High-grade pleomorphic liposarcoma of the breast

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Abstract

Liposarcoma is a mesenchymal neoplasm of uncertain pathogenesis. It is the second most common soft tissue sarcoma, found uncommonly in the breast, and constitutes less than 1% of all malignant breast tumors. We report a case of a 50-year-old woman with a pleomorphic type liposarcoma of the breast.

Keywords

Liposarcoma; pleomorphic; myxoid; round cell; mastectomy.

Introduction

Liposarcomas are the second most common malignant tumors of the soft tissues, constituting 16–18% of all malignant soft tissue tumors. However, they are rarely found as a malignancy within the breast. They may arise within a cystosarcoma, or independently from mammary adipose tissue. Approximately 17 new cases per million women are reported[1]. Of the 3% of breast tumors representing sarcomas, less than 0.3% are found to be liposarcomas. Thus, we report a case of this rare finding of a pleomorphic liposarcoma of the breast in a 50-year-old woman.

Case report

A 50-year-old woman presented with a palpable left breast mass. The mass was first noticed in October 2009, about a month prior to her examination. She had no personal risk factors of breast cancer and her only family history was in a maternal and paternal aunt. Her Gail score at 5 years was 1.2% and her lifetime risk was 10.8%. She denied history of trauma to her breast, nipple discharge, or skin changes.

On physical examination her body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters) was 61 kg/m². In the upright position, she had very large symmetrical ptotic breasts without visual deformity. In the left breast she had a palpable, freely mobile, rubbery mass in the upper inner quadrant at the 10 o’clock position about 8 cm from the nipple. The right breast was unremarkable. The left breast mass measured approximately 4–6 cm in size, and was mildly tender to palpation. Axillary and supraclavicular nodes were not palpable.

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A bilateral diagnostic mammogram was performed, and in the upper inner quadrant a superficial, smoothly marginated dense area was seen (Fig. 1a,b). Ultrasound correlation showed a 3.7 × 1.6 × 3.1 cm hyperechoic mass in the 10 o'clock position about 8 cm from the nipple (Fig. 1c). Ultrasound Doppler showed a large area of internal blood flow to the mass (Fig. 1d). A differential diagnosis of lipoma, hemangioma, or angiolipoma was suspected.

In January 27, 2010, she underwent a left excisional breast biopsy. The mass was easily enucleated out of surrounding breast tissue, and appeared as a benign lipoma. The differential diagnosis from the preliminary pathology was most consistent with angiolipoma. On final pathologic review, high-grade pleomorphic liposarcoma was reported with tumor extension into the inferolateral margin. The tumor’s greatest diameter was 4 cm. Since the tumor extended into the inferolateral margin, re-excision was recommended. With her generous breast to tumor ratio, re-excision to a 2-cm margin was felt to be adequate over a mastectomy (Fig. 2a,b) and was performed on March 10, 2010.

On gross examination, the left breast tumor was fairly well circumscribed with a thin fibrous lining. No necrosis was noted. Microscopically, on low power, the neoplasm has lipomatous features with intratumoral nodules showing increased cellularity (Fig. 3a,b). On high power, the highly cellular areas are composed of large lipoblasts with extensive differentiation and severely

![Fig. 1. (a,b) Mammograms showing an ovoid isodense mass in the upper inner left breast with predominantly well-defined margins, although partially obscured or indistinct anteriorly. Palpable BB marker located adjacent to the mass. (c,d) Grayscale ultrasonography demonstrates a wider than tall echogenic solid mass with well-defined borders. Mass located superficially in the left upper inner quadrant and corresponds to the mammographic and palpable mass. Color Doppler demonstrates hypervascular flow.](image)

![Fig. 2. (a) Breast prior to re-excision. (b) Re-excision of inferolateral 2-cm margin.](image)
pleomorphic nuclei (Fig. 3c,d). Mitotic figures are readily identified (approximately 8 in 10 high-power fields). The less cellular areas surrounding the nodules are composed of lipoblasts with mild-to-moderate nuclear atypia. No glandular/epithelial or heterologous elements are seen to suggest metaplastic carcinoma. Immunohistochemical staining is negative for CK-OSCAR, actin, CD34, CD117, HMB-45, and S-100. To exclude other histologic subtypes that could have possibly represented this tumor, fluorescent in situ hybridization (FISH) was performed. The tumor cells were negative for CPM and CHOP genes. Due to the unusual features of this tumor the case was sent to the Mayo Clinic (Rochester, MN) for external consultation, and reviewed by three pathologists, Drs A. Folpe, A. Nascimento, and A. Oliveira. They concurred with the diagnosis of a high-grade pleomorphic liposarcoma.

Subsequent staging with computed tomography (CT) scan of her chest, abdomen, and pelvis to evaluate for metastatic disease was negative. Evaluation by medical and radiation oncology was performed. She was offered radiation therapy and underwent a total of 5940 cGy in 33 fractions over 51 days. It is now 9 months since her surgery and adjuvant radiation therapy and no local or metastatic disease has been found.

**Discussion**

Primary sarcomas of the breast are rare malignant tumors arising from the mesenchymal tissue of the mammary gland, and lack a neoplastic epithelial component. Most sarcomas are made up of malignant fibrous histiocytoma, fibrosarcoma, liposarcoma, and angiosarcoma. After malignant fibrous histiocytoma, liposarcoma is the second most common type of soft tissue sarcoma in adults. They are mesenchymal neoplasms of uncertain pathogenesis, and are usually found in the retroperitoneum or extremities. They can be found in rarer locations such as the spermatocord, peritoneal cavity, axilla, vulva, and the breast. The breast is a rare site to find this entity, and liposarcomas represent 0.3% of all mammary sarcomas. Most patients are women between the ages of 40 and 60 years. Only three cases of liposarcomas in the breast have been reported in men[1].

When a sarcomatous-appearing tumor in the breast is identified, it is far more likely to be a metaplastic carcinoma or a malignant phyllodes tumor than a primary sarcoma. Metaplastic carcinomas represent a morphologically heterogeneous group of invasive breast cancers in which a portion of the glandular epithelial cells comprising the tumor have undergone transformation.
into an alternate cell type, either a non-glandular epithelial cell type (e.g., squamous cell) or a mesenchymal cell type (e.g., spindle cell, chondroid, osseous, myoid). Before diagnosing any breast tumor as a primary sarcoma, careful attention must be made to exclude metaplastic carcinoma by extensively sampling the tumor to identify foci of conventional invasive mammary carcinoma and/or ductal carcinoma in situ, and by conducting immunostains using multiple anticytokeratin antibodies. The possibility of phylloides tumor should be excluded by extensively examining the lesion to identify the benign epithelial component that characterizes these lesions[2].

Determination of the histologic type and degree of differentiation is crucial for prognosis and surgical planning of liposarcomas. Histologic features of liposarcomas were first described by Virchow in 1857. They are usually grouped in four main histologic types: myxoid/round cell, well differentiated, dedifferentiated, and pleomorphic. Myxoid liposarcomas are composed of three main tissue components: proliferating lipoblasts, a plexiform capillary pattern, and a myxoid matrix containing mucopolysaccharides. The extracellular mucoid can form large pools and can appear as a lace-like pattern. Myxoid liposarcomas are considered an intermediate grade, and include the round cell variant as its high-grade counterpart. They are of low-grade malignancy with a tendency to recur locally but have the risk of dedifferentiation. The well-differentiated type is radiolucent and can be clearly distinguished from surrounding soft tissue. They contain irregularly shaped cells with hyperchromatic nuclei. They are most common with retroperitoneal lesions. Pleomorphic liposarcomas are very aggressive high-grade sarcomas. They show a high degree of cellular pleomorphism, including bizarre giant cells. Hemorrhage and necrosis can also be seen within these kinds of tumors[3–5].

Liposarcomas have specific molecular lesions that define their subtypes. Myxoid/round cell liposarcomas are characterized by translocation t(12;16) (q13;p11) fusing genes FUS at 16p11 and CHOP at 12q13 or, rarely, translocation t(12;22) (p13;q12) fusing CHOP with EWSR1. This particular translocation and its products are found only in myxoid liposarcomas and are diagnostic for this tumor. In contrast, well-differentiated or dedifferentiated liposarcomas display amplifications of chromosome locus 12q13-15, and contain several amplified genes including MDM2, CPM, CDK4, and TSPAN 31. Pleomorphic and dedifferentiated liposarcomas share overlapping histologic features but have very different cytogenetic and expression profile studies, so it is important to decipher between the two. This case shows a predominantly lipomatous tumor component, with morphologic features supporting pleomorphic liposarcoma, high grade. In addition, the tumor cells were negative for CPM and CHOP genes, and because CPM amplification is absent, well-differentiated and dedifferentiated liposarcoma is low. The lack of CHOP (DDIT3) makes myxoid liposarcoma less likely. Pleomorphic liposarcomas lack a specific detectable genetic alteration, showing in most instances a complex karyotype[6,7]. Based on the collective findings, a diagnosis of a high-grade pleomorphic liposarcoma was made.

Liposarcomas have to be differentiated from benign entities such as a true lipoma or, in our patient with a BMI of 61, pseudosarcoma of the morbidly obese. Histologically the distinctive features of pseudosarcoma include reactive vessels at the border of the adipose and fibrous tissue, which was not identified in our specimen[8]. Compared with lipomas, liposarcomas are fast growing and are composed of denser than normal adipose tissue. Their diagnosis is suspected on clinical findings, and confirmed with tissue pathology. The use of mammography, ultrasonography, CT scan, and magnetic resonance imaging are used to provide an exact preoperative assessment of tumor extension[9].

The mainstay of treatment for sarcoma is surgery, with local control of the disease being most important. In evaluation of a patient with a breast mass suspicious for sarcoma, the diagnosis can be made via Tru-Cut biopsy, fine needle aspiration or stereotactic biopsy. The protocol for treatment of a mammary liposarcoma has not yet been determined. The finding of pseudoencapsulation intraoperatively tempts the surgeon to perform enucleation, however often there are soft tissue attachments of these tumors to the surrounding tissue that can be overlooked. Enucleation of the encapsulated mass will lead to recurrence and positive margins. Thus, surgical plans should be for wide local excision with 2-cm margins. The only current indication for mastectomy or removal of the axillary lymph nodes is when these procedures are necessary to obtain clear margins. When metastases in the axillary lymph nodes are found clinically, axillary nodal dissection is required for complete excision of the tumor. The indication for the use of
adjuvant chemotherapy and radiation therapy in this location should follow the indications for soft tissue sarcomas in general. This includes the inability to obtain negative margins, size >5 cm, or a high-grade liposarcoma, such as pleomorphic or round cell type[6,10]. These tumors do not appear to display hormone receptors, and adjuvant therapy with estrogen antagonists has no place in the treatment[11].

Prognosis is very hard to determine in these patients because of the small number of reported cases. The 5-year survival rate of liposarcoma in areas of the body other than the breast is 90% for well-differentiated lesions, 80% for myxoid lesions and 20% for round cell and pleomorphic lesions. Pleomorphic lesions are more likely to recur. Austin and Dupree[12] reported that metastasis developed in 4 of 20 patients with liposarcoma of the breast, all of which were of the pleomorphic type. Well-differentiated liposarcomas often recur locally but rarely with metastasis.

### Teaching points

- Liposarcoma of the breast is among the rarest of malignant mammary tumors.
- Determination of the histologic type and degree of differentiation is crucial for prognosis and surgical planning.
- It is important to differentiate sarcomas from breast carcinomas, as the treatment of the two conditions differ.
- The mainstay of treatment is surgical excision with at least 2-cm margins.
- Adjuvant chemotherapy and radiation should be considered in high-risk cases.
- Cytogenetic analysis is becoming the standard of care for all types of sarcomas.

### References