Surg Today (2007) 37:230–233
DOI 10.1007/s00595-006-3372-9

SURGERY TODAY

Metastatic Breast Tumor Arising from Synovial Sarcoma: Report of a Case

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Abstract
We report a case of metastatic breast tumor arising from a synovial sarcoma of the lower limb. A 27-year-old Japanese woman was diagnosed to have synovial sarcoma 14 months prior to finding a mass in her left breast. An excisional biopsy was performed and a metastatic synovial sarcoma to the breast was confirmed. Eight months after the resection of the breast lesion, the patient developed local recurrences in both her knee and breast. A tumor resection of the limb lesion and a simple mastectomy for the huge lesion, which was diagnosed to be a metastatic breast tumor without lymph node metastasis, were performed. After the operation, the patient received adjuvant systemic chemotherapy. To the best of our knowledge, this is only the second reported case of a solitary metastatic breast tumor arising from synovial sarcoma.

Key words Metastatic breast tumor · Synovial sarcoma · Young adult

Introduction

Metastases in the breast from nonmammary malignant neoplasms are rare, accounting for approximately 0.5%–1.4% of all breast tumors.[1,2] Malignant melanoma and lung carcinoma are the most commonly reported primary tumors that metastasize to breast tissue,[3] while there has only been one previous case reported of a metastatic breast tumor arising from a synovial sarcoma of the lung.[4] This report describes a patient with a synovial sarcoma of the lower limb with breast metastasis who required a simple mastectomy for local control.

Reprint requests to: Y. Kijima
Received: January 26, 2006 /Accepted: July 25, 2006

Case Report

A 27-year-old Japanese woman, diagnosed to have a synovial sarcoma of the left knee, had a resection of the tumor carried out in the Department of Orthopaedic Surgery of our hospital (Fig. 1). The tumor cells were arranged in sheets or fascicles, and had a small amount of cytoplasm and hyperchromatic nuclei. The tumor cells were positive for membranous antigen in a few areas. Many tumor cells were positive for bimentin and bcl-2, whereas they were negative for cytokeratins (CAM5.2, AE1/AE3), S-100, actins (alpha-smooth muscle actin, HHF35), desmin, and CD34. Fourteen months after this operation, the patient noticed a 20-mm diameter mass in the upper-outer quadrant of her left breast. An excisional biopsy was done at another hospital, and the breast lesion was diagnosed to be a metastasis of the synovial sarcoma. The surgical margin was free from tumor cells. Eight months after the excision of the breast lesion, the patient noticed mass lesions directly under the operation scars of her knee and left breast. The patient was diagnosed to have local recurrence of the synovial sarcoma of the knee. She was referred to our department for further examination and treatment of the breast lesion.

On physical examination, hard tumors with clear margins and poor mobility, measuring about 6×7 cm in the left knee and 9.0×8.5 cm in the left breast, were palpable. The skin within a 4-cm diameter of the breast in the vicinity of the operation scar was slightly reddish and fixed with the tumor, but no diffuse ecchymosis was seen. Ultrasonography revealed the lobulated mass to have a soft tissue density that was lower than the adjacent parenchyma in the rest of the breast, and its maximum diameter was up to 80 mm. No calcification was present (Fig. 2). The lesion was thus suspected to represent a benign or intracystic tumor or a particular type of breast carcinoma, such as a mucinous carcinoma or a breast sarcoma. Computed tomography (CT) and

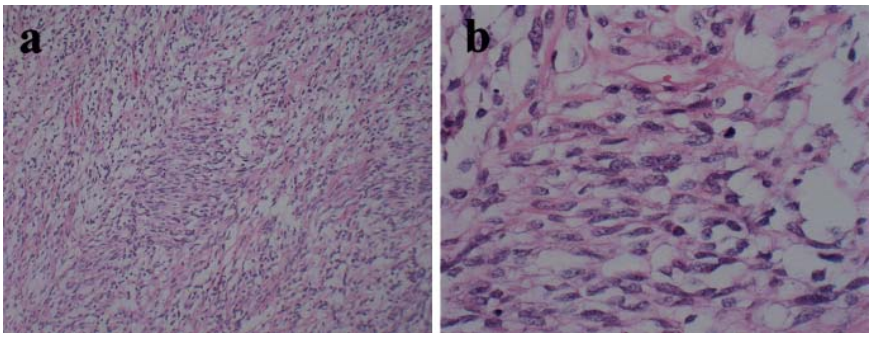

Fig. 1a,b. The tumor cells are arranged in sheets or fascicles with a small amount of cytoplasma and hyperchromatic nuclei (H&E; **a** ×100, **b** ×400)

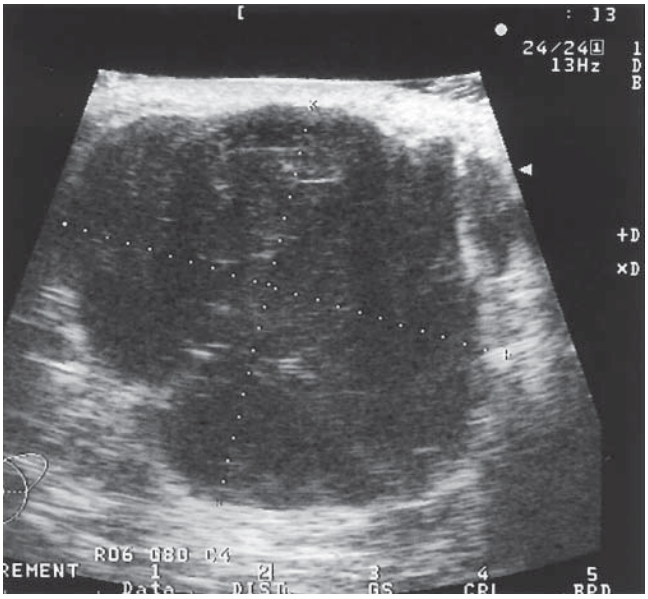

Fig. 2. Ultrasound findings of the breast tumor in October 2004. A nonhomogeneous mass with a relatively high internal echogenicity was found

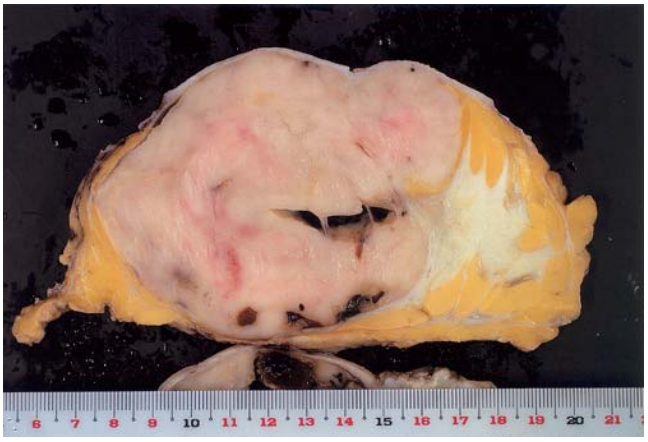

Fig. 3. Macroscopical findings of the resected breast. A relatively well circumscribed tumor with focal cystic change is seen

bone scintigraphy showed no distant metastasis, and tumor markers (CEA, CA15-3, and BCA225) were within the normal ranges. We suspected a local recurrence of the metastatic synovial sarcoma of the breast without any axillary metastasis.

Following one course of systemic chemotherapy with cisplatin (120 mg/m^2 on day 1) and doxorubicin hydrochloride (30 mg/m^2 on days 1–2), intra-arterial chemotherapy (cisplatin 100 mg/m^2, pirarubicin hydrochloride 40 mg/m^2 once a week) and irradiation with 2.0 Gy five times a week for a total amount of 50 Gy to the limb lesion were given. However, both lesions increased in size and grew rapidly for 3 months. The patient's left breast enlarged due to the large mass lesion, and diffuse ecchymosis covered most of the breast.

In January 2005, we resected the knee tumor and performed a simple mastectomy. The resected breast had a huge white mass with focal cystic change (11 × 10 × 8 cm) (Fig. 3a). Microscopically, the lesion showed a proliferation of almost uniform oval to spindle cells arranged in sheets, lobules, fascicles, or whorl-like formation (Fig. 3b). The constituent cells had a small amount of cytoplasm and hyperchromatic nuclei (Fig. 4). A reverse transcription–polymerase chain reaction analysis of the tissue specimens from both lesions, knee and breast, detected the SYT-SSX1 fusion gene transcript. The lesion in the breast was compatible with metastasis of synovial sarcoma. Although adjuvant chemotherapy with ifosfamide (3 mg/m^2 on days 1–2) and etoposide (100 mg/m^2 on days 1–2) for two courses, as well as one course of cisplatin (120 mg/m^2 on day 1) and doxorubicin hydrochloride (30 mg/m^2 on days 1–2) was given, the patient developed synovial sarcoma metastases to the lung 6 months after the mastectomy.

Discussion

The breast is the most common site of primary malignant tumors in adult women and is an unusual site for nonmammary malignancies. The incidence of metastasis to the breast from malignant neoplasms on autopsy ranges from 1.7% to 6.6% and in clinical series it

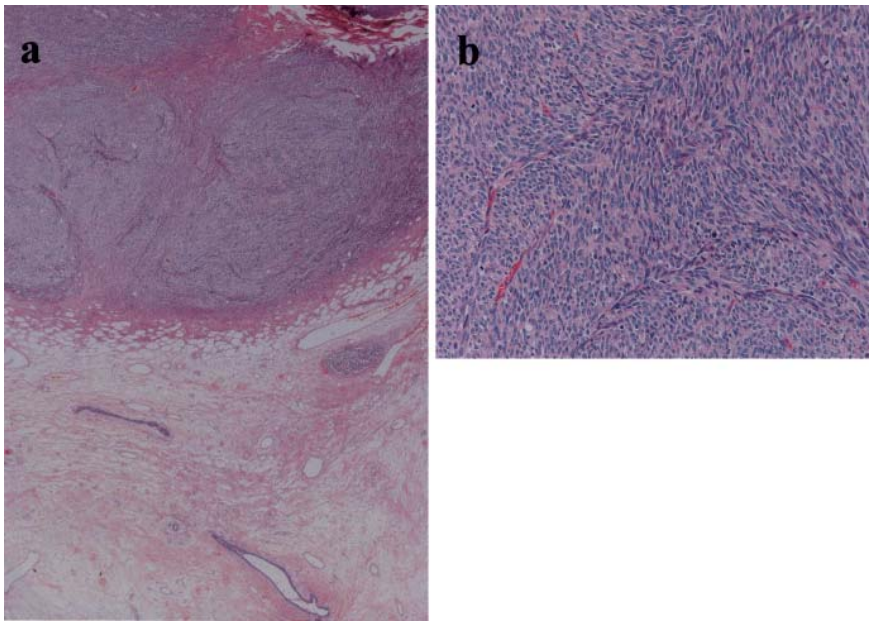

Fig. 4. **a** The relatively well circumscribed tumor is seen. The lactiferous ducts are free from tumor cells (H&E, ×20). **b** The tumor cells are arranged in sheets or fascicles. The tumor cells have a small amount of cytoplasm and hyperchromatic nuclei (H&E, × 200)

ranges from 0.5% to 1.3%.[5–7] The pathological features of metastases in the breast include absence of in situ or intraductal carcinoma, which characterizes primary breast cancer, and a histologic pattern similar to that of the extramammary primary.[1] The most common primary sites that metastasize to the breast are the contralateral breast, melanoma, lymphoma, ovary, and lung.[8,9] The average time interval between the initial diagnosis of the primary neoplasm and the biopsy of the breast for metastatic disease can range from 23 to 27 months.[10,11]

Women are affected 6 times more frequently than men; the average age at the time of metastasis is 48 years in women and 61 years in men.[2,12] In fact, over 70% of the cases occur in women younger than 50 years of age. However, malignant disease is more common after 50 years of age.[12] The relatively younger age of women with breast metastases suggests that the physiological state of the breast may provide fertile ground for metastases. In an attempt to determine why metastases in the breast are more frequent in younger patients, Deeley looked for differences in breast structure in the different age groups. The obvious differences appear to be in the blood supply of the breast and in the cellular pattern of the breast tissue.[12] The breasts of older patients have a poor blood supply and consist mainly of fat and fibrous tissue. Geschickter suggested that a regression of the mammary lobules and acini may occur toward the end of the third decade.[13] In older women, lobular elements disappear, the stroma becomes increasingly dense, and the blood vessels may become obliterated by connective tissue. It is thought that metastases to the breast are uncommon, since malignant disease is more prevalent in older women when the breast is no longer a suitable organ for metastatic cancer cells due to large areas of fibrous tissue and a relatively poor blood supply. The fact that such cases are rare in males supports this theory, particularly as most of these tumors tend to be metastases from prostatic carcinomas in patients treated with estrogens, which are known to increase the mammary blood flow.[14–16]

Synovial sarcoma originates in the deep soft tissues and primarily appears in close proximity to limb joints. The tumor accounts for 5.6%–10.0% of all soft tissue tumors, and 72% of the patients are younger than 40 years of age.[17] Metastatic lesions develop in about half of all cases, but many make their appearance many years after the initial diagnosis. As in other types of sarcoma, the principal sites of metastasis are the lungs, followed by the lymph nodes and the bone marrow. In our cases with metastasis, the lungs were involved in 94% of patients and the lymph nodes in 21%; similarly, in the series reported by Ryan et al., the lungs were affected in 94% of cases and the lymph nodes in 10%.[18] The 5-year survival rate of patients with synovial sarcoma of the extremities ranges from 36% to 64%. A poor prognosis is associated with occurrence after the age of 20 years, a primary lesion greater than 5 cm in diameter, a proximal origin, and a monophasic type.[17]

To our knowledge there has been only one other reported case of solitary metastatic synovial sarcoma to the breast in the world literature. Banerjee et al. reported a 28-year-old woman who had a left upper lobe lung resection for a synovial sarcoma 4 years prior to needing treatment for a breast lesion.[4] Our case is thus

the second one of a solitary metastatic breast tumor arising from a synovial sarcoma and is also the first reported case of metastasis from a primary of the lower extremity.

Metastatic breast tumors are often superficial, sharply limited, solitary masses with a predilection for the upper and outer quadrant.[1,2,9,19] Multiple lesions, bilateral involvement, and diffuse diseases are less common. Pain, tenderness, and/or discharge are usually absent, although Hajdu and Urban, in a review of 51 cases, stated that more than half of their patients complained of pain and discomfort.[1] Adherence to the skin and changes in the nipple are usually absent. Mammography is effective for detecting metastatic tumor in the breast in over 80% of patients.[9] Metastases are usually well circumscribed and they are difficult to distinguish from a fibroadenoma or other benign solid lesions. The rapid growth of a clinically and radiographically benign-appearing breast mass, especially with a previously treated malignant neoplasm, should raise the suspicion of a metastasis in the breast.[9,20] Axillary node involvement is frequently encountered. In an earlier series, 25%–58% of patients had nodal involvement, with an overall incidence of 48%.[1,2] Our patient had a large breast tumor located at the site of the operation scar, which had characteristics of a metastatic breast tumor clinically, on mammography, and on ultrasonography.

The survival rates are poor following the discovery of a breast metastasis. The survival rate ranges from 10.9 to 13 months in contrast to primary breast carcinoma, which has an average survival of greater than 5 years.[2,10] Hajdu and Urban concluded that metastasis to the breast apparently indicates the beginning of widespread dissemination of disease. Despite the various forms of initial treatment and chemotherapy, 41 of 51 patients died of disease within an average of 1 year after a breast biopsy.[1] McCrea et al. reported that, of their 16 patients, 11 died within 12 months or less with disseminated metastases, and 2 patients, one with leukemia and the other with Hodgkin's disease, are currently well and in clinical remission 6 years after the discovery of their primary malignancy.[11]

Although we added adjuvant chemotherapy after the local recrudescence and distant metastasis to the breast, the patient developed another distant pulmonary lesion via the hematogenous route within a short period of time after the second operation. Although good local control was achieved with the mastectomy, the presence of the metastatic lesion of the breast presages widespread neoplastic dissemination. Therefore, it is recommended that adequate systemic adjuvant therapy be given to patients with synovial sarcoma, especially in cases with poor prognostic factors.

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