Clinical Case Report

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Breast liposarcoma with solitary metastasis to the pleura

A case report

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Abstract

Rationale: Breast cancer is the most prevalent malignancy in women worldwide. Our patient presented with a history of breast liposarcoma (LPS) and was found to have pleural metastasis during the initial workup.

Patient concerns: The patient was complaining about chest pain and dyspnea that had persisted for a week.

Diagnoses: After a full evaluation and histological diagnosis, she was diagnosed as metastatic breast LPS.

Interventions: We adopted 6 cycles of pegylated liposomal doxorubicin (PLD) plus ifosfamide as 1st-line palliative chemotherapy, combined with local pleural effusion management.

Outcomes: The patient's symptoms were notably relieved, and both malignant metastatic lesions and pleural effusion were controlled.

Lessons: Although metastatic breast LPS is rarely reported and incurable, more clinical experience and use of next-generation sequencing should be helpful in finding the effective treatment for metastatic LPS.

Abbreviations: CDK = cyclin-dependent kinase, CT = computed tomography, LFS = Li–Fraumeni syndrome, LPS = liposarcoma, NCCN = the National Comprehensive Cancer Network, PLD = pegylated liposomal doxorubicin.

Keywords: breast liposarcoma, chemotherapy, solitary metastasis to pleura

1. Introduction

Breast cancer is the most prevalent malignancy in women throughout the world.[1] Liposarcoma (LPS) which originates in the breast is rare, and heterogeneous LPS differentiation in malignant phyllodes tumors is more common.[2] The patient in our study presented with breast LPS and was found to have pleural metastasis during the initial workup. The rare incidence of the condition raised the question of the proper palliative treatment for the metastatic breast LPS.

2. Case report

A 51-year-old Chinese female presented at the inpatient section of the medical breast center at Zhejiang Cancer Hospital on July 21, 2016, complaining of chest pain and dyspnea that had persisted for a week. The Eastern Cooperative Oncology Group performance score was 2. She had previously received modified radical mastectomies in both breasts, one for ductal carcinoma in situ in the left breast 7 years prior, and another for LPS in the right breast in 2014. She experienced menarche at the age of 14 and had regular cyclical periods. Menopause age was 49 years old. She had her 1st child at 26 years old and the child had been breastfed. There was no history of oral contraceptive use, and she had no family history of breast cancer.

The endocrine adjuvant therapy for her left breast ductal carcinoma in situ was tamoxifen for 5 years, and no radiotherapy had been given. The LPS mass was 1.8 cm × 1.5 cm × 1.5 cm in her right upper quadrant breast. No postoperative adjuvant therapy was administered after the surgery.

After physical and imaging examinations, bulk pleural effusion and multiple masses in the pleura were discovered by computed tomography (CT) scan when the patient came to our inpatient department. Core needle biopsy of the pleural mass identified a metastatic LPS (Fig. 1). Immunohistochemistry was positive for S100 proteins (Fig. 2).

After discussion in a breast cancer multidisciplinary team meeting, considering the relatively milder side effects of pegylated liposomal doxorubicin (PLD) than doxorubicin, we decided to treat the patient with a regimen of PLD, ifosfamide, and pleural cavity infusion of recombinant human interleukin 2. The body

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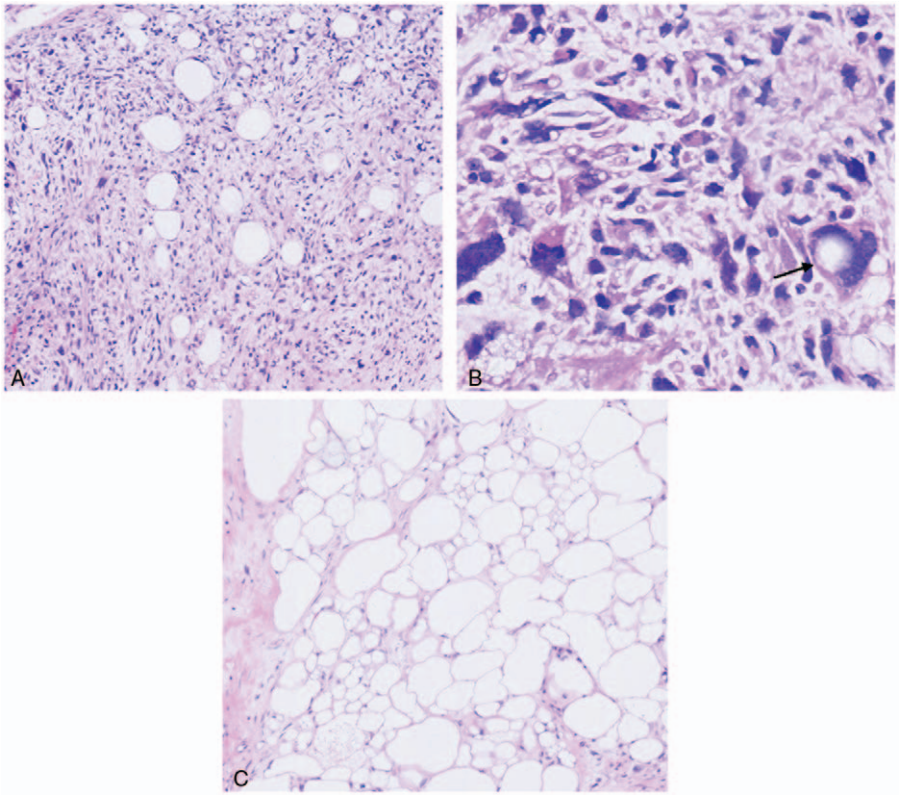

Figure 1. (A) The differentiated region of the metastatic breast LPS lesion on the pleura; residual adipose tissue is visible in the central part. H&E stain ×100. (B) Many differentiated cells are visible; black arrow points to 1. H&E stain ×400. (C) Varying sizes of adipose cells of the metastatic breast LPS lesion on the pleura. H&E stain ×100. H&E = hematoxylin and eosin, LPS = liposarcoma.

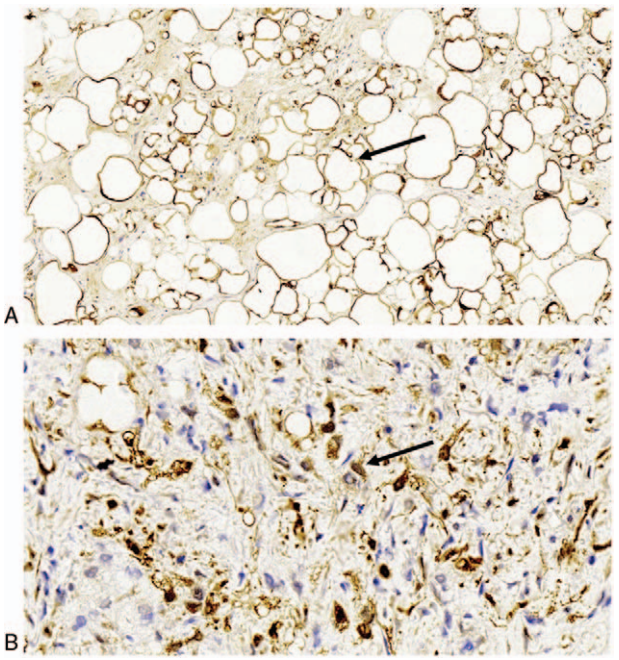

Figure 2. Metastatic breast LPS lesion on the pleura. Immature adipose tissue is seen around the differentiation region, presented as spindle-shaped and irregular-shaped cells. S100 proteins are strongly expressed, as seen by nuclear IHC staining (black arrows). IHC staining ×100 (A) and ×400 (B). IHC = immunohistochemical, LPS = liposarcoma.

surface area of the patient was 1.55 m^2, the dose and frequency of chemotherapy in detail was PLD 40 mg day 1, ifosfamide 2 g day 1 to 3, q3w. The patient responded well to palliative therapy for 6 cycles (3 weeks/cycle); the response was confirmed by CT scans (Fig. 3). The CT images showed solid masses with low densities representing fat and multiple masses in the pleura covered up by the bulk pleural effusion which resulted in the difficulty in measuring the solid masses directly. Nonetheless, the clear decrease in pleural effusion confirmed the good response to palliative therapy (Fig. 3). Although regular biological tumor marker detecting is not recommended by the National Comprehensive Cancer Network (NCCN) guidelines for soft-tissue sarcoma, we did find some change of serum tumor markers during the treatment. Carbohydrate antigen 125 had declined from 309 U/mL to normal level and neuron specific enolase from 21 ng/mL to normal level after the completion of 6 cycles of chemotherapy. This patient developed grade 1/2 gastrointestinal reaction and hematologic toxicity during chemotherapy. The side effects could be satisfactorily managed in our case. She later underwent regular follow-up for 2 months. She was recently seen at the medical breast cancer clinic with no active complaints, and her dyspnea had been relieved. Informed consent was obtained from the patient for publication of this case report and all accompanying radiographic images and pathological sections.

3. Discussion

Breast sarcoma accounts for less than 1% of all breast malignancies. The incidence of breast LPS among all breast

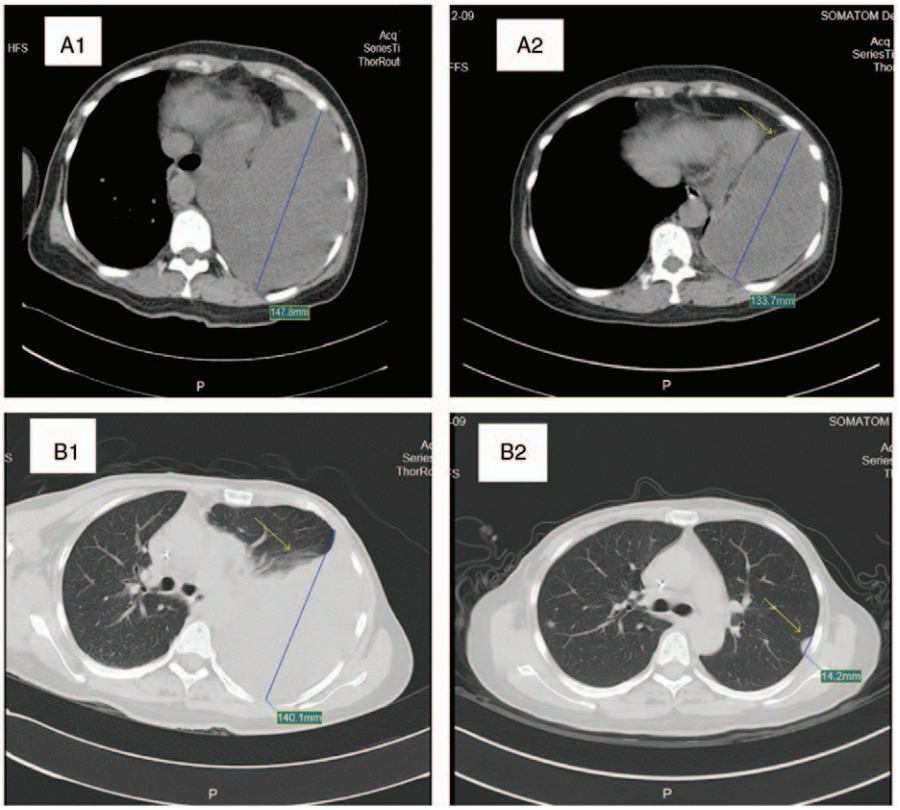

Figure 3. Computerized tomography (CT) scans. Initial CT scan of mediastinal window (A1) and pulmonary tissue (B1) with a massive pleural effusion and in the pleural cavity; later CT scan of mediastinal window (A2) and pulmonary tissue (B2) showing significant changes in tumor size and pleural effusion after 6 cycles of chemotherapy and 3 treatments with recombinant human interleukin 2 injection into the pleural cavity (yellow arrow).

sarcomas ranges from 5% to 10%. Age at diagnosis ranges from 19 to 76 years old (median age is 47 years old); the disease occurs mostly in women. Similar to other primary LPS, the metastatic rate of polymorphic breast LPS is 30% to 50%, and primary breast LPS often metastasizes to the pulmonary system.[2]

LPS tumors are of adipocytic origin, but breast LPS tumors and metastasis of soft tissue sarcoma to the breast are both rare. According to the NCCN guidelines for soft tissue sarcoma,[3] the histopathologic types of adipocytic tumors include dedifferentiated LPS, myxoid/round cell LPS, and pleomorphic LPS. Primary LPS in the breast is unusual and can occasionally transform from a malignant phyllodes tumor of the breast because it contains the heterologous stromal elements.[4,5] The etiology of breast LPS includes genetic factors such as Li–Fraumeni syndrome (LFS), environmental exposure, radiation exposure, and lymphedema after breast surgery. We found some case reports on operable breast LPS,[6–8] but a PubMed literature search yielded few metastatic breast LPS case reports.[9] The propensity of soft tissue sarcoma to metastasize to the lung is not clearly understood.[10] In this case, the breast LPS metastasized to the pleura, which may present similar peculiarities.

There are no special guidelines for the treatment of LPS yet. The principal treatment of potentially operable lesions is complete resection of the tumor by surgery, and high-risk patients should receive postoperative adjuvant therapy.[11] The treatment choices for metastatic LPS are limited, and NCCN guidelines for soft tissue sarcomas[3] offer some recommendations for treatment regimens. For example, anthracycline-based combination regimens (doxorubicin or epirubicin with ifosfamide and/or dacarbazine) can be used as 1st-line therapy; gemcitabine, docetaxel, PLD, vinorelbine, and temozolomide may be effective choices if 1st-line chemotherapy fails. In addition, eribulin, an antimitotic derived from the natural marine sponge product halichondrin B, has been approved by the US Food and Drug Administration for the treatment of advanced LPS in patients who received prior anthracycline chemotherapy. According to the recently published clinical trial results, eribulin was found to extend the median overall survival by 2 months compared with dacarbazine (13.5 vs 11.5 months, hazard ratio: 0.768), and subgroup analysis showed that the survival advantage was especially associated with LPS patients.[12] Furthermore, cyclin-dependent kinase (CDK) inhibitors, such as CDK4/6 inhibitor, have already shown promising clinical activity in breast cancer, LPS, melanoma, and mantle cell lymphoma.[13] The efficacy of CDK4/6 inhibitor in LPS may, at least in part, be attributed to the facts that LPS is a phosphorylated retinoblastoma tumor suppressor protein-positive tumor, and CDK4/6 activity is associated with phosphorylated retinoblastoma tumor suppressor protein expression.[14]

Although the prognosis for patients with metastatic LPS of the breast has been poor in the past, these patients are living much longer nowadays due to dramatic improvements in medical and surgical treatments. In addition, the treatment should be tailored to the needs of each patient, especially each patient with metastatic LPS.

In this case, we had chosen PLD to replace the conventional anthracycline because of its less toxicity and relative efficacy in metastatic breast cancer.

The purpose of testing the metastatic lesion by multigene examination was to find the possible etiology and therapeutic

target for metastatic breast LPS. The results showed that except for several gene mutations with unknown clinical meaning, such as SPEN (p.A2571G), NOTCH1 (p.R1413H), and TBX3 (p.A392V), the patient did have germline TP53 mutation as R175H, which has been reported to be connected with LFS.[15] Although the patient carried the germline TP53 mutation, breast LPS was diagnosed at the age of 49, which does not satisfy the classical diagnosis of LFS.[16] Germline mutations in genes that encode proteins involved in the DNA damage response predispose patients to a variety of tumors.[17] Although histopathological testing is required for diagnosis of the metastatic breast LPS, these novel gene mutations found by the multigene examination from the metastatic tumor in this patient may someday become the therapeutic targets in the future. In addition, the roles of these mutated genes in the pathogenesis of breast LPS and its metastasis warrant further studies.

Cytoreductive therapy to lessen the tumor burden by surgery or radiotherapy may also be beneficial treatment options in some condition. In this case, since the lesions in the pleura were too large for complete removal, we did not select palliative surgery or radiotherapy before chemotherapy. We excluded radiotherapy because the diagnosis of LFS could not be completely ruled out for this patient. Whether the maintenance chemotherapy is a viable approach for metastatic LPS or not is still unknown.

Some points in this case are worth considering. First, because of the intratumoral heterogeneity, a multilesion biopsy was important to minimize the possibility of missing more malignant parts of the primary tumor. Second, the location of LPS may affect its prognosis, so some patients with LPS at high-risk location should perhaps receive more active anticancer therapy after surgery. Third, in order to improve the outcome of breast LPS patients, especially metastatic LPS patients, more clinical experience is needed because breast LPS is rare and next-generation sequencing information should be utilized in clinical practice.

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