% and 82% for benign/ borderline types and malignant type [2], respectively. Local recurrence has been associated with a positive surgical margin, stromal overgrowth and histological classification. Stromal overgrowth was an especially predictive factor for local recurrence in cases with a positive surgical margin [13].

Many biological markers have been evaluated for their prognostic value, and cell proliferation has shown a correlation between MIB-1 positivity and histologi-

### TABLE 1.

<table>
<thead>
<tr>
<th>Material</th>
<th>AE1/AE3</th>
<th>Vimentin</th>
<th>α-SMA</th>
<th>Calponin</th>
<th>HHP35</th>
<th>CD10</th>
<th>MIB-1</th>
<th>p53</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy</td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>20.6%</td>
</tr>
<tr>
<td>Resected specimen</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The stroma of hypercellularity</td>
<td>−</td>
<td>++</td>
<td>+</td>
<td>−</td>
<td>++</td>
<td>+</td>
<td></td>
<td>50.5%</td>
</tr>
<tr>
<td>Resected specimen</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The stroma of leaf-like pattern</td>
<td>−</td>
<td>++</td>
<td>+</td>
<td>−</td>
<td>+</td>
<td>+ (focal)</td>
<td></td>
<td>8.6%</td>
</tr>
</tbody>
</table>

*Fig. 5(a,b). Histopathological findings by multiple sections: There is an epithelial component with leaf-like pattern appeared in the tumor (a: HE stain, ×40 magnification).*
cal grade. Expression of p53, commonly used as a surrogate for identification of a tumor suppressor gene mutation, has been correlated with tumor grade. Among biological markers, MIB-1 index (0.7-6% for benign types, 11.2% for borderline types and 30-31.2% for malignant types [14,15]) and p53 expression status (0-4% for benign/borderline types and 55-65% for malignant types [8,14]) may be significant prognostic factors. Table 1 summarizes immunohistochemical staining results of this case.

The tumor size and several US and MRI findings can be used to help preoperatively distinguish between malignant or benign PT. In MRI, internal non-enhanced septations, silt-like patterns in enhanced images and signal changes from T2-weighted to enhanced images correlated significantly with the histologic grade [16]. In this case, MRI findings were not characteristic of PT.

PT typically exhibits an enhanced intracanalicular growth pattern with leaf-like projections into dilated lumens. In the malignant types, the stroma shows frank sarcomatous changes, which most often are fibrosarcoma-like. Due to overgrowth of the sarcomatous components, the epithelial component may only be identified after examining multiple sections. As malignant PT grows larger and the stromal component predominates, it becomes difficult to distinguish between pure sarcoma and malignant PT.

LGMS seems to represent a distinct entity in the spectrum of low-grade myofibroblastic neoplasms and is distinguishable from fibromatosis, myofibromatosis, solitary fibrous tumor, fibrosarcoma, and leiomyosarcoma [17]. LGMS of the breast is very rare, and only seven cases have been reported in the literature [18].

The final diagnosis differed from the biopsy diagnoses due to the focal presence of an epithelial component in the resected specimen. In case of biopsy specimens showing predominately stromal lesions, it is important to thoroughly examine the resected specimen for possible epithelial components.

In conclusion, diagnosis of PT, and assignment of histological characteristics are still fraught with uncertainties, but the method described here is probably still the most practical approach [19]. Assessment of biological markers does not significantly improve prognostic prediction. Further molecular level assessment of PT may provide more insight into the biology of this tumor.

REFERENCES
