Case report

Unusual presentation of a small cell lung cancer with bilateral breast metastases: Case report and a brief review of the literature

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ABSTRACT

Small cell lung cancer (SCLC) is a smoker’s disease and occurs almost exclusively in smokers. SCLC is a high-grade neuroendocrine tumor and commonly presents as a central tumor with bulky mediastinal adenopathy. It is notorious for causing widespread disease and paraneoplastic syndromes. The usual sites of metastasis include the liver, brain, bone, and adrenals. SCLC presenting with breast metastasis is unusual; however, there are reports of unilateral and bilateral breast metastases. SCLC with bilateral breast metastases is extremely rare, with only five previously reported cases available in the literature. We are taking this opportunity to report and add to the growing literature on the unusual presentation of a small cell lung cancer with bilateral breast metastases.

1. Case presentation

The patient is a 57-year-old female, a former smoker with 20 pack-years (quit 24 years ago) with multiple sclerosis (on Teriflunomide for the past 10 years). Seven months ago, she had a telehealth visit with her primary care physician for evaluation of a dry cough of 3 weeks. After testing negative for SARS-CoV-2, she was started on bronchodilators for presumed COPD and scheduled for an outpatient pulmonary function test. Unfortunately, she was lost to follow up, and after seven months, she presented to her primary care physician again with progressive cough and dyspnea. She also reported a 20-pound weight loss over two months, progressive fatigue, and bilateral palpable breast lumps that she discovered only recently. Her primary care provider performed a breast examination that confirmed the presence of bilateral breast lumps; in the inner and upper quadrant of the right breast and the inner and lower quadrant of the left breast. She subsequently had a dedicated breast ultrasound that confirmed the presence of vascular lobulated masses in her bilateral breasts, 2.7 cm on the right and 1.6 cm on the left [Fig. 1]. Mammography also confirmed BI-RADS category 5 lobulated and irregular masses in both breasts [Fig. 2]. She was referred to a breast surgeon who requested core biopsies of the bilateral breast masses. Ultrasound-guided core biopsies of the bilateral breast masses revealed aggregates of small round cells with scant cytoplasm that stained positively for CD 56, chromogranin A, synaptophysin, and TTF-1; confirming the diagnosis of a metastatic small cell lung cancer [Image 1]. Subsequent CT chest revealed a left hilar mass of $4.5 \times 5.2 \text{ cm}^2$ with mass effect on the left main bronchus and pulmonary artery [Fig. 3]. Staging workup revealed metastatic lesions in the brain and bilateral adrenal glands. She was diagnosed with Stage IV small cell lung cancer and started on a combination of Cisplatin, Etoposide, and Atezolizumab. She was also started on radiation therapy to the chest for symptomatic relief. While on treatment, her disease progressed with significant weight loss, increasing breast masses, and frequent hospitalizations for neutropenia and pneumonia. Her condition deteriorated rapidly, requiring

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**Fig. 1.** Ultrasound bilateral breasts.

**Fig. 2.** Mammography of bilateral breasts.

**Fig. 3.** CT chest revealing left hilar mass and bilateral breast masses.
treatment discontinuation; 4 months later, she was transitioned to hospice.

2. Introduction

Primary breast cancer is the most common cancer in women and the second most common cause of cancer-related deaths in women. Though rare, breast metastasis from a non-breast primary can account for up to 0.4–1.3% of all breast cancers [4–8]. Tumors known to metastasize to the breast include leukemia, lymphoma, malignant melanoma, lung cancer, soft tissue sarcoma, ovarian cancer, thyroid cancer, osteosarcoma, neuroendocrine vaginal, and endometrial cancer cancers, gastrointestinal and genitourinary tumors [6].

3. Discussion

In the US, primary breast cancer is the most common cancer and the second leading cause of cancer deaths in women. Approximately 268,000 women receive a new breast cancer diagnosis, and close to 42,000 die of it annually. Bilateral breast cancer is invariably advanced but rare, accounting for only 1.3% of cases. Synchronous bilateral primary breast cancer is usually due to lobular carcinoma. Metastatic breast cancer from the extramammary origin is rare and accounts for only 2% of breast cancers. In most of these reported cases, the breast involvement was unilateral. Bilateral breast metastases are rare and only reported with SCLC, gastric, and pancreatic neuroendocrine tumors.

The clinical presentation of metastatic disease from a non-mammary source is similar to primary breast cancer. Patients usually present with a superficial palpable breast mass, pain, tenderness, and inflammation [5,6,8,11]. Radiographically, extramammary cancers lack calcification, spiculation, and architectural distortion and tend to involve the upper outer breast quadrants of the breast; this radiographic presentation can make the tumors appear benign on mammography [5,6,8,11]. A high index of suspicion is needed in situations like this to avoid delay in the diagnosis.

Globally, lung cancer is the most common cancer in men and the 3rd most common cancer in women, but it continues to be the leading cause of cancer deaths in men and women [12,13]. Patients with lung cancer (NSCLC and SCLC) typically present with cough (75%), dyspnea (75%), chest discomfort (50%), hemoptysis (35%), fatigue, anorexia, and weight loss [15]. SCLC is a high-grade neuroendocrine tumor and accounts for nearly 15% of the newly diagnosed lung cancer [14]. Unfortunately, most already have a systemic disease at the time of diagnosis. SCLC is commonly associated with paraneoplastic syndromes (10%) such as SIADH, Horner’s syndrome, and brachial plexopathies [15,16]. Most patients with lung cancer (NSCLC and SCLC) usually present late with locally advanced and metastatic disease. The usual sites of metastasis include the liver (20–30%), bone (20–25%), brain (15–20%), adrenal

| Author          | Year | Age | Sex  | Smoke? | Lung  | Breast |
|-----------------|------|-----|------|--------|-------|--------|
| Bartella et al. | 2003 | 65  | Female | N/A    | Right | Bilateral |
| Giarelli et al. | 1976 | N/A | Male  | N/A    | N/A   | Bilateral |
| Ko et al.       | 2020 | 64  | Female | Yes    | Right | Bilateral |
| Zinzuwadia et al. | 2021 | 52  | Female | No     | Right | Bilateral |
| Guldogan et al. | 2020 | 52  | Female | N/A    | N/A   | Bilateral |
| Bannon et al.   | 2022 | 57  | Female | Yes    | Left  | Bilateral |
Lung cancer presenting with breast metastasis is rare. After a thorough search of the existing literature, we were able to identify only 185 cases of primary lung cancer with metastasis to the breast; and only 42 (22.7%) of those cases were due to SCLC. Of the 42 cases, 5 had bilateral breast metastases, 7 had ipsilateral metastasis, 4 had contralateral metastasis, and the remaining cases did not have sufficient information on the laterality of the lung cancer or the breast involvement [Tables 1–4]. This data supports the rarity of SCLC presenting with breast metastasis, mainly bilateral breast metastases.

Approximately 70% of the patients with SCLC already have metastasis at diagnosis. Despite being a common and aggressive tumor with a tendency to metastasize, breast involvement is surprisingly rare [25–37]. The prognosis is abysmal whether one or both breasts are involved by SCLC, with an estimated five-year survival of only 2% [13]. Primary small cell carcinoma of the breast is an equally rare entity, with less than 50 cases reported in the literature [38]. Despite the rarity of these two conditions, it is still imperative to distinguish a metastatic SCLC from a primary small cell carcinoma of the breast because of the differences in the treatment options and prognosis; surgical treatment may be an option, and the prognosis may be slightly better for the primary small cell carcinoma of the breast [38]. Even though unlikely, synchronous presentation of primary lung and breast cancers should always be entertained in patients with lung and breast masses [39].

4. Conclusion

Clinicians should always consider metastatic disease while evaluating suspicious breast lumps. Metastatic disease to the breast from an extramammary source is rare but not impossible. This case should remind clinicians of the unusual presentations of cancers and add to the limited existing literature on SCLC with bilateral breast involvement.
