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Case Report

Stromal Sarcoma with Features of Giant Cell Malignant Fibrous Histiocytoma

Yuko Kijima[*1], Yoshihisa Umekita[*2], Heiji Yoshinaka[*1], Shuhei Taguchi[*2], Tetsuhiro Owaki[*1], Yawara Funasako[*1], Akihiko Sakamoto[*1], Hiroki Yoshida[*2], and Takashi Aikou[*1]

*[*1]Department of Surgical Oncology, Breast and Endocrine Surgery, Kagoshima University Graduate School of Medical and Dental Sciences, [*2]Department of Tumor Pathology, Kagoshima University Graduate School of Medical and Dental Sciences, Japan*

We report a case of primary giant cell malignant fibrous histiocytoma (GCMFH) of the breast. A 56-year-old Japanese woman presented with a firm mass in the right breast. Mammography and ultrasonography revealed a well-circumscribed and lobulated mass in the upper outer quadrant of the right breast, indicative of a benign breast tumor or mucinous carcinoma. Magnetic resonance imaging revealed a restricted breast tumor without intraductal spread. Computed tomography and bone scintigraphy found no sites of distant metastases. Fine needle aspiration biopsy showed several clusters of atypical cells associated with numerous multinucleated giant cells. Breast-conserving surgery with axillary lymph nodes dissection was performed. Histological examination showed primary GCMFH of the breast. No metastases were identified in any of the 15 left axillary lymph nodes resected and surgical margins were free from tumor cells. The tumor was negative for both estrogen and progesterone receptor. Neither adjuvant chemoendocrine therapy nor postoperative radiotherapy was given, and the patient has remained disease free for 30 months postoperatively. To our knowledge, only 30 cases of primary MFH of the breast have been reported in the literature.

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Key words: Breast sarcoma, Malignant fibrous histiocytoma, Giant cell

Introduction

Primary sarcomas occurring in breast comprise less than 1% of all malignant breast neoplasms[1, 2], and are a highly heterogeneous group including malignant fibrous histiocytoma (MFH), fibrosarcoma, angiosarcoma, leiomyosarcoma, liposarcoma, osteosarcoma, rhabdomyosarcoma and other sarcomas. There are very few reported cases of MFH of the breast that have been confirmed by immunohistochemical investigation[3]. We report a case of giant cell MFH (GCMFH) of the breast and review the literature.

Reprint requests to Yuko Kijima, Department of Surgical Oncology, Breast and Endocrine Surgery, Kagoshima University Graduate School of Medical and Dental Sciences, 8-35-1, Sakuragaoka, Kagoshima 890-8544, Japan.
E-mail: ykijima@m3.kufm.kagoshima-u.ac.jp

Abbreviations:
GCMFH, Giant cell malignant fibrous histiocytoma; MFH, Malignant fibrous histiocytoma; MPT, Malignant phyllodes tumor; FNAB, Fine needle aspiration biopsy

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Case Report

A 56-year-old postmenopausal Japanese woman was referred to our hospital with a 1-month history of a painful mass in the right breast. She had been received neither radiation therapy nor surgical treatment of the breast. On physical examination, a hard tumor with clear margins and good mobility, about 5.0 × 4.5 cm, was palpable in the right breast. Mammography revealed a well-circumscribed, lobulated mass of soft tissue density, denser than the adjacent parenchyma in the upper right quadrant, and 40 mm in maximum diameter. No calcification was present. Ultrasonography revealed a heterogenous mass with relatively high internal echogenicity (Fig 1). Benign intracystic tumor or special type of breast carcinoma such as mucinous carcinoma was suspected. Fine needle aspiration biopsy (FNAB) showed several clusters

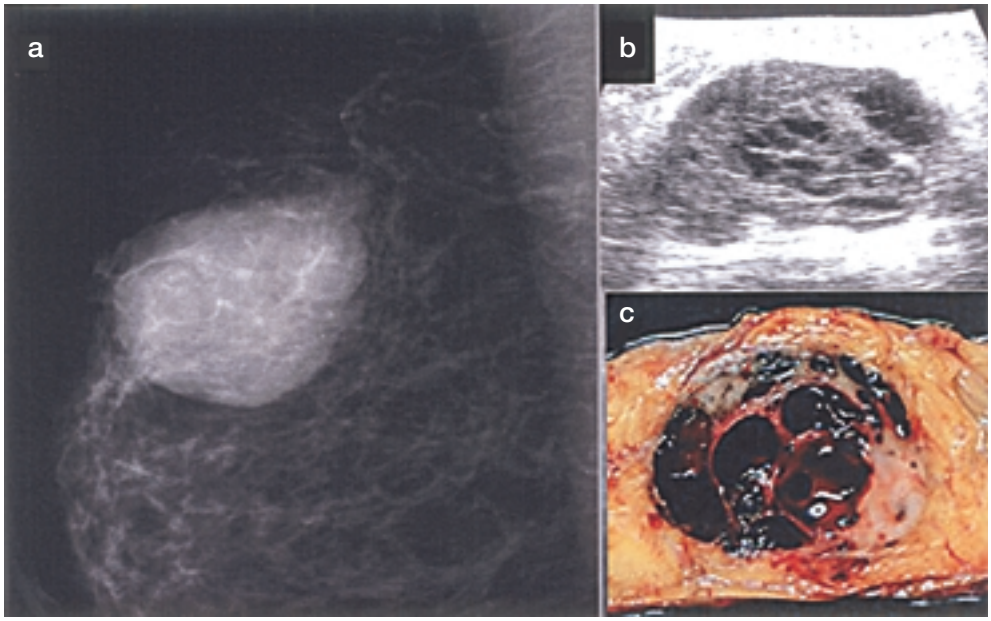

Fig 1. a) Mammography of the right breast demonstrates a well-circumscribed, lobulated mass. b) Ultrasonography of the right breast showing a restricted mass with hetero-genous high echogenicity. c) Macroscopic finding of the cut section of the tumor. Well-circumscribed, non-encapsulated tumor with cystic changes and hemorrhagic necrosis are seen.

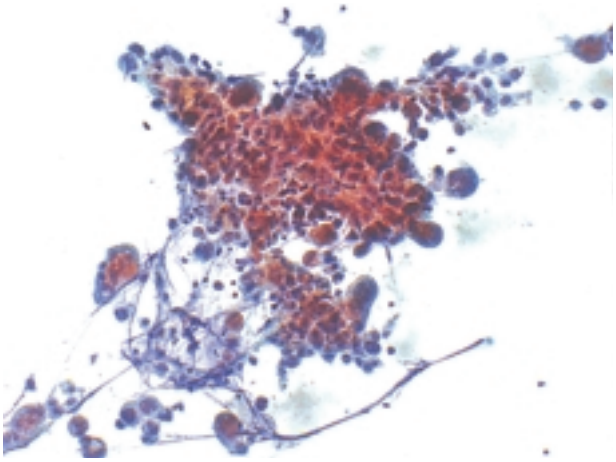

Fig 2. High cellular aspiration smears showing clusters of atypical cells and numerous multinucleated giant cells (Papanicolaou stain, ×200).

of atypical cells associated with numerous multinucleated giant cells. (Fig 2). Computed tomography and bone scintigraphy found no distant metastasis and tumor markers were within normal ranges. Preoperatively, mucinous carcinoma or invasive ductal carcinoma was diagnosed. Breast-conserving surgery with axillary lymph node dissection was performed with immediate reconstruction of the breast with latissimus dorsi muscle. The tumor was stage II, T2N0M0. for the right breast lesion.

Cut sections showed a well-circumscribed, non-encapsulated tumor with internal cystic changes and hemorrhagic necrosis (Fig 1). Complete sectioning (66 slides) was performed for a precise diagnosis. Histological examination revealed diffuse proliferation of atypical cells associated with numerous multinucleated giant cells (Fig 3a, b). No special proliferating pattern was apparent. Cystic spaces were filled with hemorrhage and cyst walls consisted of the proliferation of highly atypical cells associated with numerous multinucleated giant cells. There was no lining epithelium suggestive of phyllodes tumor. Based on these histological findings, the cyst formation may have been caused by hemorrhagic infarction of the tumor. Neither epithelial components nor normal ductal components were observed in the tumor. Mitoses or atypical mitoses were frequently noted. Osteoid formation was very focally seen (Fig 3c). Immunohistochemical staining of the tumor was positive for vimentin and negative for various cytokeratin (AE1/AE3, Cytokeratin 7, Cytokeratin 20, 34β E12, CAM5.2) (Fig 4), Desmin, S-100, CD34, Caldesmon, HHF-35, MyoD1, Myoglobin and HMB-45. α-smooth muscle actin (SMA) was focally positive (Table 1). The multinucleated giant cells were immunoreactive for the macrophage marker CD68. The average Ki-67 (MIB1) labeling index was 25%. The

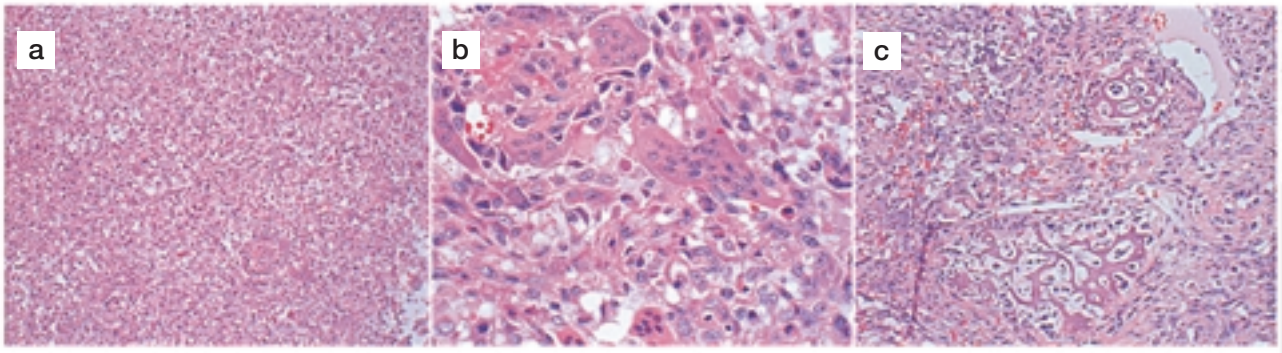

Fig 3. a) Representative histology of the tumor showing diffuse proliferation of atypical cells associated with multinucleated giant cells (HE, ×100). b) High-power view in the same section (HE, ×200). c) Osteoid formations are focally noted in the tumor (HE, ×200).

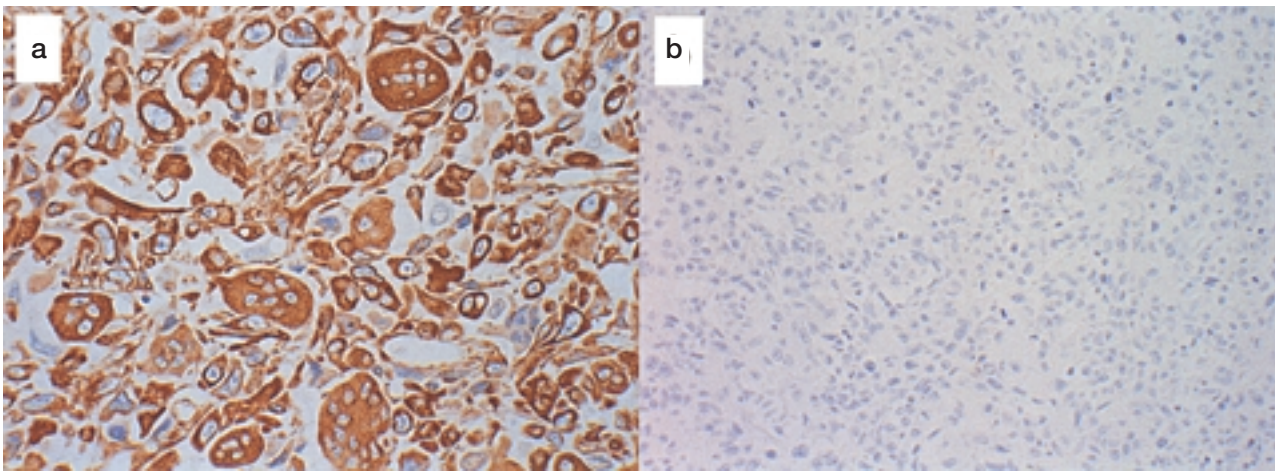

Fig 4. a) All tumor cells are positive for vimentin (immunohistochemical staining, ×200), and b) negative for cytokeratin (immunohistochemical staining, AE1/3, ×200).

tumor cells were restricted to the breast parenchyma, and the skin and pectoral fascia were free. Based on these findings, primary GCMFH of the breast was diagnosed. Surgical margins were histologically free from tumor cells and all 15 resected axillary lymph nodes were negative. The tumor was negative for both estrogen and progesterone receptors. Neither adjuvant chemo- endocrine nor postoperative radiation therapy was given, and the patient has remained disease-free for 2 years.

Discussion

MFH is a fairly common tumor in the deep soft tissues, but primary development in the breast, not in combination with any other malignancies such as malignant phyllodes tumor (MPT), or secondary to radiation therapy, is extremely rare[3]. MFH have been categorized into three subtypes: pleomorphic, giant cell and inflammatory[4]. GCMFH was formerly defined as a variant of MFH with prominent osteoclastic giant cells, but it is now appreciated that this morphologic pattern may be shared by a variety of tumor types. The term GCMFH is currently reserved for undifferentiated pleomorphic sarcomas with prominent osteoclastic giant cells. The differential diagnosis of MFH mainly includes MPT, metaplastic carcinoma, pleomorphic leiomyosarcoma, osteosarcoma and pleomorphic rhabdomyosarcoma. The tumor in our cases had cystic components suggestive of MPT, but no epithelial component was found in the tumor. Basically, a diagnosis of mammary sarcomas should be established only after metaplastic carcinoma is excluded by extensive immunohistochemical examination using epithelial markers[5]. In the case in our series, five types of epithelial markers were negative and extensive sampling revealed neither foci of usual invasive ductal carci-

Table 1. Results of Immunohistochemistry

Antigen		Clone	Dilution	Pretreatment	Source	Results
Vimentin		V9	1:50	MW	DAKO	Positive
Cytokeratin	AE1/3	AE1/3	1:50	MW	DAKO	Negative
	CK7	LP5K	1:10	MW	DAKO	Negative
	CK20	Ks20.8	1:50	MW	DAKO	Negative
	34 β E12	34 β E12	1:50	MW	DAKO	Negative
	CAM5.2	HT29	1:1	MW	Becton Dickinson	Negative
Desmine		D33	1:1	MW	DAKO	Negative
S-100		Polyclonal	1:1000	pronase	DAKO	Negative
ER		1D5	1:50	WB	DAKO	Negative
PgR		PgR636	1:800	WB	DAKO	Negative
MyoD1		5.8A	1:10	MW	DAKO	Negative
Myoglobin		polyclonal	1:2000	-	DAKO	Negative
CD68		NK-1	1:200	pronase	DAKO	Positive
α-SMA		1A4	1:50	MW	Novocastra Laboratories	focally positive
Anti-human melanoma		HMB-45	1:50	pronase	DAKO	Negative
CD34		QBEnd/10	1:50	MW	Novocastra Laboratories	Negative
Ki-67		MIB1	1:100	MW	DAKO	Positive, 25%*
h-Caldesmon		h-CD	1:50	MW	DAKO	Negative
anti-Muscle actin		HHF-35	1:100	MW	ENZO	Negative

MW, microwave heating adjusted to near-boiling in 5 mmol/L citrate buffer, 10 min at pH6.5
WB, boiling in Target Retheval Solution by water bath 95℃, 40min at pH9.0
ER, estrogen receptor
PgR, progesterone receptor
SMA, smooth muscle actin
*: Labeling index

noma nor non-invasive ductal components. Leiomyosarcoma with prominent osteoclastic giant cells has at least small areas with conventional smooth muscle cytomorphology and a fascicular growth pattern[6]. In addition, it usually shows positivity for SMA and desmin in the fascicular spindle cell component. In the case of our series showed focal positive staining for α-SMA, but was negative for desmin. In adittion, there was no area showing conventional smooth muscle cytomorphology and a fascicular growth pattern. On the other hand, pure osteosarcoma is extremely rare and many of the reported cases probably represent osteosarcomatous elements within metaplastic carcinomas[7]. From these findings, the diagnosis of GCMFH was ultimately made. There have been only 30 cases of MFH of the breast with clinical data in the English literature to our knowledge[3, 8-28] (Table 2). We reviewed and divided them into four subgroup according to Iellin's classification[12]; cases with MFH of the breast without skin invasion were classified into group I, MFH of the breast associated with cystosarcoma phyllodes were classified into group II, MFH cases arising after irradiation and/or surgery of the breast lesion were classified into group III, and MFH of the breast with secondary skin involvement was classified into group IV. The mean age was 52.3 years (33-77), the mean tumor size was 7.9 cm (1-20 cm), and the chief complaint of the 22 patients who had their complication recorded in the literature was breast mass, except for one case whose lesion was detected on mammography. Lymph node metastases were not detected in 15 patients in group I, II, and III, while one of four patients in group IV suffered from axillary involvement. Local recurrence was detected in three patients in group I and one in group III with disease-free survival ranging from 6 to 15 months. Of those patients, two cases had a good outocome after additional surgical treatment (case 1 and case 10). One had recurrence with distant lung metastasis and died 22 months postoperatively (case 7) and the other one died of thoracic invasion within one

Table 2. Malignant Fibrous Histiocytoma of the Breast in English Literature

No	year	author	Iellin's Classification[12]	age	formar lesion	tumor size(cm)	treatment	Lymph node metastasis	DFI (months)	Recurrence	Post operative period (months)	prognosis
1	1964	O'Brien JE et al.[8]	I	50	-	5	Bt	?	15	Local		A
2	1964	O'Brien JE et al.[8]	I	63	-	3	RM	?	54	-		A
3	1984	Vera-Sempere F et al.[9]	I	55	-	7	RM	no	60	-		A
4	1984	Callery CD et al.[10]	I	56	-	20	MRM	no	10	Distant (lung)	13	D
5	1984	Callery CD et al.[10]	I	67	-	19	MRM	no	108	-		A
6	1984	Callery CD et al.[10]	I	41	-	6	MRM	no	25	-		A
7	1984	Callery CD et al.[10]	I	77	-	4	Bp	no	6	Local, Distant(lung)	22	D
8	1984	Callery CD et al.[10]	I	50	-	1	Bp	no	23	-	23	DOC
9	1986	Lunde S et al.[11]	I	77	-	5	MRM	no	40	-		A
10	1986	Lunde S et al.[11]	I	49	-	4	Bp	no	12	Local	108	A
11	1986	Lunde S et al.[11]	I	71	-	6	Bt	no	197	-		D
12	1990	Iellin A et al.[12]	I	51	-	3	Bp	no	60	-		A
13	1995	Tamir G et al.[13]	I	42	-	6	MRM	no	24	-		A
14	2003	Wiriosuparto S et al.[14]	I	72	-	3	RM	no	?	?		?
15	2005	De Cesare AD et al.[15]	I	79	-	1.5	Bt	?	48	-		A
16	2005	De Cesare AD et al.[15]	I	42	-	1.5	MRM	no	288	-		A
17	2005	Yao MS et al.[16]	I	46	-	-	MRM	no	8	-		A
18	1980	Hanada M et al.[17]	II	33	-	32	MRM	post ope.	1	Distant (Bone)	1.5	D
19	1978	Dinner MI et al.[18]	III	46	cancer	8	Tm	post ope.	?	?		?
20	1979	Tsuneyoshi M et al.[19]	III	52	cancer	2.5	Tm	post ope.	28	-		A
21	1984	Vera-Sempere F et al.[9]	III	34	cancer	7	Tm	post ope.	<12	Local (thoracia)	<12	D
22	1986	Luzzatto R et al.[20]	III	43	cancer	2.5	Tm	post ope.	36	-		A
23	2000	Horii R et al.[21]	III	41	cancer	4	Tm	post ope.	18	-		A
24	1984	Langham MR et al.[22]	III	51	benign	1	MRM	no	11	-		A
25	1982	Liebert CW et al.[23]	III	51	NA	15	Tm	?	12	Distant (lung)		?
26	2005	Meshikhes AWN et al.[24]	III	14	benign	4	Bt	?	12	-		A
27	1987	Ostyn C et al.[25]	IV	45	-	4	Bt	no	3	Distant (lung)	16	D
28	1987	Van Nieckerk JLM et al.[26]	IV	70	-	12	RM	yes	2	Distant (lung)	2	D
29	2002	Ajisaka H et al.[27]	IV	52	-	20	RM	no	36	-		A
30	2004	Oh SJ et al.[28]	IV	48	-	12	RM	no	2	Distant (lung)	2	D
31	2006	Present case	I	56	-	5	Bp	no	30	-		A

DFI, disease free interval; NA, not available; Bt, simple mastectomy; RM, radical mastectomy; RMR, modified radical mastectomy; Bp, partial resection; Tm, tumorectomy; A, alive without evidence of disease; D, dead of disease; DOC, dead of other couase

year (case 21). Distant recurrence without local recurrence was detected in three patients in group I, II, and III. Three of four patients with skin invasion were suffered from lung metastases shortly after initial surgery (2-3 months) and died of their disease.

It was considered from the literature that the poor prognostic factors may be a huge tumor or skin invasion even if lymph nodes are negative for metastasis. However, the prognosis of MFH of the breast is difficult to predict because of the problems with classification of these tumors. We were not able to diagnose GCMFH preoperatively because the cytological similarity of breast GCMFH on FNAB to other malignant breast neoplasms makes the preoperative diagnosis challenging[14] and the sonographic findings of MFH of the breast are non-specific[17]. Further series of cases based on strictly defined diagnostic criteria are required to better understand the prognosis.

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