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CASE REPORT

Preoperative diagnosis of a giant cell tumor of soft tissue arising from the breast by ultrasound-guided core needle biopsy

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Abstract
Giant cell tumors of soft tissue (GCT-ST) arising in the breast are extremely rare. Herein, we report a case of a 45-year-old woman with a 5-cm mass in her left breast. Ultrasonography revealed a mainly well-circumscribed mass that contained a cystic lesion. Magnetic resonance imaging showed a fibrous capsule-covered mass that contained a high-intensity area, suggesting hemorrhaging. Ultrasound-guided core needle biopsy (CNB) revealed mononuclear histiocytic cells with a round shape or spindled appearance that was mixed with multinucleated giant cells. Immunohistochemical analysis revealed CD68-positive staining in the mononuclear and giant cells but negative staining for pancytokeratin. Preoperatively, the tumor was highly suspected of being GCT-ST. Histopathological results after a left mastectomy showed similar findings to CNB. The final diagnosis was GCT-ST in the breast. To the best of our knowledge, this is the first case report of a GCT-ST arising in the breast diagnosed by ultrasound-guided CNB.

Keywords Giant cell tumor · Giant cell tumor of soft tissue in breast · Breast tumor

Introduction

In 1972, Salm and Sissons reported a case series of giant cell tumors of soft tissue (GCT-ST) as distinct entities [1]. GCT-ST most frequently develop in the long bones as osteolytic tumors, usually after closure of the epiphyses, but extraosseous manifestations of GCT-ST at various sites have been described, including the skin, salivary glands, lung, pancreas, female genital tract, breast, thyroid, larynx, and heart [2]. However, to the best of our knowledge, GCT-ST arising in the breast is exceedingly rare, with only six cases having been previously reported [3–8]. Here, we report on a unique case of primary breast GCT-ST that was preoperatively diagnosed via ultrasonography, magnetic resonance imaging (MRI), and ultrasound-guided core needle biopsy (CNB).

Case report

A 45-year-old woman presented with a rapidly enlarging lump, pain, and bloody nipple discharge in her left breast. She had no previous history of breast disease but had been diagnosed with a benign ovarian cyst and endometriosis. On physical examination, a firm lump, approximately 5 cm in size, was palpable in the central portion of the left breast with no fixity to the chest wall or skin, but no palpable axillary lymph nodes were noted. Ultrasonography revealed a mainly well-circumscribed 5-cm mass under the left nipple (Fig. 1a). Internal echoes were heterogeneous and hypervascular (Fig. 1b). The mass contained a cystic lesion ascribed to necrosis, while only reactive swelling was found in the axillary lymph node. On MRI, the mass had a high-intensity area suggestive of hemorrhaging on T1- and T2-weighted images (Fig. 2a, b) along with a fibrous capsule that was gradually enhanced after administration of a radiopaque dye (Fig. 2c). Ultrasound-guided CNB was done, and pathology showed

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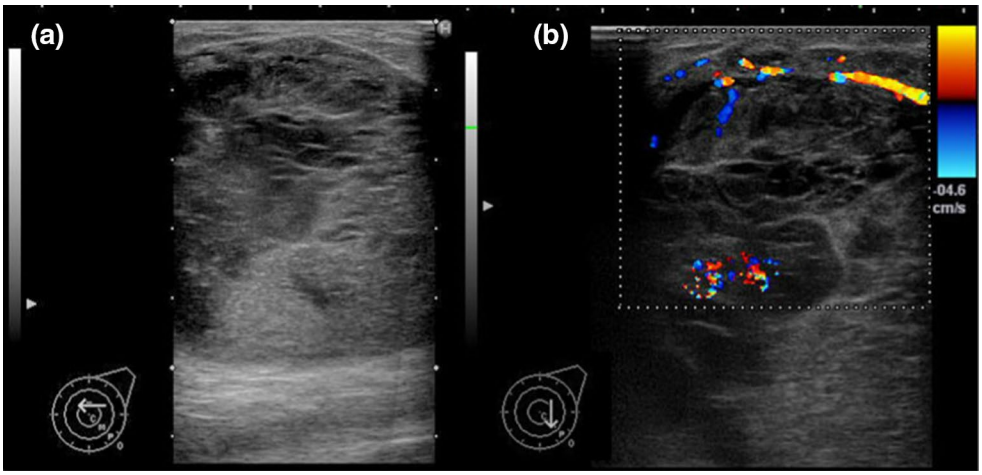

Fig. 1 Ultrasonography showing a mainly well-circumscribed, hypoechoic tumor (**a**). Internal echoing was heterogeneous and hypervascular (**b**)

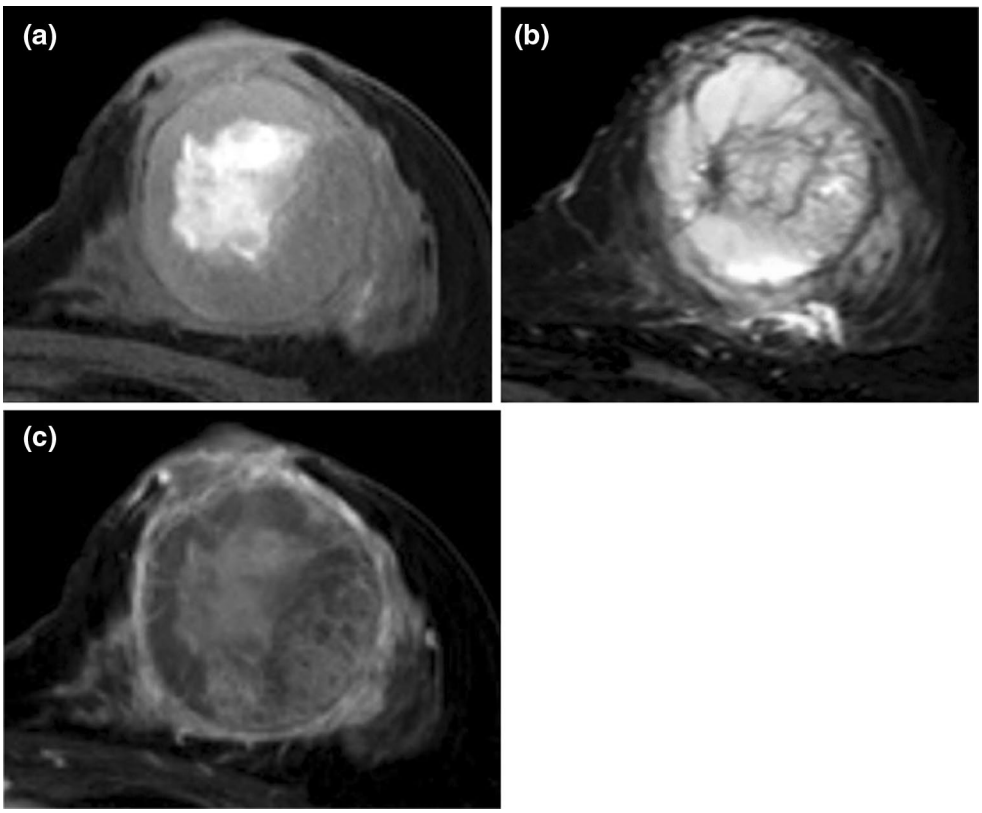

Fig. 2 Magnetic resonance imaging showing a well-demarcated, 5-cm tumor in the left breast. A high-intensity area on T1- (**a**) and T2-weighted (**b**) imaging suggested hemorrhaging. The tumor had a fibrous capsule that was enhanced gradually after administration of a radiopaque dye (**c**)

mononuclear histiocytic cells mixed with multinucleated giant cells (Fig. 3a). These mononuclear cells had eosinophilic cytoplasm and oval or spindled nuclei that resembled the giant cell nuclei with easily identifiable mitotic figures (Fig. 3b). Immunostaining for CD68 was positive in the mononuclear and giant cells (Fig. 3c) but negative for pancytokeratin, S100, ER, PgR, HER2, SMA, and desmin. Ki-67-positive staining was found in approximately 30% of the mononuclear and giant cells. Because of these findings, GCT-ST was highly suspected preoperatively. A left mastectomy and an axillary lymph node dissection were performed, and gross pathological

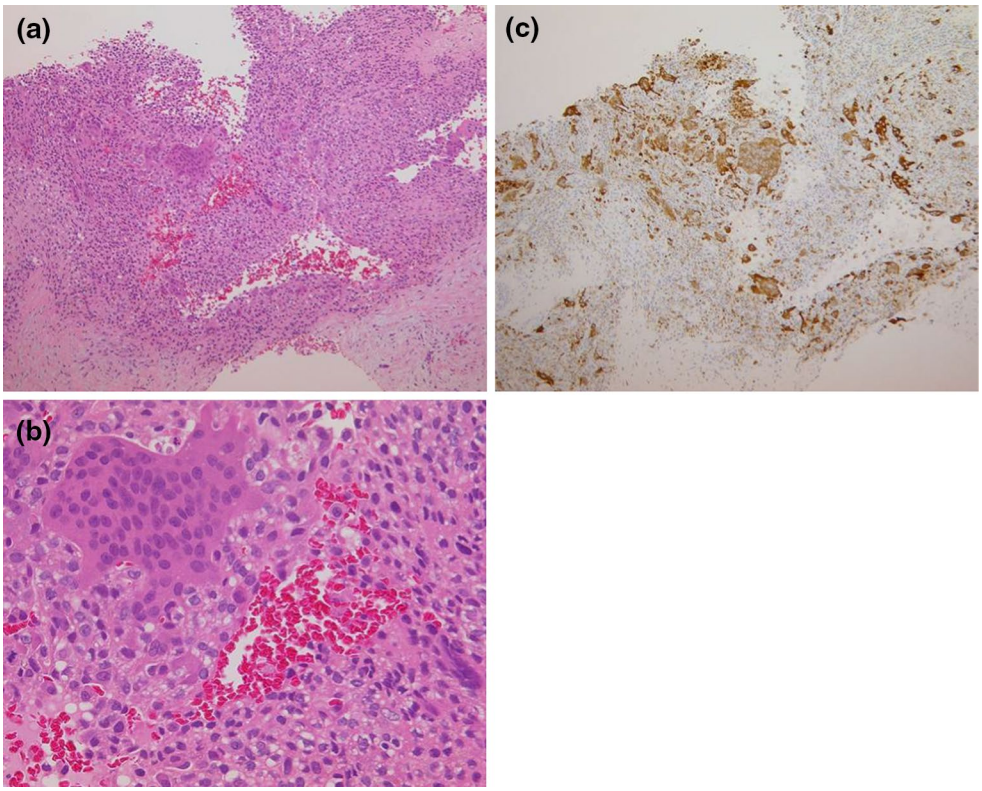

Fig. 3 Pathological findings of CNB showing mononuclear histiocytic cells with a round shape or spindled appearance mixed with multinucleated giant cells. The mononuclear cells contained eosinophilic cytoplasm and oval nuclei that resembled the giant cell nuclei (**a** hematoxylin and eosin, × 100, **b** hematoxylin and eosin, × 400). The mononuclear and giant cells stained positively for CD68 via immunohistochemistry (**c** CD68 immunostaining, × 100)

findings showed an encapsulated tumor with hemorrhaging and necrosis (Fig. 4), while round and spindle cells with multinucleated giant cells were also found on surgical specimens. No proliferation of atypical epithelial components was noted. The surgical margins were free and axillary lymph nodes were negative for metastasis. Immunohistochemical findings of the mass showed positive staining for CD68 and CD1a but negative staining for pancytokeratin, CD34, ER, PgR, and HER2. The final diagnosis was GCT-ST in the breast. As of this report, the patient has remained disease-free for 5 years and undergoes regular follow-up exams.

Discussion

Giant cell tumors of soft tissue are uncommon tumors composed of multinucleated osteoclast-like giant cells surrounded by oval and spindle mononuclear cells. Although GCT-ST ranges from benign to malignant, recent reports suggest that GCT-ST actually possesses only low malignant potential [2, 8]. It usually develops in the superficial and deep soft tissues of the extremities but has also been reported to arise at various sites such as the skin, salivary glands, lung, pancreas, female genital tract, breast, thyroid, larynx, and heart [2]. However, GCT-ST in the female breast is exceedingly rare; to the best of our knowledge, only six

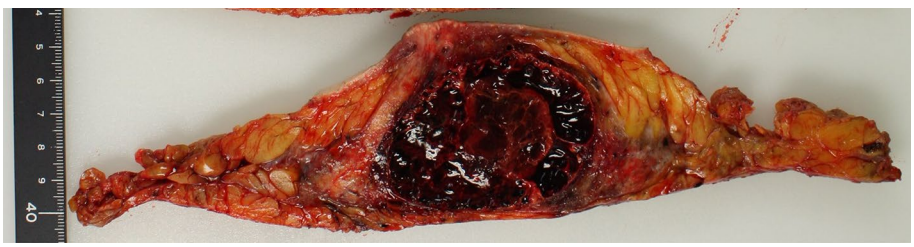

Fig. 4 Cut surface of the specimen showing an encapsulated tumor with hemorrhage and necrosis

cases of GCT-ST involving the breast have been reported (Table 1), and presentation tends to be as a rapidly growing lump without axillary lymphadenopathy [3–8]. In these cases, mammography revealed a well-circumscribed mass in four of seven cases, but ultrasonography showed various findings of well-circumscribed lesions, cystic lesions, and irregular hypoechoic areas [5–8]. In six of the previously reported cases, MRI was not performed. Our case is unique in that it was preoperatively diagnosed via ultrasound-guided CNB. Four patients were treated via mastectomy, while three were treated with wide excision. There was no recurrence except for one patient who developed pulmonary metastases and died 10 months after the initial presentation.

Macroscopically, GCT-ST presents as a well-circumscribed, mostly solid, nodular mass with a fleshy, red-brown cut surface that indicates focal hemorrhaging [9]. Microscopically, GCT-ST displays a multinodular architecture, with the nodules ranging in size from microscopic dimensions to 15 mm. These nodules are composed of a mixture of mononuclear round and oval cells and osteoclast-like multinucleated giant cells, both groups of which possess nuclei of similar appearance. Mitotic activity is generally present, but atypia, pleomorphism, and necrosis are rarely found. Additional histological features include stromal hemorrhaging and regressive changes in the form of marked stromal fibrosis and clusters of foamy macrophages. Immunohistochemically, GCT-ST displays immunoreactivity for vimentin, CD68, and smooth muscle actin. The mononuclear cells show only focal staining, while the multinucleated giant cells show positivity for CD68 staining, indicating a pluripotential, mesenchymal stromal cell origin from the monocytic/histiocytic lineage. Meanwhile, GCT-ST are uniformly negative for pancytoketatin, epithelial membrane antigen, desmin, and estrogen receptors. Melanocytic origin is excluded via negative immunohistochemistry with S-100 and melan-A antibodies. Atypical mitotic figures can be confirmed if a high proportion of these cells stain positively with the proliferation marker MIB-1/Ki67.

In our case, we initially suspected the rapidly growing lump to be a phyllodes tumor upon physical examination. However, in contrast to phyllodes tumors, ultrasonography showed a partially uncircumscribed margin, cystic component, and heterogeneous internal echoing. CNB histological results showed histiocytic cells with a round shape or spindled appearance that was mixed with multinucleated giant cells. Other differential diagnoses to be considered included mammary carcinoma with osteoclast-like giant cells (which may be a variant of metaplastic mammary carcinoma), giant cell-rich leiomyosarcoma, malignant fibrous histiocytoma, or metastatic GCT of bone. Carcinoma was ruled out based on the lack of staining of epithelial markers and components. Because the present tumor was negative for SMA and desmin, leiomyosarcoma was also ruled out. The absence of marked cellular atypia and pleomorphism eliminated the possibility of malignant fibrous histiocytoma, while diagnostic imaging did not indicate a bone tumor. Finally, preoperative ultrasound-guided CNB provided a definitive diagnosis of GCT-ST arising in the breast.

Similar to other sites, complete tumor excision is the treatment modality of choice for GCT arising in the breast. Moreover, a paucity of cases makes for difficulties in

Table 1 Clinical characteristics of the seven patients with GCT-ST in the breast

Age/gender [references]	Size (cm)	Mammogram	Ultrasonography	MRI	Clinical diagnosis	Treatment	Follow-up	Recurrence
72/M [3]	13	Not shown	Not shown	Not shown	Not shown	Mastectomy	6 months	Absent
68/F [4]	3	Not shown	Not shown	Not shown	Intracystic papilloma	Mastectomy	Not shown	Unknown
59/F [5]	3.7	Well-circumscribed lesion	Well-circumscribed lesion	Not shown	Soft tissue tumor	Wide-local excision	2 years	Absent
60/F [6]	3	Well-demarcated mass	Cystic mass with mixed echogenicity	Not shown	Not shown	Mastectomy	6 months	Pulmonary metastases
50/F [7]	2.5	Well-defined opacity	Irregular hypoechoic area	Not shown	Not shown	Excisional biopsy	Not shown	Unknown
36/F [8]	6	Well-defined hyperdense mass	Not shown	Not shown	Phyllodes tumor	Wide-local excision	1 year	Absent
45/F (present case)	5	Not shown	Partially poor circumscribed hypoechoic mass	Capsule-enhanced mass	GCT-ST	Mastectomy	5 years	Absent

predicting clinical behavior, and long-term follow-up is required for these tumors.

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Compliance with ethical standards

Conflict of interest Aya Sawa, Tatsuhiko Ikeda, Emika Ichioka, Yukiko Tsushima, Akiko Iguchi, Hiroko Bando, Yuzuru Kondo, and Hisato Hara declare that they have no conflicts of interest.

Ethical statement All procedures followed were in accordance with the ethical standards of the responsible committees on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent was obtained from all patients prior to inclusion in the study.

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