



Relapse of Infiltrating Lobular Carcinoma with Distant Metastasis and Malignant Pleural Effusion after 7 Years of Disease-Free Survival: A Case Report

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Abstract

Breast cancer relapse remains a common cause of morbidity and mortality in patients who initially underwent surgical treatment with or without chemotherapy and radiation. Rates of recurrence are highest in the first two years after diagnosis but the rate of relapse remains persistent more than a decade after diagnosis. Additionally, pleural metastasis of breast cancer, which often presents as a malignant pleural effusion, typically occurs during the first few years after diagnosis but is not common after a long period of disease-free survival. This is a case of breast cancer relapse after 7 years of disease-free survival with lung metastasis and malignant pleural effusion secondary to pleural metastasis and without locoregional recurrence.

Keywords: *breast cancer relapse, pleural metastasis, malignant pleural effusion, breast cancer, mastectomy*

Introduction

Breast cancer is the leading cause of cancer deaths in women worldwide. While screening guidelines and advances in surgical modalities, radiation, and chemotherapy have all contributed to a drastic decrease in the number of deaths due to breast cancer, breast cancer relapse is still a common cause of mortality in patients who have completed treatment [1].

The frequency of locoregional recurrence is cumulatively less than 1% annually and identifying it early may be the most feasible way to decrease the number of cancer deaths as we have seen with screening in patients without a history of cancer. Clinical-pathologic features that increase the risk of locoregional recurrence are the number of lymph nodes involved, the size of the primary tumor and stage as well as hormone receptor status and oncogene expression, receipt of chemotherapy or radiation, and margin size after surgery. The type of surgical approach also affects the presentation of locoregional recurrence. With breast conservation therapy recurrence is likely seen on imaging, whereas with mastectomy locoregional recurrence is clinically apparent. Locoregional recurrence can be either local, regional, or both. In breast conservation therapy, local recurrence is defined as presence in the ipsilateral breast, while in those treated with mastectomy, local recurrence occurs along the chest wall. Regional recurrences involve sentinel lymph nodes. Distant metastases are present in a large portion of patients with locoregional recurrence and can

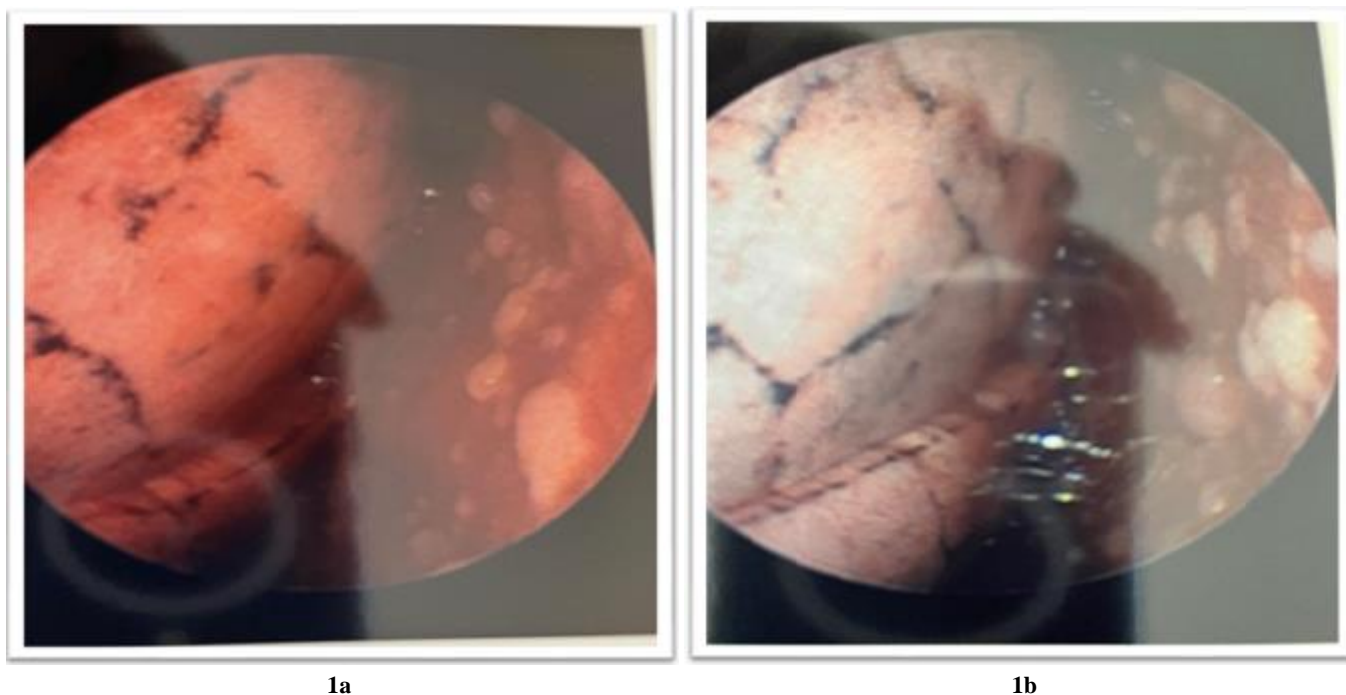
occur anywhere in the body although most commonly in the bone, liver, and lungs for all types of breast cancer. Rates of recurrence are highest in the first two years after diagnosis but the rate of relapse remains persistent more than a decade after diagnosis [2]. Additionally, pleural metastasis of breast cancer, which often presents as a malignant pleural effusion, typically occurs during the first few years after diagnosis but is not common after a long period of disease-free survival [1]. Survival time of patients with malignant pleural effusion due to breast cancer is about 15 months. With such a poor prognosis, typical treatments for pleural effusion are not considered as they are mostly invasive such as pleurectomy or chemotherapy. Therefore, malignant pleural effusions in this population are most commonly managed symptomatically with regular thoracentesis or, if appropriate, indwelling pleural catheter or pleurodesis. The goal of these interventions is to improve quality of life rather than to decrease morbidity or mortality [1]. Here, we present a case of breast cancer relapse after 7 years of disease-free survival with lung metastasis and malignant pleural effusion secondary to pleural metastasis and without locoregional recurrence.

Case Presentation

A 77 year-old Caucasian woman presented to the emergency department in early 2021 with complaints of non-productive cough and a pressure-like sensation in the chest. The patient was

diagnosed with estrogen-receptor (ER) positive, human epidermal growth factor receptor-2 (HER-2) negative infiltrating lobular carcinoma (ILC) in 2007 which was treated with left lumpectomy and radiation in 2005, followed by right lumpectomy with radiation and chemotherapy in 2010, and definitively with a bilateral mastectomy in 2014. She was doing well 14 years after initial diagnosis until a computed tomography (CT) of the chest to evaluate nonspecific respiratory complaints revealed lung nodules. She denied hemoptysis, sputum production, fever or chills, rigor, sweats, weight loss, and loss of appetite. Physical examination showed no abnormalities with normal percussion of the chest and good air entry on auscultation bilaterally without wheezing, rales, or crackles. There was no inguinal or cervical lymphadenopathy and inspection of the digits and nails showed no evidence of clubbing, cyanosis, or ischemia. Subsequent positron emission tomography (PET) scan showed significant PET uptake in numerous lung nodules primarily on the left side most of which were new when compared with the previous CT Chest as well as pleural nodules. A navigation bronchoscopy with biopsy of the

PET avid-positive nodules of the left upper lobe and endobronchial ultrasound with biopsy of the station 7 lymph node were performed in January 2021. Cytology of cells from fine needle aspiration of the left upper lung nodule showed atypical cells. However, cytology of the station 7 lymph node was negative for malignancy. Numerous pleural metastases were visualized on subsequent thoracoscopy [Figures 1a and 1b] which were biopsied and a sample of pleural fluid was obtained for analysis. Pleural biopsy samples were positive for involvement by carcinoma. Cells from the pleural fluid were noted to have enlarged atypical nuclei with prominent nucleoli, consistent with malignancy. Immunohistochemical stain was performed to further characterize the cells which were positive for CK-7, ER, and GATA-3 as well as weakly positive for GCDPF-15 but negative for TTF-1. The patient was determined to have distant metastasis of the previous primary breast cancer to the lung and pleura without locoregional recurrence as PET did not reveal any uptake in breast tissue or sentinel nodes.



Figures 1a and 1b: Pleural metastases are seen near the left lower lobe on thoracoscopy.

Discussion

Infiltrating lobular carcinoma (ILC) is a subtype of comprises up to 14% of all breast cancer diagnoses and its incidence is increasing [3]. ILC is challenging to diagnose by palpation or mammogram as its cells surround normal breast tissue in a single-file formation which does not result in the destruction of anatomic structures or form distinct masses [3]. This is because infiltrating lobular carcinoma is histologically a monomorphic population of small round cells with scant cytoplasm which are contained within the basement membrane of the benign breast cells they invade, maintaining the cells architecture [4]. The lack of a singular mass, multifocal and multicentric distribution, tendency for bilaterality makes breast conservation therapy less likely to be successful. ILC is diagnosed in older patients compared with other types of breast cancer, possibly due to the difficulty in detection and low proliferative rate. Although similar to ductal carcinoma in many ways, ILC has a different distribution of metastasis and typically metastasizes to the peritoneum, ovary, and gastrointestinal system,

unlike ductal carcinoma that is commonly found in the lungs, pleura, and central nervous system. The overall survival rate in ILC is 95.6% with a disease-free survival rate of 85.7% after initial treatment [3]. Further, recurrence of ILC occurs in about 32% of patients within 5 years [3] and has been shown to be dependent on the surgical approach used [4].

This case demonstrates the importance of considering delayed breast cancer relapse in a patient with a lengthy period of disease-free survival. Although case reports have demonstrated delayed relapses of decades, breast cancer relapse typically has a bimodal distribution with most relapses occurring 2 years and 6-9 years after initial treatment. A case series by Rawindraraj et al. in 2018 described two cases of delayed breast cancer relapse in patients with infiltrating lobular carcinoma which presented with malignant pleural effusion. One of the cases was treated with modified radical unilateral mastectomy and adjuvant chemotherapy and radiation 21 years prior. The other patient underwent a bilateral simple mastectomies with adjuvant chemotherapy for left invasive ductal carcinoma as well as right in-situ ductal and lobular carcinoma and relapsed 14 years later [1]. Neither of the cases in

that series mentioned whether other sites of recurrence were found. Additionally, in these cases with disease-free survivals more than a decade, there is the possibility that treatment modalities have greatly improved since the patients' diagnoses.

Our case is unique in that the breast cancer relapse presented as distant metastasis without locoregional recurrence despite bilateral mastectomy, chemotherapy, and radiation. Few studies have compared local recurrence rates of infiltrating lobular carcinoma after breast conservation therapy and mastectomy [1]. A retrospective study showed a rate 42% recurrence with breast conservation therapy versus 5% with mastectomy [4]. Because infiltrating lobular carcinoma and ductal carcinoma in-situ (DCIS) are similar, they are often compared and misdiagnosed. One of the characteristics they share is their risk factors for distant metastasis such as age under 40 years, lymph node metastasis, ER negativity, and previous or simultaneous local recurrence. These risk factors are, however, hard to define as the rate of distant metastasis as a delayed recurrence after surgery is less than 1% [5].

Conclusion

Distant metastasis and malignant pleural effusion in relapsed breast cancer have a poor prognosis, warranting only symptomatic treatment that has no effect on morbidity or mortality. Patients with a history of invasive lobular carcinoma should be monitored for relapse with consideration to locoregional recurrence, regardless of treatment methods employed or long periods of disease-free survival.

HCA Healthcare Disclaimer

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Ethics approval and consent to participate

Research conducted for this study involving human participants was performed in accordance with the principles embodied in the Declaration of Helsinki and in accordance with local statutory requirements. This study was determined exempt from ethical review by HCA Graduate Medical Education Institutional Review Board. Written consent for this case report and associated imaging was obtained from the patient. This article does not contain any studies with animals performed by any of the authors.

List of Abbreviations

ER: Estrogen-receptor
HER-2: Human epidermal growth factor receptor-2
ILC: Infiltrating lobular carcinoma
CT: Computed tomography
PET: Positron emission tomography

Conflicts of Interests

The authors declare that they have no competing interests.

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Authors' Contributions

JK: Conception of the work, Design of the work, Acquisition of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

SG: Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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