

Case Report

The Role of Pulmonary Metastasectomy in Breast Cancer with Limited Progression Following CDK4/6 Inhibitor Therapy: A Case Report

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Abstract

Metastatic breast cancer is primarily managed with systemic therapy; however, the role of pulmonary metastasectomy (PM) in patients with pulmonary oligometastases remains uncertain. We present the case of a 56-year-old postmenopausal woman who developed lung and bone metastases 4 years after resection of her primary tumor. Due to the progression of pulmonary metastasis following combined therapy with ribociclib and fulvestrant for advanced disease, she underwent PM, which histologically confirmed breast cancer metastasis. Following the procedure, she continued the same combined therapy and achieved stable disease. This case highlights that PM can aid in the accurate differential diagnosis of lung nodules in breast cancer patients. For selected individuals, particularly those with limited progression following CDK4/6 inhibitor therapy, PM may be considered an additional treatment option.

Keywords: Breast cancer, oligometastatic disease, progression-free survival, pulmonary metastasectomy

INTRODUCTION

Metastatic breast cancer is a systemic disease, and the primary treatment modalities are chemotherapy, endocrine therapy, immune checkpoint inhibitors, and targeted therapies (e.g., CDK4/6 inhibitors).^[1] Distant metastasis from breast cancer predominantly occurs in the bones, lungs, and liver, with one study reporting pulmonary metastasis in 23.8% to 47.1% of patients with metastatic disease.^[2] In recent decades, the development of effective anticancer agents has

significantly enhanced the prognosis for individuals diagnosed with metastatic breast cancer.^[3]

Oligometastatic disease is characterized by the presence of one or a limited number of detectable metastatic lesions.^[4] It is a type of distant metastasis, for which local therapies may provide potential curative options. For selected patients with pulmonary metastases, pulmonary metastasectomy (PM) is a viable

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treatment approach.^[5] However, the lack of randomized studies demonstrating the survival benefits of PM has led to controversy regarding its effectiveness and role in the management of patients with breast cancer and pulmonary metastases.^[6]

Here, we report a case of breast cancer with metastases to the bones and lungs that developed 4 years after resection of the primary tumor. Shortly after initiating combination treatment with fulvestrant and ribociclib for disease control, the pulmonary metastasis progressed. The patient subsequently underwent PM and achieved stable disease with continued endocrine therapy following the surgery.

CASE REPORT

A 56-year-old postmenopausal woman presented in 2018 with a palpable mass in her right breast. Breast ultrasound revealed a 3.1 cm × 1.5 cm irregular tumor in the right breast with right axillary lymphadenopathy. A core biopsy confirmed the diagnosis of invasive ductal carcinoma. Further evaluation with chest computed tomography (CT) showed no evidence of lung metastasis, and a whole-body bone scan ruled out bone metastasis. In April 2018, she underwent a right modified radical mastectomy. A pathological examination revealed a 4.2 cm invasive ductal carcinoma with metastasis to eight of the dissected lymph nodes. The tumor was positive for estrogen receptor (ER) and progesterone receptor (PR), with a human epidermal growth factor receptor 2 (HER2) score of 0 on immunohistochemical staining. Postoperatively, she received adjuvant chemotherapy consisting of four cycles of doxorubicin and cyclophosphamide, followed by four cycles of docetaxel. She also completed 1 month of adjuvant radiotherapy and began endocrine therapy with letrozole.

In April 2022, she reported moderate low back pain, and an X-ray of the spine revealed an L1 compression fracture, and a bone mineral density test indicated the presence of osteoporosis. To mitigate the adverse effects of osteoporosis associated with letrozole, tamoxifen was substituted. A surveillance abdominal CT scan conducted in July 2022 showed a new bone lesion in the L3 vertebra. A subsequent bone biopsy confirmed metastatic adenocarcinoma of the breast origin; the lesion was ER positive but PR negative and the HER2 score was 0. On identification of the new bone metastases, she was started on a treatment regimen of fulvestrant and ribociclib. Meanwhile, a surveillance chest

CT scan identified a 1.6 cm subpleural nodule in the right lower lobe (RLL), with no nodules detected in the right upper lobe (RUL) [Figure 1]. The nature of the new nodule was uncertain; however, due to its proximity to the heart, a biopsy was deemed challenging, and close follow-up was recommended.

Unfortunately, a follow-up chest CT 3 months later revealed several new grouped subpleural nodules of up to 1.5 cm in the RUL [Figure 2], while the RLL subpleural nodule remained stable. No pleural effusion or mediastinal lymphadenopathy was detected. To further evaluate these findings, she underwent video-assisted thoracoscopic surgery with wedge resection of the RUL in December 2022. A pathological examination confirmed that the RUL tumor was a metastasis from breast cancer, with immunohistochemical staining showing positive ER status, negative PR status, and a HER2 score of 0. The surgical margins were clear. Following the surgery, she continued to receive fulvestrant and ribociclib combination therapy. The latest surveillance chest CT scan in March 2024 showed that the RLL subpleural nodule remained stable in size, with no new intrathoracic lesions identified.

DISCUSSION

In breast cancer patients with lung nodules, PM may be considered for two primary purposes: to achieve histological confirmation and assess molecular status and to explore potential therapeutic benefits. Conventionally, new lung nodules identified after breast cancer treatment are presumed to be metastatic lesions. However, the incidence of second primary neoplasms after breast cancer treatment is increasing, with lung cancers accounting for approximately 5% of these secondary malignancies.^[7] Making a differential diagnosis by radiological examination can be challenging, as some pulmonary metastases may have irregular shapes similar to those of primary lung cancers.^[8] In a retrospective review of resected pulmonary nodules in breast cancer patients, breast cancer metastasis was the most common final diagnosis (75%), followed by primary lung cancer (11.5%) and other histologies including infection and benign tumors (13.5%).^[9] Surgical intervention remains the most effective method for obtaining adequate tissue for histological confirmation and for assessing hormone receptor expression and HER2 status.^[10] Given that pulmonary nodules in breast cancer patients are not always

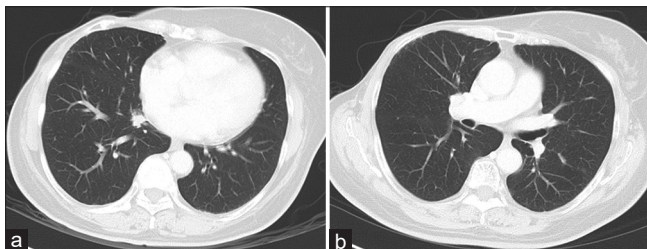


Figure 1: Computed tomography (July 2022) showing (a) a 1.6 cm right lower lobe subpleural nodule (b) with no nodules detected in the right upper lobe

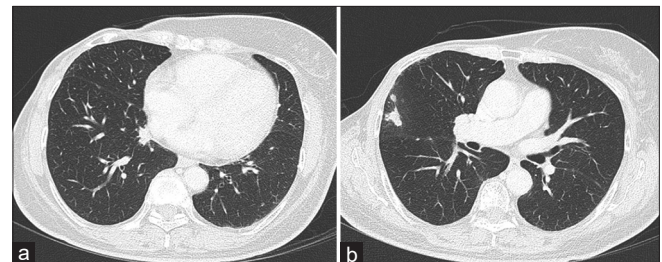


Figure 2: Computed tomography (October 2022) showing (a) stable size of the right lower lobe subpleural nodule but (b) new nodules of up to 1.5 cm in size in the right upper lobe

indicative of metastasis, confirming the pathological diagnosis through surgery remains a viable option.

Except for certain cancers, such as colorectal cancer, metastatic disease is generally considered incurable, and as such metastasectomy is not considered to offer a survival benefit for these patients.^[11] However, with the emergence of targeted therapies in cancer treatment, several studies have shown that metastasectomy or other local therapies can extend survival outcomes for patients undergoing targeted therapy, particularly in non-small cell lung cancer (NSCLC).^[12,13] These approaches are now recommended in the National Comprehensive Cancer Network guidelines for NSCLC.^[14] However, the prognostic impact of PM for metastases originating from breast cancer appears less definitive. A retrospective study of consecutive patients with recurrent breast cancer and oligometastatic lung metastases found that those who underwent PM followed by systemic treatment had a significantly longer 4-year overall survival compared to those who received systemic treatment alone (82.1% vs. 31.6%, $P=0.001$).^[15] However, some studies have suggested that incomplete resection of lung metastases does not significantly impact survival, indicating a potentially limited benefit of PM.^[16-18] The reported 5-year survival rates for metastatic breast cancer patients undergoing PM range from 35% to 72%.^[10] Favorable prognostic factors often include a longer disease-free interval, hormone receptor positivity, a smaller number of pulmonary metastases, and smaller tumor size.^[16] Given the potential survival benefits associated with PM in breast cancer, it should be considered an optional treatment for pulmonary metastases. However, clear selection criteria have not been established, and expert consensus recommends a multidisciplinary team discussion and individualized treatment approach.^[19]

In conclusion, for breast cancer patients with oligometastatic lung metastases, systemic therapy remains the cornerstone of treatment. PM can offer valuable insights into the definitive diagnosis and molecular characteristics. Patients who may benefit from PM could be selected based on criteria such as positive hormone receptor status, a prolonged disease-free interval, and a limited number and size of lung metastases. This approach is particularly relevant for patients showing limited progression following CDK4/6 inhibitor therapy. For these patients, PM may be considered an optional treatment, provided it is discussed comprehensively within a multidisciplinary team.

Declaration of patient consent

This study was performed in accordance with and conforming to the Declaration of Helsinki. The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Data availability statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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