A case report of synchronous breast and lung cancer with three different pathologic diagnoses

Nawal Khan[1], Maria de la Torre[1], Houyar Moghaddas[2], Nelli Fromer[3], Siarhei Melnikau[1]

[1]Department of Surgery, Wyckoff Heights Medical Center, Brooklyn, NY, USA; [2]St George's University School of Medicine, Saint George, Grenada; [3]Department of Oncology, Wyckoff Heights Medical Center, Brooklyn, NY, USA

Contributions: (I) Conception and design: All authors; (II) Administrative support: N Fromer, S Melnikau, H Moghaddas; (III) Provision of study materials or patients: N Fromer, S Melnikau; (IV) Collection and assembly of data: N Khan, M de la Torre, H Moghaddas; (V) Data analysis and interpretation: N Khan, M de la Torre, N Fromer; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Maria de la Torre, MD. Department of Surgery, Wyckoff Heights Medical Center, 374 Stockholm St, Brooklyn, NY 11237, USA. Email: mpdelatorre22@gmail.com.

Background: Multiple primary malignant tumors (MPMTs) pose a significant clinical challenge, denoting the occurrence of two or more distinct malignant tumors with differing histological characteristics, all diagnosed within a 6-month timeframe. MPMT is a rare condition and due to the unique treatment requirements for each specific cancer type, it is crucial for healthcare professionals to accurately differentiate between metastatic growth and distinct primary tumors.

Case Description: In this case report, we present a 41-year-old female patient who received diagnoses of three separate synchronous primary tumors. The patient presented for evaluation of a right breast mass that had been present for 1 year. Initial diagnostic tests, including mammography and ultrasound, did not provide any conclusive results. Subsequent magnetic resonance imaging (MRI) of the breast prompted an ultrasound-guided biopsy which confirmed moderately differentiated invasive ductal carcinoma (IDC). During pre-surgical testing, a suspicious opacity was detected on a chest X-ray, prompting further investigation with a computed tomography (CT) scan of the chest to distinguish between metastatic disease and a potential new primary tumor. Clinical and pathological examinations revealed the presence of bilateral masses originating from two different origins: invasive mucinous pulmonary adenocarcinoma in the left lower lobe and a neuroendocrine carcinoma in the right middle lobe of the lung.

Conclusions: Cases of this nature present a complex challenge to physicians and underscore the critical importance of maintaining a high level of clinical suspicion to ensure the delivery of high-quality care. Effective management of such patients requires a multidisciplinary collaboration among breast surgeons, thoracic surgeons, and medical and radiation oncologists.

Keywords: Breast cancer; lung cancer; case report

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Introduction

Background

Multiple primary malignant tumors (MPMTs) are a clinical challenge that refers to the presence of two or more histologically different, malignant tumors that have been diagnosed within 6 months of each other and are not due to metastasis, recurrence, or local spread (1,2). Its incidence ranges from 0.73% to 11.7% (3).

Rationale and knowledge gap

Since the treatment strategies for each cancer type vary, it is imperative that clinicians can distinguish between metastasis

versus primary tumors.

Objective

Herein, we describe a 41-year-old female who was diagnosed with three synchronous primary tumors. We present this case in accordance with the CARE reporting checklist (available at https://acr.amegroups.com/article/view/10.21037/acr-23-194/rc).

Case presentation

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

In July 2022, a 41-year-old premenopausal female with a past medical history of polycystic ovarian syndrome, hypothyroidism, and psoriasis presented to the breast surgery clinic for evaluation of the right breast mass that had been present for 1 year. Family history was significant for breast cancer in her sister after age 50. No other risk factors such as smoking, radiation or asbestos exposure, or previously known mutations were found. Physical exam was contributory for a palpable 2 cm mass at the 6 o'clock position in the right breast.

The initial screening mammogram was incomplete (BIRADS 0). A subsequent diagnostic mammogram and breast ultrasound showed a complex cyst, and a repeat mammogram was recommended in six months. Thereafter, repeat imaging demonstrated an indeterminate hypoechogenic mass. To further delineate anatomy, a magnetic resonance imaging (MRI) of the right breast was performed which showed an enhancing 7 o'clock mass and an additional small mass at 9 o'clock in the right breast (BIRADS 4) (see *Figure 1*).

The patient underwent an ultrasound-guided biopsy of the 7 o'clock mass and the pathology revealed moderately differentiated invasive ductal carcinoma (IDC), estrogen receptor (ER) and progesterone receptor (PR) positive and Her2 receptor-negative. Meanwhile, she was referred to the oncology clinic where multi-cancer germline mutation testing was ordered and returned negative for any cancer-associated mutations.

She was then scheduled to undergo breast-conserving surgery with bracket localization and sentinel lymph node biopsy, however during the pre-surgical testing routine, a chest X-ray revealed a mass-like opacity projecting over the lingula as well as haziness within the right lung base. Subsequently, chest computed tomography (CT) showed a lobulated mass lesion in the superior segment of the left lower lobe, 4.3 cm × 4.3 cm in size, and a non-specific indeterminate right middle lobe pulmonary nodule, 1.5 cm × 1.2 cm (*Figures 2,3*).

Bilateral CT-guided biopsies of both lesions were recommended to distinguish between a new primary tumor versus metastasis from the known breast cancer. A biopsy of the left lung mass revealed a primary mucinous adenocarcinoma of the lung [programmed death-ligand 1 (PDL-1) 1%]. A biopsy of the right lung mass revealed a neuroendocrine tumor (NET).

After a multidisciplinary discussion, a decision was made to proceed with the right breast lumpectomy with seed localization and sentinel lymph node biopsy, followed by left lower lobe lobectomy and excision of the right middle lobe mass. Surgical pathology of the right breast showed stage IIA, pT1c N1a Mx, hormone receptor-positive and Her2/neu negative, IDC. The left lower lobe mass demonstrated grade II invasive mucinous pulmonary adenocarcinoma with visceral pleural involvement and lymphovascular invasion.

Highlight box

Key findings

- Multiple synchronous primary malignant tumors.

What is known and what is new?

- Multiple primary malignant tumor (MPMT) is a rare condition, however, its incidence has increased due to advancements in diagnostic modalities, genetic predisposition, and longer life expectancy. Females with breast cancer who are discovered with pulmonary nodules exhibit primary lung cancer in 55% of cases.
- In this case, we identified 2 tumors with different cellular origins.

What is the implication, and what should change now?

- There is a paucity of literature regarding the management plan of a patient with synchronous lung and breast cancer. And these patients have a worse prognosis. High clinical suspicion is essential when confronting any anomalies in imaging studies, as this vigilance is key for obtaining appropriate tissue diagnosis and treatment.
- These statistics show that concurrent lung mass in breast cancer patients merits tissue sampling and pathologic diagnosis that plays an essential role in prognostication and treatment planning.

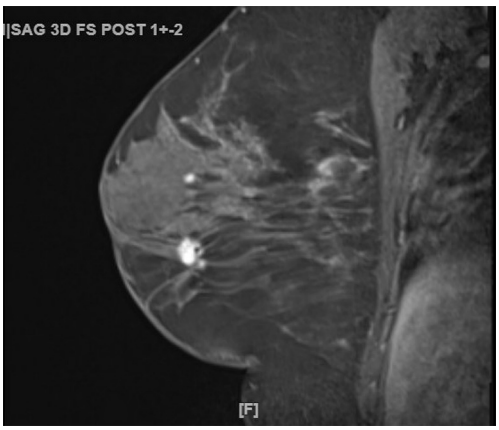

Figure 1 Right breast MRI, enhancing 7 o'clock mass and an additional small mass at 9 o'clock (BIRADS 4). MRI, magnetic resonance imaging.

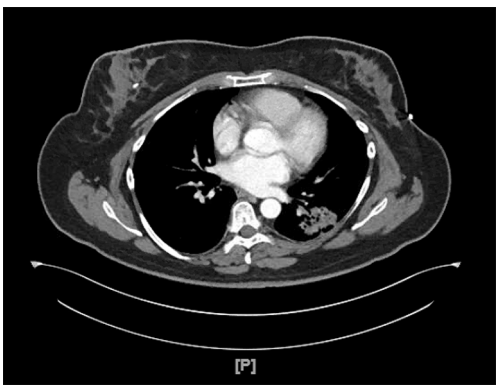

Figure 2 CT chest with intravenous contrast, lobulated mass lesion in the superior segment of the left lower lobe. CT, computed tomography.

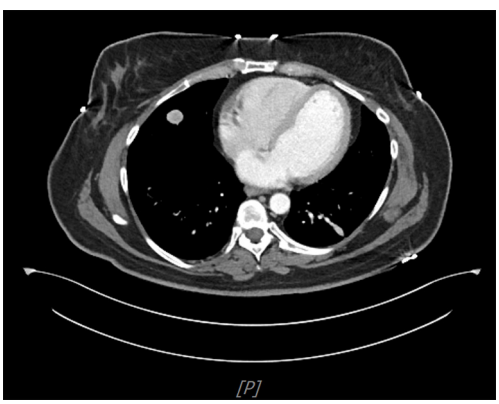

Figure 3 CT chest with intravenous contrast, non-specific indeterminate right middle lobe pulmonary nodule. CT, computed tomography.

All margins and lymph nodes were negative for carcinoma, thus making it stage IIB, pT3N0. Surgical pathology of the right middle lobe lung mass revealed a 2.3-cm unifocal neuroendocrine carcinoma with a Ki67 of 2%, no visceral pleural or lymphovascular invasion, and negative lymph node involvement, making it stage IA.

After recovering from all her surgeries, she underwent radiation therapy to the right breast. The patient did not require adjuvant chemotherapy for breast cancer since the Oncotype Dx recurrence score was low-risk. After completion of radiation, she proceeded with four cycles of adjuvant chemotherapy with cisplatin and pemetrexed for stage IIB adenocarcinoma of the left lung (3-5). She was started on immunotherapy, atezolizumab, however, it was stopped after three cycles as she developed lower extremity weakness attributed to toxicity. Adjuvant chemotherapy was not indicated for the right lung NET. She is now on adjuvant endocrine therapy with tamoxifen for breast cancer, planned for 10 years as she is premenopausal. Please see *Figure 4* for the timeline.

Discussion

Key findings

When encountering a patient with multiple malignancies, simultaneously, the management must be tailored to obtain the best response from all tumors and to stratify or triage based on the current literature. Our patient presented with a right breast mass and two lung masses were found 6 months later during presurgical testing.

Strengths and limitations

To differentiate between primary lung tumors and breast cancer metastatic deposits, a CT-guided biopsy of both lung masses was performed. Tissue diagnosis revealed a neuroendocrine carcinoma and a mucinous adenocarcinoma. She had three primary cancers that required different surgical and systemic approaches to management.

Comparison with similar researchers

The incidence of synchronous breast and lung cancer is rare, affecting less than 0.5% of patients diagnosed with breast cancer (2,4). In recent years, however, the incidence of MPMT has increased due to advancements in diagnostic

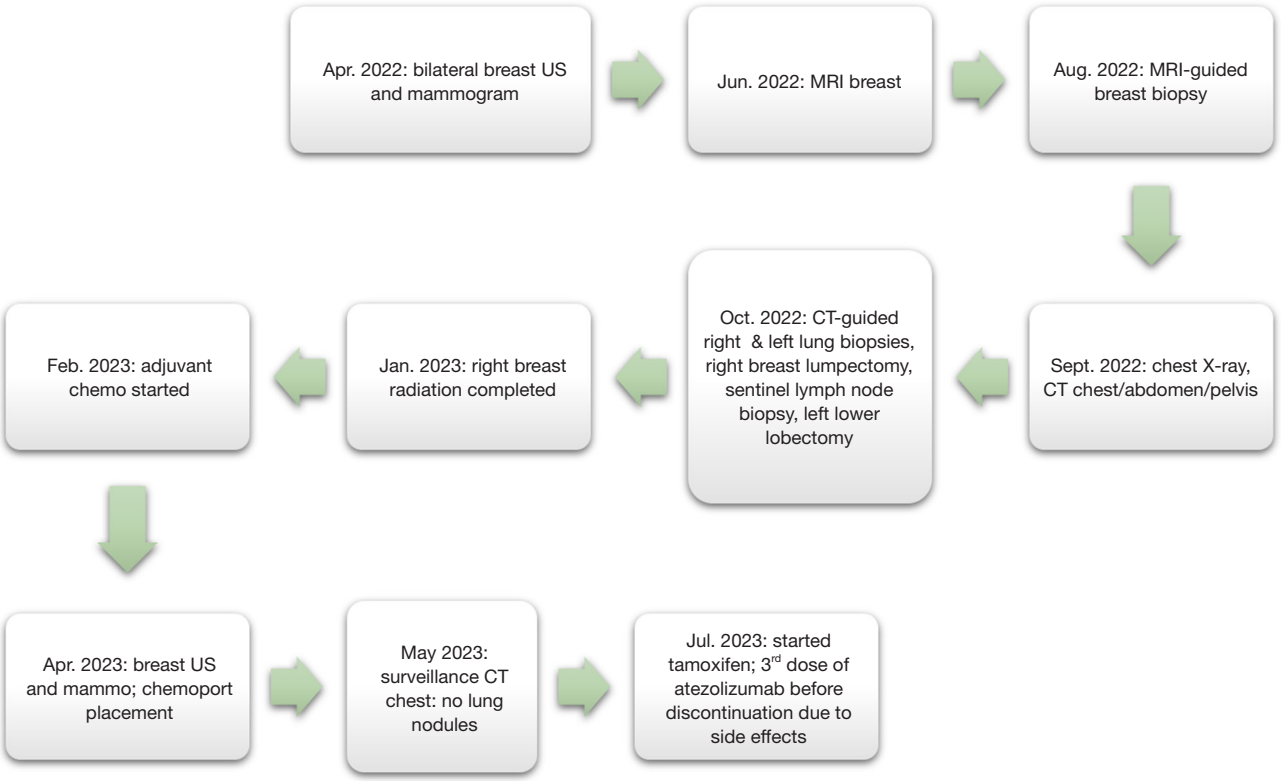

Figure 4 Timeline. US, ultrasound; MRI, magnetic resonance imaging; CT, computed tomography.

modalities, access to health care, genetic predisposition, and longer life expectancy (3). Additional risk factors such as unhealthy lifestyle, cancer treatments, or interactions between any of these factors have also contributed to the development of MPTP (5).

Females with breast cancer who are discovered with pulmonary nodules have been observed to exhibit primary lung cancer in 55% of cases, metastatic disease in 37% of cases, and benign lesions in eight percent of cases (6). Therefore, it is recommended to assess the pathology of these lesions, as approximately half of them could potentially be candidates for curative treatment (3,4,7). The statistics above signify that a concurrent lung mass in breast cancer patients merits tissue sampling and pathologic diagnosis that plays an essential role in prognostication and treatment planning (4,6).

Explanations of findings

Management of patients with invasive carcinoma of the breast involves addressing both the breast and axilla through surgery, radiation therapy, or a combination of both. For patients with clinical stage I and II breast carcinoma, adjuvant therapy should be considered after local treatment involving mastectomy or breast conservation therapy (BCT) (8,9). BCT entails partial mastectomy, axillary surgical staging, and whole breast irradiation. Randomized clinical trials have demonstrated similar effectiveness between BCT and modified radical mastectomy for these patients (10-12). Sentinel lymph node biopsy has emerged as a consideration in breast conservation when axillary nodes are clinically negative (13-16).

Systemic treatment options, such as hormonal or cytotoxic therapy, are considered based on various factors like clinical stage, microscopic findings, tumor biology, evidence of metastatic disease, and the patient's overall condition. For tumors between 0.6 and 1.0 cm in diameter, adjuvant therapy is often considered. The Oncotype Dx score is often used to predict the benefit of cytotoxic chemotherapy in early-stage hormone receptor-positive breast cancers. Premenopausal patients with hormone-positive breast cancers require 10 years of adjuvant tamoxifen therapy.

The second diagnosis of our patient, mucinous

adenocarcinoma of the lung, is a rare histological variant of lung cancer, previously known as bronchoalveolar carcinoma. It constitutes approximately five percent of resected lung cancer cases (17,18). Diagnosis can be challenging on small biopsy specimens, and they may resemble pneumonia on imaging, leading to delayed diagnosis. Combination platinum-based therapy with pemetrexed is used as first-line chemotherapy in patients with lung adenocarcinoma (19).

On the other hand, NETs of the lung account for approximately 20–25% of all primary lung neoplasms and arise from neuroendocrine cells of the bronchopulmonary epithelium (18,20). The latest WHO classification categorizes lung NETs into four subtypes: typical carcinoid (TC), atypical carcinoid (AC), large cell neuroendocrine lung carcinoma (LCNELC), and small cell lung carcinoma (SCLC) (17). SCLC is a poorly differentiated NET with a grave prognosis and represents the majority (80%) of lung NETs (21,22). Treatment plans for lung NETs depend on histologic subtype and disease extent. ACs tend to have a greater propensity for nodal involvement and distant spread compared to TCs (22,23).

Functionality is another factor affecting treatment decisions, as some lung cancers can cause secretory syndromes, such as carcinoid syndrome or Cushing's syndrome (22,24). Surgical removal remains the primary treatment for localized NETs with various approaches such as complete anatomic resection (lobectomy, bilobectomy, and pneumonectomy), sublobar resection (segmentectomy, wedge resection), and lung parenchyma-sparing surgery (bronchial sleeve resection, sleeve lobectomy), depending on the size, location, histological subtype, and patient's overall health (18,20,25). Adjuvant chemotherapy is generally not indicated for localized NETs.

As seen in our patient, when managing patients with MPMT, a multidisciplinary cohesive treatment approach tailored to the patient needs to be undertaken. As indicated for ER/PR + stage IIA invasive breast cancer, we performed a right breast lumpectomy with seed localization and sentinel lymph node biopsy, followed by left lower lobe lobectomy and excision of the right middle lobe mass indicated for lung tumors. Thereafter, she underwent whole breast radiation on the right side and then began chemotherapy for lung adenocarcinoma. Due to hormone receptor positivity, she is currently taking hormone therapy. A stepwise management approach that takes into account the associated morbidity and mortality of each cancer type and its treatment is required. This approach concurrently plans the next steps to ensure comprehensive and effective care for these patients.

Implications and actions needed

There is a paucity of literature regarding the management plan of a patient with synchronous lung and breast cancer (6). Breast cancer patients with synchronous primary lung cancer have a worse prognosis because lung cancer has a higher mortality than breast cancer (2,23). By presenting this case, we want to emphasize that even though synchronous primary tumors are rare, physicians should always be aware of and consider this possibility during the staging workup of tumors. Delayed or inadequate treatment due to a missed diagnosis can impact the patient's survival and prognosis.

Conclusions

Synchronous primary breast and lung cancers are rare, and management of such patients can present a complex challenge to physicians. Multidisciplinary collaboration between breast surgeons, thoracic surgeons, and medical and radiation oncologists is crucial in the management of these patients.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://acr.amegroups.com/article/view/10.21037/acr-23-194/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://acr.amegroups.com/article/view/10.21037/acr-23-194/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are 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. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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