Pathol. Oncol. Res. (2009) 15:467–471
DOI 10.1007/s12253-008-9121-1

ORIGINAL PAPER

Breast Carcinoma Metastasis in Recurrent Myxoid Liposarcoma

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Received: 19 October 2008 / Accepted: 21 October 2008 / Published online: 6 November 2008

Abstract Tumor to tumor metastasis is a rare, but well recognized entity, most commonly involving a carcinoma metastasis to a benign or low grade mesenchymal tumor. A case of breast carcinoma metastasis in a recurrent myxoid liposarcoma is presented in this study. A 52-year-old female patient with a history of breast carcinoma (70% invasive lobular carcinoma and 30% invasive ductal carcinoma) presented with a mass in the right lumbar region. The excised mass was diagnosed as myxoid liposarcoma. The tumor recurred twice and was reexcised. Microscopic examination of the second recurrence revealed multiple foci of breast carcinoma metastases in myxoid liposarcoma. Immunohistochemical study showed staining for CK19, GCDFP-15, estrogen and progesterone in metastases. Both breast carcinoma metastasis and myxoid liposarcoma were immunoreactive for E-cadherin and beta-catenin. To our knowledge, this is the first reported case of breast carcinoma metastasis in myxoid liposarcoma, and the first occurrence of metastasis in a liposarcoma.

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Keywords Beta-catenin · Breast cancer · E-cadherin · Liposarcoma · Tumor to tumor metastasis

Introduction

Tumor to tumor metastasis is a rare but well recognized entity [1–3]. The metastatic tumor is commonly an aggressive carcinoma and the recipient tumor is a benign or a low-grade mesenchymal neoplasm [4–7]. Lung, breast, melanoma and renal cell carcinoma are the most common metastatic tumors and the target of metastasis is a tumor like meningioma [8–11], leiomyoma, fibroma or an adenoma. Renal cell carcinoma may also act as a recipient [12].

A case of breast carcinoma metastasis in recurrent myxoid liposarcoma is presented in this study. To our knowledge, this is the first case in the literature with this combination of a donor and a host tumor and the first occurrence of metastasis in liposarcoma.

Materials and Methods

A 52-year-old female patient referred to the hospital with the complaint of a palpable painless mass in her left breast. Ultrasonographic examination of the breast showed a solid vascular lesion. Mammography showed an ill-defined stellate mass with calcification. Atypical epithelial cells were detected with fine needle aspiration cytology. There wasn't any finding of metastasis with abdominal ultrasonography and bone scintigraphy. Histopathological findings of frozen section were consistent with invasive carcinoma. Modified radical mastectomy and axillary curettage were performed. Gross examination showed a 5.5×4.5×2 cm tan to yellow colored, ill-defined mass with firm consistency

localized in the upper outer quadrant and extending to the lower outer quadrant. The nearest surgical margin to the fascia was 0.8 cm. The skin and the nipple showed no pathological findings. The rest of the breast tissue was fibro-adipose and no other mass was defined. With dissection of the axillary curettage material, 13 lymph nodes with the largest one 2 cm in diameter were dissected. Microscopic examination of the mass showed malignant tumor infiltration in the breast tissue composed of round to ovoid noncohesive cells dispersed in a fibrous stroma or cells arranged in linear cords presenting in a concentric pattern around the ducts (Fig. 1). Focal necrosis and microcalcifications were present. Widespread vascular and lymphatic invasion and perineural invasion were observed.

Results

The tumor was interpreted as mixed form of invasive breast carcinoma (70% invasive lobular carcinoma and 30% invasive ductal carcinoma). The histological grade of invasive ductal carcinoma was II/III and nuclear grade was II/III. Immunohistochemical study for hormone receptors showed +/+++ expression for estrogen (Neomarkers, 1/400) and +/+++ expression for progesterone (Neomarkers, 1/400). C erb 2 (Neomarkers, 1/400) did not show membranous staining in the tumor cells. The tumor was multicentric in the upper inner, lower outer and upper outer quadrants. There was lymphatic invasion in the superficial dermis. The tumor was adjacent to the fascial surgical margin. There was tumor invasion in the pectoral muscle. All of the lymph nodes showed carcinoma metastasis with pericapsular lymph node infiltration. Fibrocystic changes were present in the non-tumoral breast tissue. Postoperative local radiotherapy, hormonotherapy (tamoxifen) and chemotherapy (six cures of epidoxorubicin, cyclophosphamide and fluorouracil) were performed.

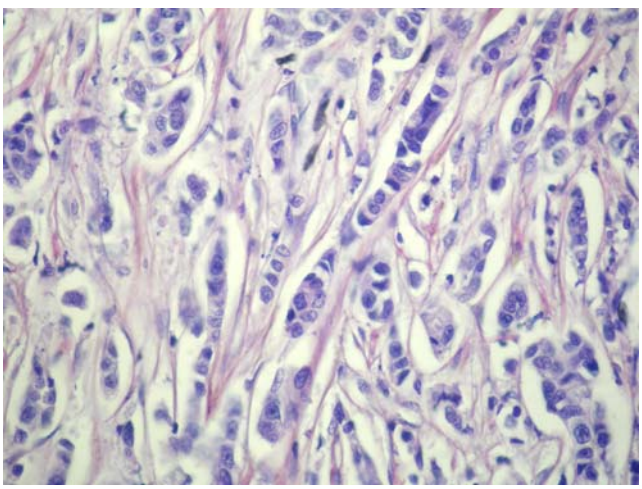

Fig. 1 Breast carcinoma consisting of round to ovoid cells arranged in linear cords (H & E, ×200)

Seven months later the patient referred to the hospital again for a slowly growing painless mass in the right lumbar region. The computerized axial tomography examination showed a 7 cm lobulated soft tissue mass in the subcutaneous fatty tissue, extending to latissimus dorsi and superficial fascia. The magnetic resonance image of the region showed a 7 cm lobulated soft tissue mass in subcutaneous adipose tissue extending to quadratus lumborum muscle. It showed high signal intensity with T_1 and low signal intensity with T_2 weighted image. The mass was totally excised. It was a well circumscribed lobulated mass measuring 7 cm in diameter. On section it was multilobular and myxoid in appearance with foci of hemorrhage. Histopathological examination showed a proliferation of uniform round to oval shaped mesenchymal cells in a myxoid stroma having a rich plexiform vascular network. Occasional lipoblasts were dispersed throughout the tumor. The lesion was diagnosed as myxoid liposarcoma with positive surgical margins. Three months later the lesion recurred and was reexcised. Grossly it was a lobulated mass 5 cm in diameter. On cut section, it was similar in appearance with the primary tumor. On histopathological examination, similar findings were observed and the lesion was diagnosed as myxoid liposarcoma. The lesion was 0.3 cm from the nearest surgical margin. One year later the lesion recurred again. The excised mass was 6 cm in diameter and gelatinous in appearance. Histopathologically it was consistent with myxoid liposarcoma. Surprisingly, there were multiple foci of atypical ductal appearing structures inside the tumor (Fig. 2a,b). Immunohistochemical study showed positive staining for CK 19 (Neomarkers; 1:200; Fig. 3) and GCDFP-15 (Neomarkers; prediluted; Fig. 4), and faint staining for estrogen (Neomarkers; 1/400) and progesterone (Neomarkers; 1/400) receptors. E-cadherin (Immunovision, clone ECH-6, 1:200) and beta-catenin (Immunovision, clone cat-a 1, prediluted) showed staining both in the ductal structures and liposarcoma (Fig. 5a,b). The findings were interpreted as invasive breast carcinoma metastasis in recurrent myxoid liposarcoma. Membranous staining for E-cadherin suggested ductal pattern of metastasis.

During her 5 month follow-up, lymph nodes in the paratracheal and perigastric regions, nodular densities in the lower lobes of the lungs, and ascites were detected, and the patient died of widespread breast carcinoma metastasis.

Discussion

Metastasis, well known as the formation of secondary tumor implants in distant organs, involves a complex

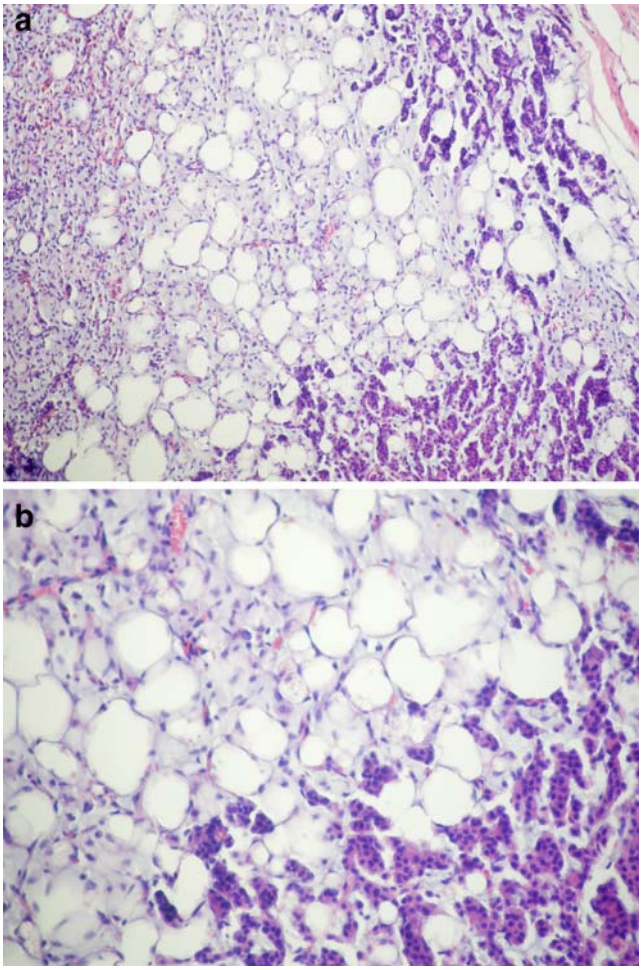

Fig. 2 **a** Atypical ductal structures in myxoid liposarcoma (H & E, ×100). **b** The same structures with higher magnification (H & E, ×200)

multistep process. The tumor penetrates the stroma and the vessels, aggregates with the platelets, adheres to distant endothelia and results with extravasation and recolonization [13]. In general, the more aggressive and the larger the primary neoplasm, the greater is the likelihood that it will metastasize. However, some well differentiated, slowly growing, small lesions metastasize, while some rapidly growing large lesions may remain silent. The ability of a neoplasm to metastasize depends on several factors, which include production of collagenases, secretion of free soluble adhesion molecules by the tumor cells and the production of peptides inducing angiogenesis [14, 15].

Tumor to tumor metastasis is an infrequent condition. Criteria for tumor to tumor metastasis have been proposed by Chambers et al. [16]. More than one primary tumor must exist. The metastasizing tumor should be compatible with the primary tumor. The metastatic tumor should not be a contiguous growth or embolization of tumor cells and be at least partially enclosed by a rim of histologically distinct

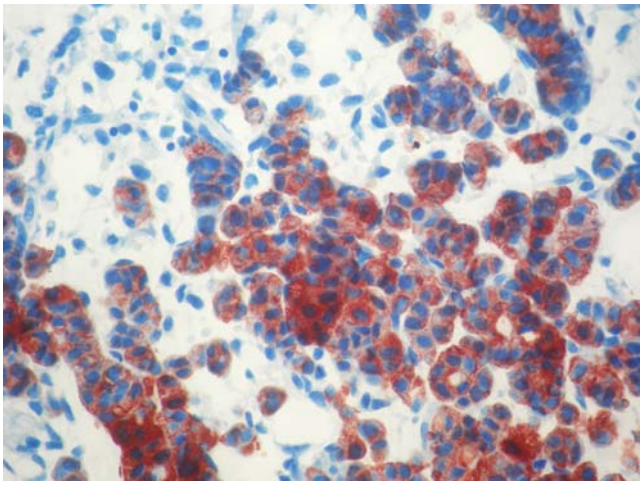

Fig. 3 Immunoreaction for CK 19 in metastasis of breast carcinoma

tumor tissue. Tumors that have metastasized to the lymphatic systems, where lymphoreticular malignant tumors already exist are not excepted in this category.

Meningiomas have been the primary recipient tumor of metastatic tumors [17, 18]. The highly vascular architecture, slow growth rate, high collagen and lipid content of meningiomas provide a medium for seeding of tumor cells. Noncompetitive metabolic environment, and cell to cell interaction from hormonal, enzymatic and immunologic aspects have been ascribed [19]. These criteria can also be applied for other recipient tumors. Abundant vascularization and slow growth of a low grade tumor make it vulnerable to blood borne metastases. Benign and low-grade tumors generally proliferate slowly and remain unnoticed for a long period, thus become candidates for a focus of metastasis [10]. Rich vascularity and high lipid content of the myxoid liposarcoma might have provided a suitable environment for metastasis in the presented case.

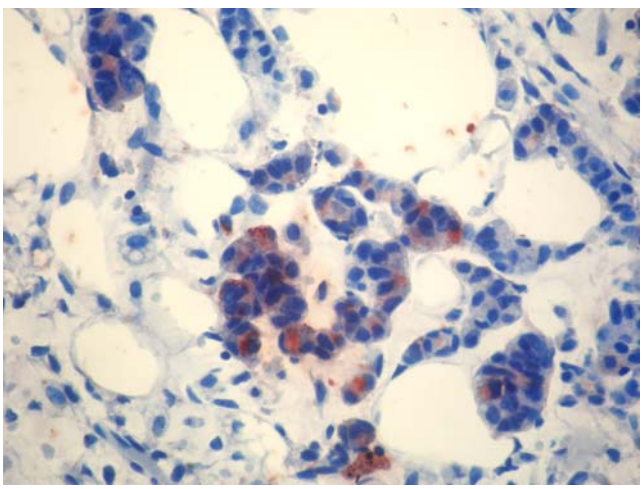

Fig. 4 Immunoreaction for GCDFP-15 in metastasis of breast carcinoma

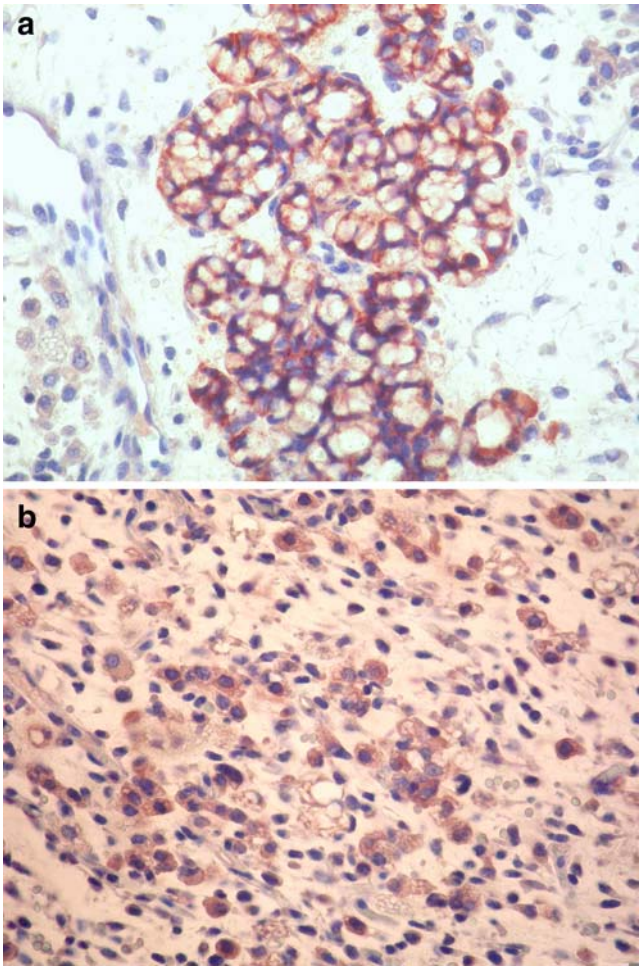

Fig. 5 **a** Membranous staining pattern of E-cadherin in ductal structures. **b** Immunoreaction for E-cadherin in liposarcoma

Alteration in cell adhesion molecules is important in metastasis [14, 20]. Loss of intercellular adhesion and increased cell motility promote tumor cell invasion. E-cadherin is an epithelial subtype of cadherin family that works as a cell adhesion molecule. Its expression has been identified in most types of normal epithelia and cancers. Loss of a reduced expression of E-cadherin cause distraction of tumor cells with correlation to invasiveness and metastasis. The expression on the contrary may promote cell adhesion if the recipient cells also express E-cadherin. This expression has also been described in intratumoral metastasis [18, 19]. The immunoreactivity of E-cadherin was both detected in breast cancer cells and meningioma. Both the carcinoma and liposarcoma showed immunoreaction for E-cadherin and beta-catenin in the presented case. As far as we know, E-cadherin expression in liposarcoma hasn't been reported before. On the other hand, positive staining for beta-catenin was found in 42% of dedifferentiated liposarcoma and 28% of well differentiated liposarcoma cases in a study [21]. The expression of cell adhesion molecules may be one of the factors that promote tumor to tumor metastasis.

The prognosis of invasive ductal carcinoma is influenced by classical prognostic variables of histological grade, tumor size, lymph node state and vascular invasion. The status of the axillary lymph nodes is the most single prognostic factor. Tumor size is an important prognostic factor for axillary lymph node involvement and prognosis. All of the 13 lymph nodes showed carcinoma metastasis with perivascular lymph node infiltration. The tumor tissue had a considerably large diameter as 5.5 cm, also correlating with aggressive behavior. There is a higher frequency of tumor metastasis in invasive lobular carcinoma. Seventy percent invasive lobular component of the tumor presented also plays a role in widespread metastasis. Breast carcinoma is the most common origin of cutaneous metastasis in women [22]. A low grade tumor located in subcutaneous tissue might have been another target of metastasis in this case.

Myxoid liposarcoma is the second most common type of liposarcoma representing approximately one third of all liposarcomas and 10% of all adult soft tissue sarcomas. It is a slow growing, deep seated tumor, mostly in the lower extremity of a relatively young adult patient. Metastases are often in other deep soft tissue, retroperitoneum and extremities. Myxoid liposarcoma and round cell liposarcoma represent the ends of a spectrum of the same entity. Myxoid liposarcoma with a round cell component has a higher tendency to recur and metastasize. Pure myxoid liposarcoma is considered a low-grade sarcoma [23].

In a study by Heuvel et al. [24] on myxoid liposarcoma, tumor size, age at presentation, and tumor grade had a negative influence on survival. Tumor grade was the only independent prognostic factor that remained significant by multivariate analysis. The risk of local recurrence was associated with tumor location, 86% of the patients with a nonextremity location developed a local recurrence, compared with 24% of tumors in extremity location. Surgical margins and postoperative radiotherapy are the main factors associated with development of local recurrence. In the Mayo Clinic study, no significant difference was seen in local recurrence rate between patients treated with marginal resection with radiotherapy included versus wide resection alone [25]. Although metastasis in a pure myxoid liposarcoma with no round cell component is reported, marginal resection and nonextremity location of the tumor was probably the reasons for the recurrences.

Although tumor to tumor metastasis is rare, this possibility should be kept in mind when an unusual dimorphic pattern is detected in a tumor. History of a previous tumor and immunohistochemical study can be helpful in analyzing the morphologic findings.

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