INTRODUCTION

Primary breast sarcomas are rare, histologically heterogenous nonepithelial malignancies that arise from the connective tissue within the breast [1]. Like soft tissue sarcomas originating in other parts of the body, breast sarcomas consist of a heterogeneous group of several subtypes: liposarcoma, fibrosarcoma, pleomorphic sarcoma, leiomyosarcoma, rhabomyosarcoma, angiosarcoma, and osteosarcoma, sarcomas of uncertain differentiation [2].

Undifferentiated pleomorphic sarcoma has been defined as a group of pleomorphic, high-grade sarcomas in which any attempt to disclose their line of differentiation has failed. It constitutes less than 5% of all sarcomas in adults [3] and has been rarely seen in breast [4]. The clinical features of this rare tumor mimic those of breast carcinoma and often present diagnostic challenges [5].

Herein, we report a case of primary undifferentiated pleomorphic sarcoma in a 76-year-old man; this case highlights a rare and interesting variant of primary breast sarcoma and the diagnostic difficulty that physician and pathologist may encounter with it.

CASE REPORT

We report a case of spindle cell sarcoma of the breast in a 76-year-old man. He presented to the Daegu Catholic University Hospital with a lump in his left breast that had been present for the previous two months. He had been taking medication for hypertension and benign prostate hypertrophy and had not suffered trauma to his chest wall. Further, he had no family history of malignancy, including breast cancer.

On physical examination, the patient had a poorly demarcated, mobile, firm mass in his left breast. The mass was non-tender, approximately 1 cm in diameter, and was detected in the subareolar area of the left breast. There was no clinical evidence of regional lymphadenopathy, and there were no abnormal findings in the right breast. Mammography revealed a dense lesion occupying the subareolar region; this lesion was consistent with prominent fibroglandular tissue and suggested asymmetric left gynecomastia (Figure 1A). Ultrasonography revealed a poorly demarcated and highly suspicious malignant lesion in the periareolar area of his left breast, and the lesion was categorized according to Breast Imaging Report and Data System for Screening (BIRADS) as category 5, suggestive of malignancy. The lesion was then excised by wide local excision. Histologically, the lesion was found to be a pleomorphic sarcoma with atypical spindle cells and areas of necrosis.

Based on these findings, the final diagnosis was undifferentiated pleomorphic sarcoma. Immunohistochemical staining for CD34, actin, S100, and desmin showed diffuse and strong positivity for CD34, which is consistent with the diagnosis of sarcoma. The patient was referred to a medical oncologist for further management, and chemotherapy was initiated.

Key Words: Breast neoplasms, Male, Malignant fibrous histiocytoma, Sarcoma
YoungJuJeong, et al.

Preoperative examination consisted of a complete blood count, serum kidney and liver function test, thyroid function test, and tests for the levels of several hormones related to the development of gynecomastia, including estrogen, testosterone, prolactin, and gonadotrophic hormones. All results were within the normal limits.

The patient underwent wide excision of the lesion, including removal of normal breast tissue to provide a safety margin and he did not require subsequent axillary lymph node dissection. Gross examination of the specimen revealed a whitish, fibrotic nodular lesion, measuring 1.5×1 cm in size including surrounding adipose tissue. The specimen was fixed in 10% formalin. Paraffin sections were prepared and stained with haematoxylin and eosin (H&E). Microscopic examination of the sections from the specimen showed nodular proliferation of fibrous tissue with focal infiltrating margins (Figure 3A). There were no ductal components and epithelial tissues. The nodules were composed of plump to spindle-shaped fibroblasts, many lymphplasma cells, eosinophilic infiltrate, and many keloid-like collagen bundles (Figure 3B). A few atypical multinuclear giant cells and pleomorphic cells were noted; however, abnormal mitosis was not identified. Immunohistochemical staining for desmin, smooth muscle actin (SMA), and S-100 protein was negative (Figure 3C). These diverse histological and immunohistochemical findings established the diagnosis of atypical spindle cell lesion with uncertain malignant potential, exhibiting features of a reactive fibroblastic lesion.

The patient's progress was monitored after the operation, and no specific adjuvant treatment was administered. One year later, he returned with a recurrent mass at the previous surgical site. On physical examination, a firm mass of about 2 cm in diameter was palpated in the wound from the previous surgery. Radiological studies, including computed tomography (CT) and positron emission tomography-CT (PET-CT), were conducted, and PET-CT showed faint fluorodeoxyglucose uptake in the area of the left breast that corresponded to the lesion seen on the CT scan (Figure 4). There was no evidence of either regional lymphadenopathy or distant metastasis. The lesion was surgically removed using wide excision.

A histological assay showed that the recurrent tumor was 3.8 cm sized in diameter and had an irregular margin. On sectioning, the cut surface showed fibrous bands and lobular adipose tissue with focal congestion without necrosis. The nodules

Figure 1. Initial radiologic findings. (A) Mammography showing prominent fibroglandular tissue in the subareolar area of left breast. (B) Ultrasonographic scan showing heterogeneous hypoechoic lesion with diffuse skin thickening and fatty infiltration.

Figure 2. Histological findings of the left breast mass by core needle biopsy. Marked infiltration of plasma cells and eosinophils have been shown. Many atypical cells with large nuclei in the abundant collagenous stroma can be seen (H&E stain, ×400).

(BIRADS) as BIRADS 4C (Figure 1B). He underwent ultrasound-guided core needle biopsy, which indicated the presence of atypical cells in the fibrous, proliferative lesion (Figure 2).

http://ejbc.kr

http://dx.doi.org/10.4048/jbc.2011.14.3.241
were composed of plump to spindle-shaped fibroblasts, many lymphoplasma cells, eosinophilic infiltrate, and many keloid-like collagen bundles. Microscopic findings were similar to the previous histological findings (Figure 5A), but many atypical cells and abnormal mitotic activity ranging from 6 to 10 mitotic figures per 10 high power fields (hpf) were noted and the re-

Figure 3. Initial histological appearance of the left breast mass after wide excision. (A, B) Microscopic findings of the specimen showing nodular proliferation of fibrous tissue with focal infiltrating margins. Spindle fibroblasts with many lymphoplasma cells and eosinophils were apparent. A few atypical cells and pleomorphic cells were noted, but abnormal mitosis was not identified (H&E stain; A, ×40; B, ×400). (C) Immunohistochemical staining for S-100 protein shows negative staining in tumors (×200).

Figure 4. Radiologic findings of a recurrent mass in left breast. (A) Computed tomography (CT) image showing a low attenuating mass in the subareolar area of the left breast (arrow) without significant lymph node enlargement. (B) Positron emission tomography-CT image showing faint FDG uptake area in the left breast (arrow) without other metabolically significant FDG uptake lesions that would suggest axillary nodal or distant organ metastasis.
sected margins were involved with the tumor (Figure 5B, C). Based on the rapid recurrence of the mass, increase in tumor size, high degree of cellularity, presence of atypical cells, many abnormal mitotic figures, and infiltrating growth pattern, malignancy was indicated. The immunohistochemical staining for CD34 showed focal positivity; however, the cells were not reactive for other immunomarkers including cytokeratin (CK), epithelial membrane antigen (EMA), SMA, murine double-minute protein 2 (MDM2), desmin, S-100 protein, CD68 and anaplastic lymphoma kinase (ALK). These established histological features of malignant pleomorphic spindle cell tumor in addition to the immunohistochemical results demonstrated no line of differentiation and led to the diagnosis of undifferentiated pleomorphic sarcoma of the breast. Due to the involvement of the resected margin, the patient underwent simple mastectomy.

**DISCUSSION**

Primary breast sarcoma is a rare type of cancer arising from the mesenchymal tissue of the breast and represents less than 1% of all breast malignancies. It includes a heterogeneous group of disease entities. According to the World Health Organization (WHO) classification, malignant fibrous histiocytoma (MFH) is a morphological pattern rather than a distinct clinicopathological entity. Many neoplasms diagnosed as MFH previously are actually classified as pleomorphic subtypes of other sarcomas [2]. Pleomorphic MFH/undifferentiated pleomorphic sarcoma is defined as a group of pleomorphic, high-grade sarcomas showing no line of differentiation. Undifferentiated pleomorphic sarcoma has been a diagnosis of exclusion following thorough sampling and critical use of ancillary diagnostic techniques. In the previous reports, it consisted of 10.5-24% of all primary breast sarcomas [4,6]. Most undifferentiated pleomorphic sarcomas have appeared in patients who are in their sixth and seventh decade of life [2]. Neither the symptoms nor the physical findings of undifferentiated pleomorphic sarcoma of the breast present any characteristic pattern that would easily suggest the diagnosis. Immunohistochemistry may be useful to distinguish primary breast sarcomas from non-mesenchymal malignant tumors and to delineate the level of differentiation of primary breast sarco-

**Figure 5.** Histological appearance of the recurrent left breast mass, diagnosed as pleomorphic spindle cell sarcoma. (A) Fibrous bands and lobular adipose tissue with focal congestion and no necrosis (H&E stain, × 40). (B) Microscopic findings showed spindle tumor cells with many lymphoplasmacytic infiltrates (H&E stain, × 200). (C) Many atypical cells and abnormal mitoses were noted (H&E stain, × 400).
mas [5]. Desmin, vimentin, smooth muscle antigen, CK, leukocyte common antigen, CD34, HMB-45, SMA, EMA, and S-100 protein should all be analyzed in sarcoma patients.

Undifferentiated pleomorphic sarcomas often grow rapidly and then may be painful. Imaging methods and macroscopy have revealed well-circumscribed masses with heterogeneous composition. Further, they have been identified as pale fibrous and fleshy areas admixed with zones of (cystic) necrosis, hemorrhage, or myxoid features [7]. Microscopically, lesions exhibit cells showing marked pleomorphism admixed with bizarre giant cells, spindle cells, and variable foamy cells [8]. A storiform growth pattern and variable chronic inflammatory cells are also common [7].

Limited data on undifferentiated pleomorphic sarcoma have indicated that this neoplasm has an aggressive clinical course and high incidence of recurrence and metastasis. Overall 5-year survival of patients with undifferentiated pleomorphic sarcoma has been roughly 50% [7]. Local surgical resection is the choice of treatment and negative margins are particularly important, although the extent of the surgery has been controversial. Axillary dissection has been generally thought to be unnecessary for undifferentiated pleomorphic sarcoma of the breast, since these tumors rarely metastasize via the lymphatics [9,10]. The role of adjuvant chemotherapy and radiation also has been unclear [9,10]. In our case, the patient was subjected to wide local excision for recurrent mass without axillary dissection and will undergo simple mastectomy due to involvement of the resected margin.

Differential diagnosis should include metaplastic (sarcomatoid) carcinoma, malignant phyllodes tumor, inflammatory myofibroblastic tumor (IMT), and myofibrosarcoma.

Metaplastic (sarcomatoid) carcinoma, also called spindle cell carcinoma, is a rare heterogeneous neoplasm generally characterized by a mixture of adenocarcinoma with dominant areas of spindle cells, squamous and other mesenchymal differentiation [11]. CK positivity of the spindle cells confirms the epithelial origin of this tumor.

Malignant phyllodes tumor consists of malignant mesenchymal cells and a benign epithelial component [5]. The tumor shows overgrowth of the stroma in relation to the epithelial component, cellular pleomorphism with sarcomatous elements and frequent mitoses, and invasion of the surrounding tissues. The tumor can be differentiated from undifferentiated pleomorphic sarcoma by more extensive sampling for identifying epithelial component.

IMT is a neoplasm of myofibroblastic origin, often admixed with prominent inflammatory infiltrate consisting of lymphocytes, plasma cells, macrophages, eosinophils and histiocytes. An IMT is a low-grade neoplastic lesion showing lack of atypia, hyperchromasia, and abnormal mitotic figures [12]. Immunohistochemistry of IMT shows strong SMA reactivity within the spindle cells frequently and occasional immunoreactivity for ALK, and negative or focal positivity for pankeratin.

Myofibrosarcomas are malignant tumors of myofibroblasts. Electron microscopy examination has been considered a gold standard for diagnosis of myofibrosarcoma, and ultrastructurally, the neoplastic cells have variable rough endoplasmic reticulum (RER) as well as peripheral filament bundles resembling stress fibers, collagen secretion granules and, rarely fibronectin fibrils and a fibronexus junction [13]. Most myofibrosarcomas are immunoreactive for SMA and expression of CK, EMA, CD34, desmin or S100 protein is seen sporadically.

Although rare, benign spindled cell lesions of the breast may show malignant progression as in our case; however, breast sarcoma may be misdiagnosed as benign spindle cell lesions such as myofibroblastoma, nodular fasciitis and fibromatosis. The histological criteria for the diagnosis of benign spindled cell neoplasms includes well-circumscribed cells, monomorphic, bland-looking spindle to oval-shaped cells, minimal to moderate cytological atypia, fasicular and/or haphazard growth pattern; absence of epithelial and myoepithelial components; mitotic activity of 2 or less per 10 hpf, and the absence of both atypical mitosis and necrosis [14].

Myofibroblastoma is a benign prototypic tumor of mammary stroma [13]. Currently, it is believed that myofibroblastoma occurs mainly in older men and postmenopausal women. Morphologic features of classic-type myofibroblastoma are purely mesenchymal tumor with no epimyoepithelial components, interspersed thick hyalinized collagen bundles, low mitotic count, lack of marked cytologic atypia, no atypical mitoses, and the absence of necrosis. Most myofibroblastomas are typically positive to vimentin, desmin, and CD34 and immunoreactivity for SMA, bcl-2, and CD99 is frequently obtained [13].

Nodular fasciitis is a rapidly growing lesion, which is usually subcutaneous and does not reach a large size. Microscopically, the lesion is fairly well circumscribed. It consists of plump active fibroblasts and myofibroblasts arranged in short, loose and irregular bundles. Nodular fascitis is less cellular and uniform than undifferentiated pleomorphic sarcoma and does not infiltrate into surrounding tissue. Unlike in undifferentiated pleomorphic sarcoma, nuclear atypia and necrosis are not seen [5,14].

Fibromatosis is non-encapsulated well-differentiated fibroblastic lesion composed of relatively uniform fibroblasts and collagen forming a firm, solitary, or multinodular mass with an infiltrative growth pattern. Immunohistochemically, fibromatosis exhibits positivity for SMA and vimentin and negativity

http://dx.doi.org/10.4048/jbc.2011.14.3.241
tumor with adequate margins seems to be the most significant
ated pleomorphic sarcoma of the breast, surgical excision of the
undifferentiated pleomorphic sarcoma. In case of undifferen-
tial results of the tumor, we diagnosed the recurrent mass as
ally in men. Also, undifferentiated pleomorphic sarcoma, one
subtype of primary breast sarcoma has been uncommon and
these lesions represent special diagnostic difficulties. Herein,
we reported a case of the undifferentiated pleomorphic sar-
coma occurring in the male breast. Initially, it was difficult to
classify the lesion as undifferentiated pleomorphic sarcoma; fi-
ally, based on histological findings and the immunohistochem-
ical results of the tumor, we diagnosed the recurrent mass as
undifferentiated pleomorphic sarcoma. In case of undifferen-
tated pleomorphic sarcoma of the breast, surgical excision of
the tumor with adequate margins seems to be the most significant
prognostic factor; therefore, it will be necessary to treat this pa-
tient with repeated excision or simple mastectomy to prevent
local recurrence and to improve his chances of survival.

REFERENCES

1. Moore MP, Kinne DW. Breast sarcoma. Surg Clin North Am 1996;76:
383-92.
2. Fletcher CD, Unni KK, Mertens F. World Health Organization Classifi-
cation of Tumors: Pathology and Genetics of Tumors of Soft Tissue and
Bone. Lyon: IARC Press; 2002. p.9-154.
3. Fletcher CD. The evolving classification of soft tissue tumours: an up-
date based on the new WHO classification. Histopathology 2006;48:3-
12.
4. Adem C, Reynolds C, Ingle JN, Nascimento AG. Primary breast sar-
coma: clinicopathologic series from the Mayo Clinic and review of the
literature. Br J Cancer 2004;91:237-41.
5. Al-Nafussi A. Spindle cell tumours of the breast: practical approach to
diagnosis. Histopathology 1999;35:1-13.
6. Pandey M, Mathew A, Abraham HK, Rajan B. Primary sarcoma of the
breast. J Surg Oncol 2004;87:121-5.
7. Zelger B, Burgdorf WH. Fibrohistiocytic tumors. In: Nouri K, editor.
Skin Cancer. 1st ed. New York: McGraw-Hill; 2007. p.205-7.
8. Jain M, Malhan P. Cytology of soft tissue tumors: pleomorphic sarcoma.
J Cytol 2008;25:93-6.
9. McGowan TS, Gammins BI, O’Sullivan B, Catton CN, Miller N, Pan-
zarella T. An analysis of 78 breast sarcoma patients without distant me-
tastases at presentation. Int J Radiat Oncol Biol Phys 2000;46:383-90.
10. Shabahang M, Franceschi D, Sundaram M, Castillo MH, Moffat FL,
Frank DS, et al. Surgical management of primary breast sarcoma. Am
Surg 2002;68:673-7.
11. Guarino M, Tricomi P, Giordano F, Cristofori E. Sarcomatoid carcino-
mas: pathological and histopathogenetic considerations. Pathology 1996;
28:298-305.
12. Coffin CM, Dehner LP, Meis-Kindblom JM. Inflammatory myofibro-
blastic tumor, inflammatory fibrosarcoma, and related lesions: an his-
torical review with differential diagnostic considerations. Semin Diagn
Pathol 1998:15:102-10.
13. Magro G. Mammary myofibroblastoma: a tumor with a wide morph-
ologic spectrum. Arch Pathol Lab Med 2008;132:1813-20.
14. Magro G, Michal M, Bisciglia M. Benign spindle cell tumors of the
mammary stroma: diagnostic criteria, classification, and histogenesis.
Pathol Res Pract 2001;197:453-66.
15. Wargotz ES, Norris HJ, Austin RM, Enzinger FM. Fibromatosis of the
breast. A clinical and pathological study of 28 cases. Am J Surg Pathol
1987;11:38-45.