

Case Report

Breast Metastasis from Neuroendocrine Carcinoma of the Lung: A Case Report and Review of the Literature

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Keywords

Metastasis · Relapse · Histology

Abstract

Breast metastasis originating from non-mammary tumors is an uncommon event accounting for 0.5–6.6% of all breast neoplasms. The primary malignancies that reportedly metastasize to the breast most frequently are hematologic malignancies, such as leukemia and lymphoma and malignant melanoma. Breast cancer metastasis resulting from a primary lung neoplasm is significantly less commonly described in the literature. Herein, we present the unusual case of a patient with metastatic disease to the breast from a primary lung tumor.

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Introduction

Primary breast cancer represents the most common malignancy in women and the second leading cause of cancer-related death after lung cancer [1]. Nevertheless, metastases from other primary cancer sites are rare. Since the first report of a breast metastasis [2], a variety of neoplasms have been reported to metastasize to the breast, including malignant melanoma, lymphoma, lung, ovary, prostate, kidney, stomach, ileum, thyroid, and cervical cancer [3–5]. Despite being reported rather scarcely, metastatic disease to the breast repre-

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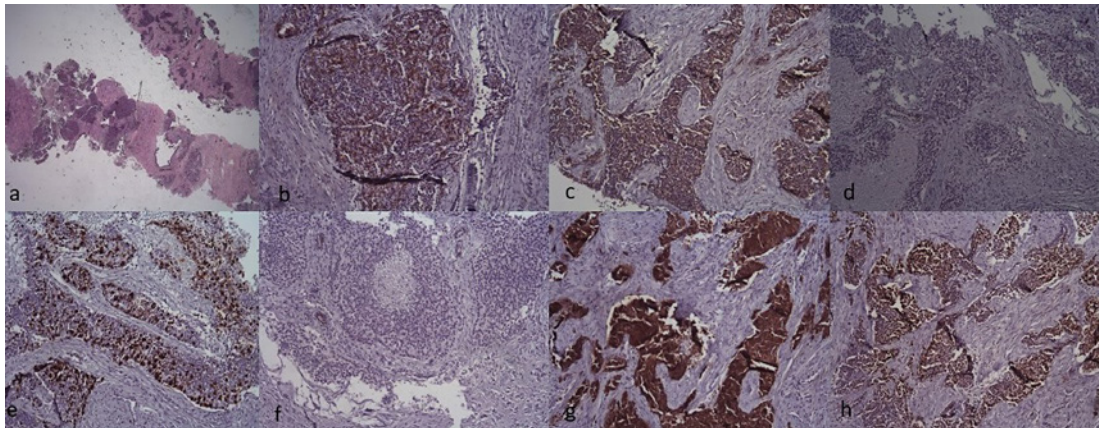


Fig. 1. Pathology features of breast metastasis: H&E staining (a), membrane CD56 staining (b), chromogranin staining (c), ER staining (d), Ki67 staining (e), PR staining (f), synaptophysin staining (g), and TTF-1 staining (h).

sents an important diagnostic issue because medical management is different compared to a primary breast tumor.

Breast metastases from lung cancer have been rarely reported in the literature. Interestingly, differential diagnosis of breast metastasis might be perplexing when the pathology report is consistent with adenocarcinoma, because it could be mistaken for a primary triple-negative breast tumor.

Herein, we report an unusual case of a patient who presented with neuroendocrine carcinoma of the lung and a synchronous breast nodule that was shown to be a metastasis from her primary lung tumor.

Case Report

A 42-year-old female smoker with a history of a limited-stage small cell lung cancer of the right middle lobe in remission, for which she had previously received chemotherapy with cisplatin-etoposide and radiotherapy in 2017, presented at the Oncology Unit in January 2020 with mild dyspnea and chest pain. She had undergone a CT scan of the lung that showed a new lesion at the right hilum and right pleural effusion. The patient underwent new bronchoscopy that revealed a neuroendocrine carcinoma with immunohistochemical markers consistent with the previous small cell carcinoma (CD56 (+), chromogranin (+), synaptophysin (+), thyroid transcription factor-1 – TTF-1 (+), Ki67: 40%).

In addition, the patient complained of a left breast mass of a 5-month duration and therefore was referred to the Breast Unit. On examination, there was a small solid palpable mass in the upper outer quadrant of her left breast. Axillary and supraclavicular lymph nodes were not palpable. Ultrasonography showed a hypoechoic solid nodule 3 cm in the left breast, and the patient underwent a core needle biopsy. Pathology revealed a malignant neoplasm with morphological and immunohistochemical characteristics (CD56 (+), chromogranin (+), synaptophysin (+), TTF-1 (+), Ki67: 70%, ER (–), PR (–)) suggestive of a neuroendocrine carcinoma (shown in Fig. 1).

Additional staging with CT scans of the brain/abdomen and bone scan demonstrated osseous metastases, and the patient was started on chemotherapy in combination with anti-PD-L1 inhibitor.

Discussion/Conclusion

Liver, bones, adrenal glands, and brain are usually the most common sites of metastases from primary lung cancer. In contrast, breast metastases are extremely rare, accounting for 0.6–6.6% of breast tumors [6, 7]. Several tumors can cause metastases to breast tissue including hematologic malignancies, malignant melanoma, rhabdomyosarcoma, and lung malignancies [8]. Dissemination can occur via lymphatic and hematologic routes [9, 10]. Hematologic metastases most commonly appear as palpable single masses that do not display skin changes or nipple discharge [9].

Herein, we present an unusual case of a patient with recurrence of a lung neuroendocrine carcinoma that presented with a breast metastasis. Breast metastases from a primary lung tumor have been reported since 1977 [11]. In 2003, Bartella et al. [12] described a case of a 65-year-old female that presented with a synchronous single-breast metastasis originating from a small cell carcinoma of the mediastinum. Shukla et al. [13] reported two cases of 40-year-old women with small cell lung carcinomas metastatic to the breast; in one case, the primary lung tumor was detected later. Lee [14] reported a series of breast metastases and included two young women with small cell carcinoma that developed breast masses approximately 10 months after diagnosis of the primary tumor. Babu et al. [7] described two cases of lung neuroendocrine carcinomas who presented with breast lumps. Finally, Crona et al. [15] reported 8 women with lung neuroendocrine tumors (either carcinoids or large cell neuroendocrine tumors) that developed breast metastases several months after diagnosis in the majority of cases.

Lung carcinomas can spread to the ipsilateral breast through lymphatic vessels once they infiltrate ipsilateral axillary lymph nodes [16]. Interestingly, in the case of our patient, breast metastasis was located at the contralateral breast, which indicates that the tumor has probably spread through the hematogenous route.

Diagnosing a breast metastasis can be very challenging because it has to be distinguished from a primary malignancy or even a benign tumor. Histopathologic characteristics are crucial for differentiation and diagnosis. H&E-stained sections are very useful for the diagnosis of small cell carcinoma and traditionally show piles of cells with spotted chromatin, scant cytoplasm, necrosis, and many mitoses. Immunohistochemical markers, such as CD56 and synaptophysin most commonly display positivity in neuroendocrine carcinoma. In addition, TTF-1 is positive in approximately 80% of lung adenocarcinomas and small cell carcinomas [14]. TTF-1 can also be present in primary mammary small cell carcinoma, which is extremely rare; moreover, it usually co-expresses Estrogen Receptor (ER) and GCDFP-15 and includes elements of ductal carcinoma in situ [17].

Because squamous cell carcinoma of the breast is very rarely diagnosed, metastasis should always be excluded in those cases. Breast metastasis from large cell carcinoma/adenocarcinoma of the lung can be hard to distinguish from triple-negative breast carcinoma, and clinical information should always be provided to help differential diagnosis.

In the case of our patient, TTF-1 and neuroendocrine markers (synaptophysin, chromogranin) were positive in both primary lung tumor and breast tumor. In addition, breast metastasis developed synchronously with the primary tumor, making differential diagnosis easier.

In conclusion, we present the unusual case of a young woman with breast metastasis from a relapsed neuroendocrine carcinoma of the lung. Diagnosis of a breast metastasis represents a challenge for the treating physician, since it can mimic primary breast cancer.

Statement of Ethics

The patient has given written informed consent to publish her case. This research is in accordance with the World Medical Association Declaration of Helsinki.

Conflict of Interest Statement

The authors declare that there is no conflict of interest.

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None.

Author Contributions

Manuscript draft: P.E., A.C. Data acquisition, analysis, and interpretation: K.G., I.P., A.P., I.K., N.A. Conception and design: N.V.M. Final approval: all authors.

References

- McPherson K, Steel CM, Dixon JM. ABC of breast diseases. Breast cancer-epidemiology, risk factors, and genetics. *BMJ*. 2000 Sep 9;321(7261):624–8.
- Sitzenfrey A. Mammakarzinom zwei Jahre nach abdominaler radikal Operation wegen doppelseitigen Carcinoma ovarii. *Prag Med Wochenschr*. 1907;32:221–35.
- Georgiannos SN, Chin J, Goode AW, Sheaff M. Secondary neoplasms of the breast: a survey of the 20th Century. *Cancer*. 2001 Nov 1;92(9):2259–66.
- Klingen TA, Klaasen H, Aas H, Chen Y, Akslen LA. Secondary breast cancer: a 5-year population-based study with review of the literature. *APMIS*. 2009 Oct;117(10):762–7.
- Wang L, Wang SL, Shen HH, Niu FT, Niu Y. Breast metastasis from lung cancer: a report of two cases and literature review. *Cancer Biol Med*. 2014 Sep;11(3):208–15.
- Amichetti M, Perani B, Boi S. Metastases to the breast from extramammary malignancies. *Oncology*. 1990; 47(3):257–60.
- Babu KS, Roberts F, Bryden F, McCafferty A, Downer P, Hansell DT, et al. Metastases to breast from primary lung cancer. *J Thorac Oncol*. 2009 Apr;4(4):540–2.
- Vizcaino I, Torregrosa A, Higuera V, Morote V, Cremades A, Torres V, et al. Metastasis to the breast from extramammary malignancies: a report of four cases and a review of literature. *Eur Radiol*. 2001;11(9):1659–65. [not available]
- Lee SH, Park JM, Kook SH, Han BK, Moon WK. Metastatic tumors to the breast: mammographic and ultrasonographic findings. *J Ultrasound Med*. 2000 Apr;19(4):257–62.
- Malek D, Buccheri S, Dey CB, Samli B, Plemmons J. Lung cancer metastasis to the breast mimicking inflammatory breast carcinoma on imaging. *Radiol Case Rep*. 2019 Dec;14(12):1500–5.
- Toombs BD, Kalisher L. Metastatic disease to the breast: clinical, pathologic, and radiographic features. *AJR Am J Roentgenol*. 1977 Oct;129(4):673–6.
- Bartella L, Kaye J, Perry NM, Malhotra A, Evans D, Ryan D, et al. Metastases to the breast revisited: radiological-histopathological correlation. *Clin Radiol*. 2003 Jul;58(7):524–31.
- Shukla R, Pooja B, Radhika S, Nijhawan R, Rajwanshi A. Fine-needle aspiration cytology of extramammary neoplasms metastatic to the breast. *Diagn Cytopathol*. 2005 Apr;32(4):193–7.
- Lee AH. The histological diagnosis of metastases to the breast from extramammary malignancies. *J Clin Pathol*. 2007 Dec;60(12):1333–41.
- Crona J, Granberg D, Norlén O, Wärnberg F, Stålberg P, Hellman P, et al. Metastases from neuroendocrine tumors to the breast are more common than previously thought. A diagnostic pitfall? *World J Surg*. 2013 Jul; 37(7):1701–6.
- Huang HC, Hang JF, Wu MH, Chou TY, Chiu CH. Lung adenocarcinoma with ipsilateral breast metastasis: a simple coincidence? *J Thorac Oncol*. 2013 Jul;8(7):974–9.
- Shin SJ, DeLellis RA, Ying L, Rosen PP. Small cell carcinoma of the breast: a clinicopathologic and immunohistochemical study of nine patients. *Am J Surg Pathol*. 2000 Sep;24(9):1231–8.