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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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A B S T R A C T

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 × 5.2 cm² 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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Received 5 May 2022; Accepted 20 June 2022

Available online 27 June 2022

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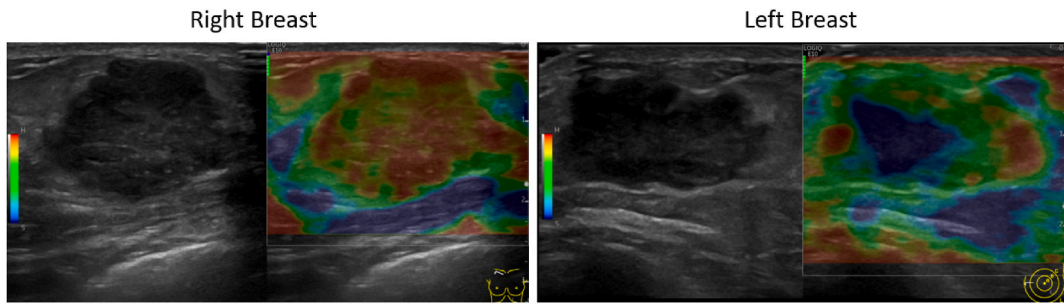


Fig. 1. Ultrasound bilateral breasts.

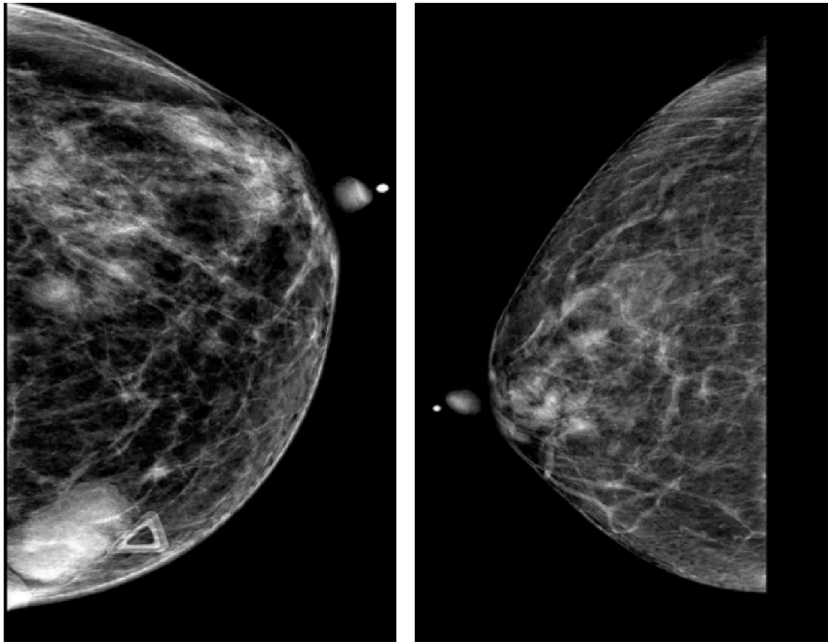


Fig. 2. Mammography of bilateral breasts.

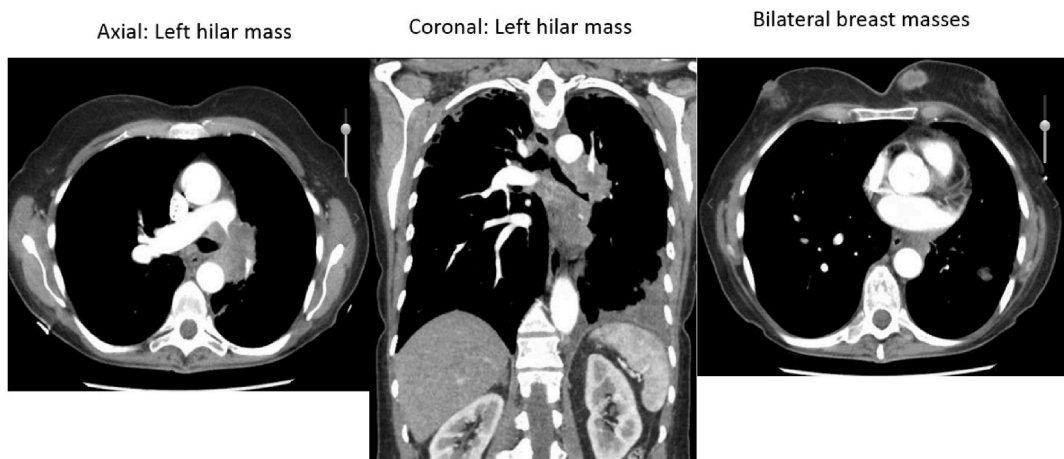


Fig. 3. CT chest revealing left hilar mass and bilateral breast masses.

A: H&E showing the characteristic small round to oval and short spindle-shaped cells arranged in sheets, without distinct nuclei representative of small cell lung cancer

B: TTF-1

C: Synaptophysin

D: CD56

E: Chromogranin A

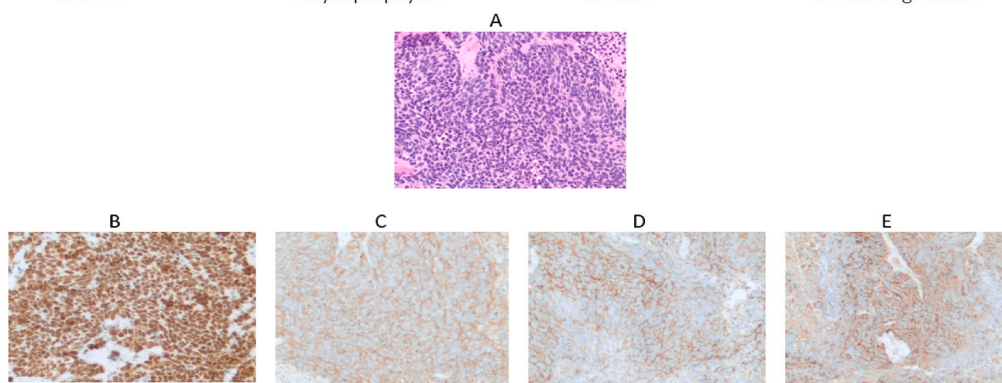


Image 1. A: H&E showing the characteristic small to oval and short spindle-shaped cells arranged in sheets, without distinct nuclei representative of small cell lung cancer.

Table 1

Documented cases of SCLC Metastasis to Bilateral Breasts at time of Clinical Presentation.

Author	Year	Age	Sex	Smoke?	Lung	Breast
Bartella et al. [1]	2003	65	Female	N/A	Right	Bilateral
Giarelli et al. [2]	1976	N/A	Male	N/A	N/A	Bilateral
Ko et al. [3]	2020	64	Female	Yes	Right	Bilateral
Zinzuwadia et al. [4]	2021	52	Female	No	Right	Bilateral
Guldogan et al. [5]	2020	52	Female	N/A	N/A	Bilateral
Bannon et al. (our case)	2022	57	Female	Yes	Left	Bilateral

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

Table 2
Documented Cases of SCLC Metastasis to Ipsilateral Breasts at time of Clinical Presentation.

Author	Year	Age	Sex	Smoke?	Lung	Breast
Liu et al. [6]	2009	45	Female	N/A	Bilateral	Right
Guldogan et al. [5]	2020	64	Female	Yes	Left	Left
Luh et al. [7]	2007	66	Female	N/A	Left	Left
Kelly et al. [8]	1988	64	Female	N/A	Left	Left
Babu et al. [9]	2009	69	Female	Yes	Right	Right
Wang et al. [10]	2014	49	Female	No	Right	Right
Noguera et al. [40]	2007	51	Female	N/A	N/A	“Unilateral”

Table 3
Documented Cases of Contralateral Metastasis of SCLC to the Breast at time of Clinical Presentation.

Author	Year	Age	Sex	Smoke?	Lung	Breast
Altintoprak et al. [12]	2011	47	Male	Yes	Left	Right
Lin et al. [13]	2016	49	Male	Yes	Left	Right
Courtney et al. [14]	1989	59	Female	Yes	Right	Left
Economopoulou et al. [15]	2020	42	Female	Yes	Right	Left

Table 4
Documented Cases of Metastasis of SCLC without adequate information on the laterality.

Author	Year	Age	Sex	Smoke?	Lung	Breast
Inoue et al. [16]	2006	55	Female	N/A	N/A	“Multiple”
Kelly et al. [8]	1988	39	Female	N/A	N/A	Left
Shukla et al. [17]	2005	40	Female	N/A	N/A	Left
Wood et al. [18]	2008	75	Female	N/A	N/A	Left
Wood et al. [18]	2008	60	Female	N/A	N/A	Left
Klingen et al. [19]	2009	54	Female	N/A	N/A	Right
Shukla et al. [17]	2005	42	Female	N/A	N/A	Right
Vaughan et al. [20]	2007	83	Female	N/A	N/A	Right
Wood Et al [18]	2008	47	Female	N/A	N/A	Right
Zhao et al. [21]	2018	58	Female	Yes	N/A	Right
Jakovljevic et al. [22]	2003	44	N/A	N/A	N/A	N/A
Lee [23]	2007	49	Female	N/A	N/A	N/A
Lee [23]	2007	49	Female	N/A	N/A	N/A
Domanski et al. [24]	1996	N/A	N/A	N/A	N/A	N/A
Toombs et al. [18]	2007	12 Patients	N/A	N/A	N/A	N/A

N/A: information not available.

glands (5–6%), and the lymph nodes [15,16]; but, breast involvement is uncommon.

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.

Declaration of competing interest

We have no conflicts to declare.

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