Breast Cancer
Vol. 12 No. 2 April 2005

Case Report

A Case of Carcinosarcoma of the Breast

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Carcinosarcoma is a rare malignant tumor of the breast. A 59-year-old woman was admitted to our hospital with a complaint of a right breast mass for one month. The mass grew rapidly, and modified radical mastectomy was performed. Based on the histological findings of carcinomatous and sarcomatous components entangled without a transition area, and the results of immunohistochemical staining, carcinosarcoma of the breast was diagnosed. Within 9 months of the surgery, a recurrent lesion appeared in her chest wall. As shown by local resection, this recurrent tumor had only a carcinomatous component.

Such tumors are very rare, and there have been no detailed reports of recurrence patterns of carcinosarcoma. Here we report our pathological findings in detail.

Breast Cancer 12:149-153, 2005.

Key words: Carcinosarcoma, Breast

True carcinosarcoma is rare and aggressive. It is strictly defined as a mixed tumor consisting of a carcinomatous component and a malignant nonepitherial component of mesenchymal origin without a transition zone between the two elements. This tumor should be differentiated from other metaplastic carcinomas, including spindle cell carcinoma (so-called carcinosarcoma), malignant phyllodes tumor and stromal sarcoma.

We report here our experience with a case of carcinosarcoma of the breast, describing our pathological and immunohistochemical findings.

Case Report

A 59-year-old-woman was admitted to our institute due to a right breast mass that she had noticed a month previously. Her elder brother had had gastric cancer. Her obstetric history was noncontributory.

On physical examination, an irregularly shaped mass measuring 5 × 4 cm was palpable in the upper outer quadrant of the right breast. It was uneven on the surface and not sharply demarcated, with good mobility. There was no adhesion to the skin or the pectoral muscle. Regional lymphadenopathy was not noticed. Mammography showed a high-density mass with marginal irregularity and pleomorphic calcification (Fig 1). A 4.0 × 3.9 × 2.0 cm solid mass was revealed by ultrasonography (Fig 2). Solid-tubular carcinoma was diagnosed by needle biopsy, and showed rapid growth in the preoperative period. A modified radical mastectomy was performed.

Macroscopically, the cut surface of the tumor was 3.5 × 1.3 cm in size, elastic and soft in consistency. The cut surface was grayish white, showing solid and lobulated features. There was no adhesion to the skin.

After macroscopic examination, the tissue sample was fixed in 10% formalin. Paraffin sections were prepared and stained with hematoxylin and eosin. Sections were immunostained according to the avidin-biotin peroxidase method with anti-cytokeratin AE1/AE3 antibody (Dako Corporation, Carpenteria, CA, 1:100 dilution), anti-cytokeratin CAM5.2 antibody (Dako Corporation, Carpenteria, CA, 1:1 dilution), anti-vimentin antibody (Dako Corporation, Carpenteria, CA, 1:100 dilution), anti-human smooth muscle actin antibody (Dako Corporation, Carpenteria, CA, 1:400 dilution). Microscopically, the tumor consisted of intermingled carcinomatous and sarcomatous

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Received March 13, 2004; accepted November 19, 2004

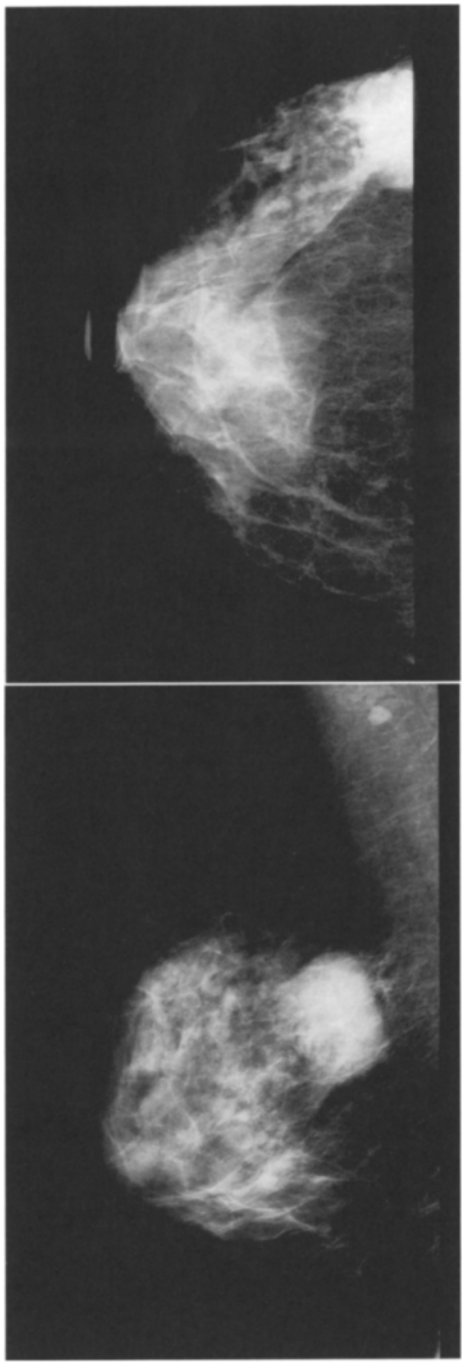

Fig 1. A high-density irregular mass with pleomorphic calcification can be seen in this mammogram.

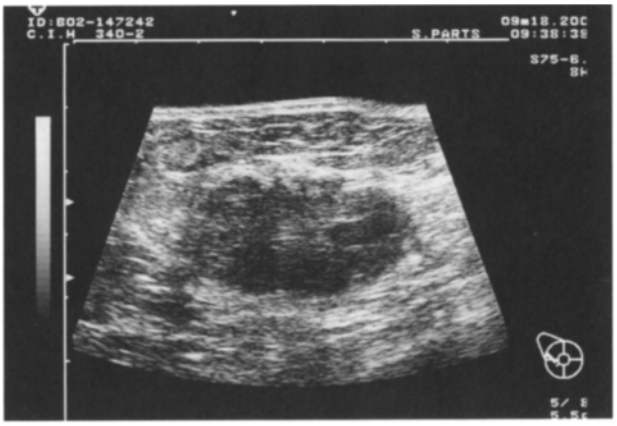

Fig 2. Ultrasonography showed a 40 × 39 × 20 mm solid and nonhomogenous mass.

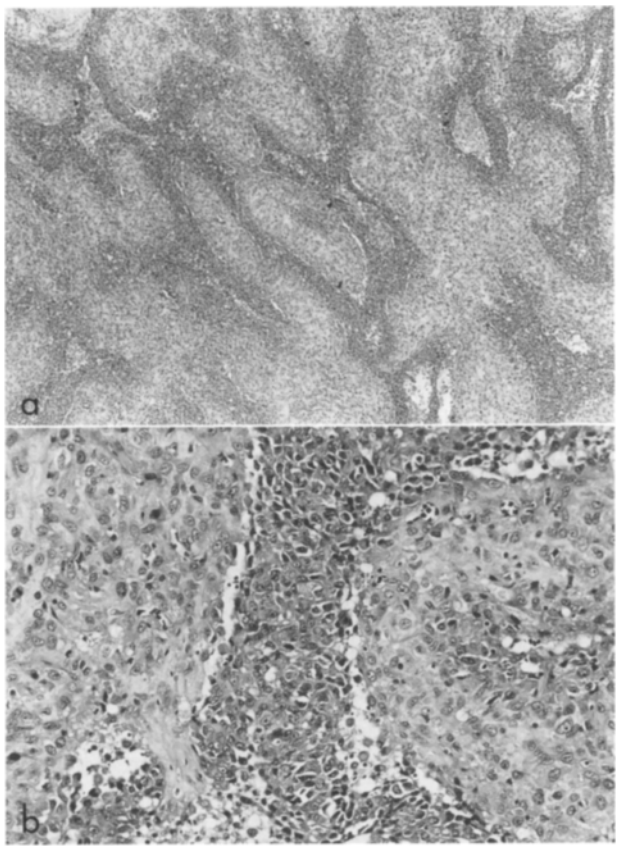

Fig 3. Microscopic view of the tumor demonstrated that tumor consisted of intermingled carcinomatous and sarcomatous areas such as this leaf-like structure (Fig 3a H.E., original magnification ×4). Mitosis are plentiful in both areas. There was no transition area between these two components (Fig 3b, H.E., original magnification ×20).

areas such as a leaf-like structure of phyllodes tumor (Fig 3a). The atypical nests of invasive carcinoma extended into the sarcomatous structure of the tumor with pleomorphic spindle cells. These sarcomatous areas showed pleomorphism with bizarre and giant hyperchromatic nuclei, but there were no obvious sarcomatous features such as liposarcomatous, chondrosarcomatous, and osteosarcomatous findings. These two components interlocked with each other without transition areas (Fig 3b). Central necrosis and infiltration to fat tissue were seen, but there was no obvi-

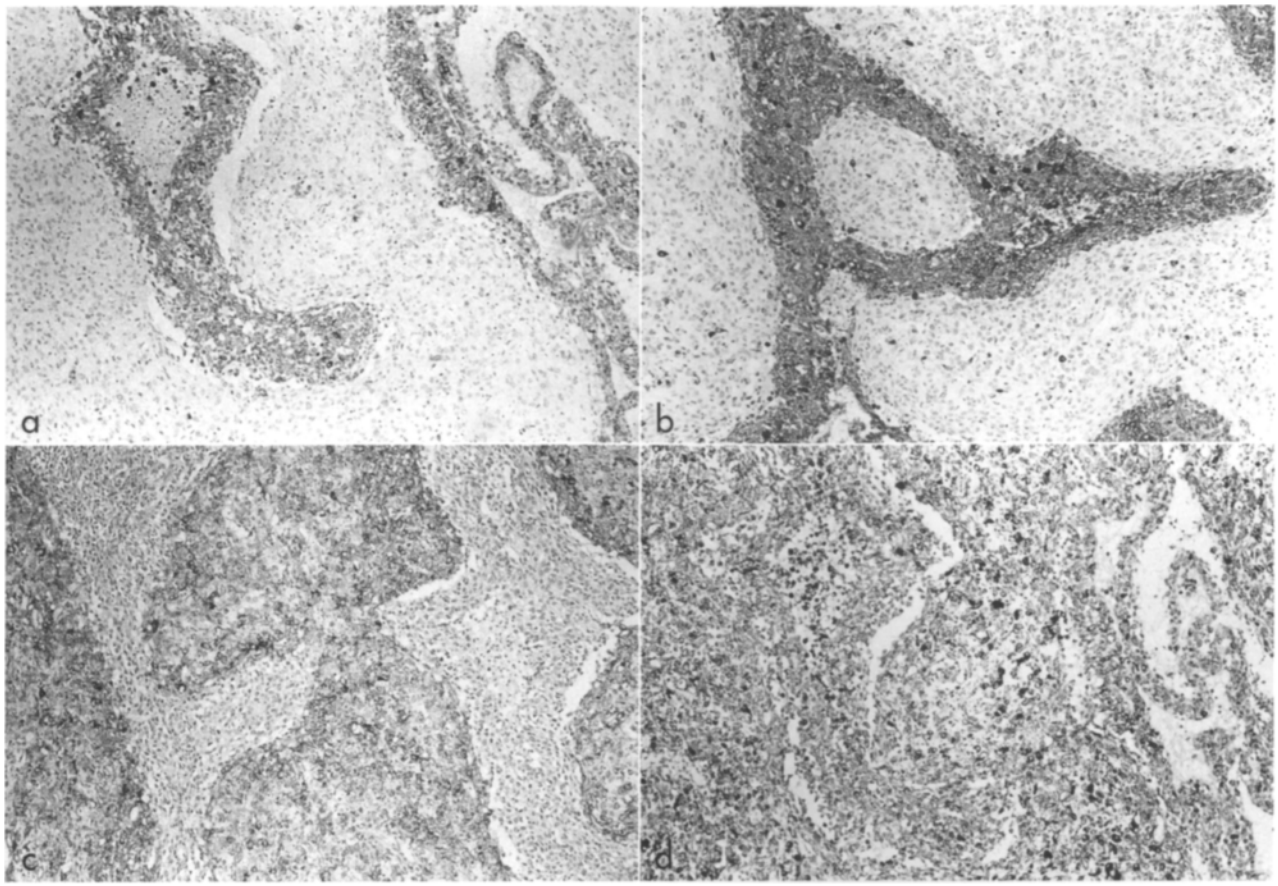

Fig 4. Immunohistochemical staining was positive in the epithelial component with AE1/AE3 (Fig 4a, original magnification × 10) and CAM5.2 (Fig 4b, original magnification ×10), while sarcomatous cells were positive for smooth-muscle actin (SMA) (Fig 4c, original magnification ×10), and both components were positive for vimentin (Fig 4d, original magnification ×10).

ous vascular invasion in this tumor. Marked mitosis was seen, 25/high power field (HPF) in the carcinomatous component and 8/HPF in the sarcomatous component. No metastasis to lymph nodes was noted (0/30). Hormonal recepter assay revealed the tumor to be negative for both estrogen and progesterone receptors in both the carcinomatous and sarcomatous components. Immunohistochemical staining revealed positive reaction in the epithelial component for cytokeratins (AE1/AE3, CAM5.2) (Fig 4a, 4b), while sarcomatous cells were positive for smooth-muscle actin (SMA) (Fig 4c), and both components were positive for vimentin (Fig 4d). Carcinosarcoma of the breast was diagnosed.

The patient was treated with cyclophosphamide (100 mg/m^2 orally, days 1-14), methotrexate (40 mg/m^2, days 1, 8) and 5-fluorouracil (600 mg/m^2, days 1, 8) for 6 cycles as adjuvant chemotherapy and followed. Ten months after surgery, she noticed an elevated mass beneath the scar. On ultrasonography, an irregularly shaped and hypoechoic mass, 3.8 × 3.6 × 2.6 cm in size was revealed. Fine-needle aspiration cytology was performed, and local recurrence was diagnosed. Magnetic resonance imaging showed peritumoral invasion (Fig 5). After systemic screening for distant metastasis, a local resection of surrounding tissue, including parts of the pectoralis major, serratus anterior, external intercostals and external oblique muscles, was performed. The resected tumor measured 4.0 × 3.0 cm. Microscopically, the component of this recurrent tumor showed proliferation of carcinoma cells, resembling the epithelial component of the breast tumor without any sarcoma (Fig 6).

Radiation therapy was delivered postoperatively to the chest wall, with a total dose of 50 Gy. She is being closely followed, and she has remained free of disease for 5 months after the second surgery.

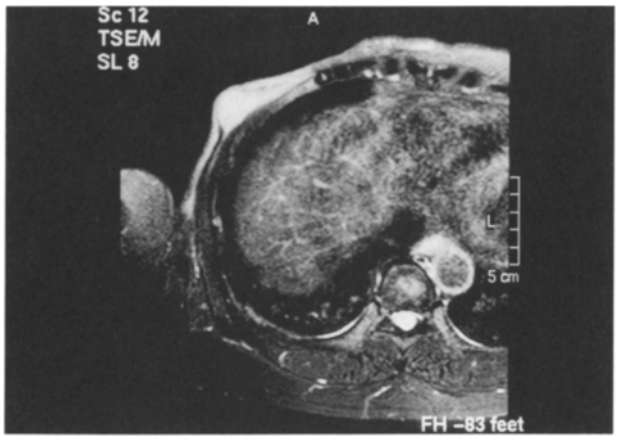

Fig 5. Magnetic resonance imaging revealed a recurrent tumor 25 × 17 mm with peritumoral invasion.

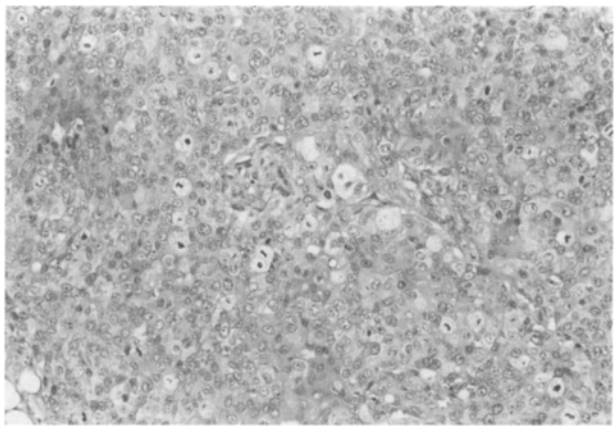

Fig 6. Microscopically, the recurrent tumor consisted of a proliferation of carcinoma cells, similar to the epithelial component of the original breast tumor and without a sarcomatous component (H.E., original magnification ×20).

Discussion

True carcinosarcoma of the breast is extremely rare. The strict definition of this tumor requires both a carcinomatous component and a malignant non-epithelial component of mesenchymal origin, without evidence of a transition zone between the two elements[1,2]. Primary sarcoma of the breast is also rare and constitutes 0.6 to 1.2% of the total number of malignant breast tumors[3]. The incidence of carcinosarcoma has been reported as to be 0.1 to 0.2% of breast carcinomas[3,4].

The origin of this tumor has not been proven; one controversial idea is that a proliferation of myoepithelial cell develops into this tumor[1,5]. In the present case, immunohistochemical staining showed the epithelial component to be positive for cytokeratin, while sarcomatous cells were positive for smooth muscle actin, and both components were positive for vimentin. Therefore, the possibility of the tumor being derived from a cell with potential biphasic differentiation was considered. On the other hand, several reported cases of carcinosarcoma were suggested to arise from pre-existing fibroadenomas or phyllodes tumors[2,5]. In the present case, neither fibroadenoma nor phyllodes tumor were detected in post-operative material, but the structure of the tumor was similar to a phyllodes pattern, so a pre-existing phyllodes tumor must have existed. Malignant phyllodes tumor, which has a malignant epithelial component, is thought to a subtype of true carcinosarcoma. Such cases of malignant phyllodes tumor are also very rare, and Nishimura *et al.* reported only three cases[6,7]. The present case may be a subtype of malignant phyllodes tumor with a malignant epithelial component.

Carcinosarcoma of the breast should be distinguished from metaplastic carcinoma, including spindle cell carcinoma, carcinoma with cartilaginous or osseous metaplasia, matrix producing carcinoma, fibrosarcoma and other types of sarcoma. The most important finding to differentiate metaplastic carcinoma from carcinosarcoma is whether a transition zone exists[1,2]. Carcinoma of the breast can undergo spindle-cell and other metaplasia, such as fibroblastic, chondroid, osseous, or osteoblastic. Although these metaplastic and infiltrative cancer cells form pseudosarcomatous stroma, as if carcinomatous components are admixed with sarcomatous components, a transition zone is always seen between these two components. The cumulative 5-year survival rate of carcinosarcoma is 49%. The survival rate for spindle cell carcinoma and matrix-producing carcinoma is 64% and 68%, respectively, so these tumors should be distinguishable other than by the difference in their prognosis[1].

Though any type of sarcoma arising from mesenchymal tissue can be confused with carcinosarcoma, there is no proof of malignant epithelial elements in these sarcomas. A carcinomatous component may be very minor in carcinosarcoma; therefore, carcinomatous elements can be lost by inadequate sampling and diagnosed as sarcomas, making careful study necessary to corroborate the diagnosis[5].

Treatment strategies for carcinosarcoma resemble those for breast cancer. In almost all of

the reported cases, mastectomy was performed, with or without axillary dissection[1-4]. Carcinosarcoma metastasizes by the lymphogenous route, and Wargotz and Norris reported that involved axillaly lymph nodes in which carcinomatous and/or sarcomatous components were present occurred in about 26% of all cases[1]. Therefore axillary dissection was suggested. Postoperative radiation and chemotherapy in various combinations have been used, but do not seem to be effective[1]. The prognosis of carcinosarcoma is poor. This tumor also shows hematogenous metastasis. Pleural and pulmonary metastasis are more common than skeletal, liver, or brain metastasis. Any distant metastasis is ominous for patients, because of the fatal potential[1], but local recurrence is not as threatening and can generally be treated surgically[1]. Although surgical resection, intensive chemotherapy, and radiation have all been reported for recurrence, there is no established treatment modality[1]. In the present case, interestingly, the recurrent tumor consisted of a carcinomatous element only. Even after surgical resection and radiation therapy, careful follow up is needed because recurrence can be rapid.

In conclusion, we report a case of carcinosarcoma arising in the breast. This is a very rare, malignant tumor, the diagnosis of which is made less difficult with detailed histological investigation to differentiate it from other, similar tumors.

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