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EGFR-Mutated Breast Metastasis of Lung Adenocarcinoma: A Case Report

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Key Words
Lung adenocarcinoma · Breast metastasis · EGFR mutation · Triple-negative breast cancer · EGFR tyrosine kinase inhibitors

Abstract
Breast metastasis from other primary carcinoma is very rare and could be difficult to identify despite immunohistochemistry analysis. Breast metastasis from lung adenocarcinoma can mimic triple-negative breast cancer. Given the prognosis and therapeutic challenges, a correct diagnosis appears essential, and molecular biomarkers could be useful. We report the case of a 52-year-old woman with a breast mass initially diagnosed as primary breast cancer and secondarily attached to breast metastasis from an EGFR-mutated lung adenocarcinoma. The same activating EGFR mutations were identified in both the primary lung carcinoma and the breast metastasis.

Introduction

Most metastases of lung cancer are localized in the liver, bone, brain and adrenal glands, but a large variety of atypical metastasis has also been reported. Breast metastasis from squamous cell carcinoma, adenocarcinoma and small-cell carcinoma of the lung is very rare

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and can mimic primary breast cancer. Breast metastasis from lung adenocarcinoma could be difficult to distinguish from triple-negative breast cancer (TNBC). Clinical, imaging and molecular correlations are necessary for an effective management of these patients with rare and atypical metastasis.

Case Report

An inflammatory left breast mass with a left axillar adenopathy was diagnosed in a nonsmoking 52-year-old woman. Mammography and breast ultrasonography revealed a 26-mm mass in the left lower quadrant compatible with primary breast cancer. The serum cancer antigen 15-3 (CA 15-3) level was slightly elevated. Ultrasound-guided core biopsy pointed to an adenocarcinoma with negative immunohistochemistry staining for ER, PR and HER2. There were no liver or bone lesions, but a moderate asymptomatic pleural effusion was discovered on chest X-ray. First-line chemotherapy with fluorouracil-epirubicin-cyclophosphamide (FEC) was prescribed for this presumed metastatic TNBC. After three cycles of FEC, a progression of the breast mass was noted. Due to massive pleural effusion, a thoracoscopy for biopsies and talc pleurodesis was performed (fig. 1). Biopsies pointed to a pleural metastasis from a thyroid transcription factor-1 (TTF1)-positive lung adenocarcinoma with EGFR-activating mutation detected by PCR analysis (deletion of exon 19). A chest CT scan performed after complete pleural drainage demonstrated an upper left lobe primary lung cancer (fig. 2). Considering these thoracic findings and the lack of efficacy of chemotherapy for the breast lesion, a new breast biopsy was performed. Histology features and immunostaining profile (TTF1+, GATA3–, GCDFP15–, PAX8–) were consistent with breast metastasis from the lung adenocarcinoma rather than a primary breast carcinoma (fig. 3). PCR analysis of the breast lesion identified the same EGFR-activating mutation (deletion of exon 19) as in the primary lung tumor. Afatinib 40 mg once a day was started. Major clinical and ultrasonographic reduction of the breast mass and thoracic objective response were found after 2 months of afatinib (fig. 4).

Discussion

Breast metastasis from other primary carcinoma is very rare, with an incidence ranging between 0.5 and 1% of all breast tumors. Histological and immunohistochemical features are useful to diagnose metastasis to the breast from extramammary malignancies [1]. Primary sites are mainly malignant melanoma, lymphoma, ovarian and lung carcinoma. All histological subtypes of lung carcinoma may metastasize to the breast [2–4]. Breast metastasis from lung adenocarcinoma is exceptional and represents less than 0.1% of breast cancers [5]. Breast metastasis from lung adenocarcinoma can mimic TNBC. EGFR-activating mutations have been reported in 1.4 and 11.4%, respectively, in two series of Asian patients with TNBC but in none of the European patients [6–8]. Clinical, imaging, histological and immunohistochemical features must be taken into account to optimize the management of these rare lesions. Mirrielees et al. [9] published a systematic review of the literature on breast metastasis from primary lung carcinoma. They identified 31 case reports of non-small-cell lung cancer (NSCLC) and 8 cases of small-cell lung cancer (SCLC) metastasis to the breast. Synchronous metastasis to the breast was detected in 33 and 80%, respectively, of NSCLC and SCLC. TTF1 was expressed in 58% of all NSCLC breast metastases, including 83% of those of adenocarcinoma subtype. The predictive value of EGFR-activating mutations for

EGFR tyrosine kinase inhibitor (EGFR-TKI) efficacy is well recognized. EGFR-TKIs are currently recommended as first-line treatment for EGFR-mutated NSCLC. The LUX-Lung 3 study demonstrated a significant superiority of afatinib on cisplatin-pemetrexed in terms of response rate and progression-free survival [10]. In our case report, a rapid and objective response was noted under afatinib both in the primary and the breast metastatic lesion. Fukumoto et al. [11] have reported a case of late breast metastasis from a previously resected EGFR-mutated lung adenocarcinoma. As in our case report, these authors highlighted that the same EGFR mutation was detected in both the primary lung cancer and the breast tumor. However, in their case report, the patient did not receive EGFR-TKIs, and no further information was available. Sato et al. [12] reported the case of a woman treated as first-line with gefitinib for an EGFR-mutated lung adenocarcinoma. After 12 months of gefitinib, the patient developed breast metastasis in which the second mutation resistant to EGFR-TKIs (T790M) was detected [12]. To our knowledge our case report is the first of a synchronous breast metastasis from a lung adenocarcinoma with an EGFR mutation detected both in the primary and the metastatic lesion. Our case report highlights the usefulness of EGFR mutation detection for appropriate diagnosis and targeted treatment.

Disclosure Statement

The authors declare that they have no conflicts of interest.

References

1 Lee AH: The histological diagnosis of metastases to the breast from extramammary malignancies. J Clin Pathol 2007;60:1333–1341.
2 Hsu W, Sheen-Chen SM, Wang JL, Huang CC, Ko SF: Squamous cell lung carcinoma metastatic to the breast. Anticancer Res 2008;28:1299–1301.
3 Masmoudi A, Mathieu MC, Soria JC: Breast metastasis from lung adenocarcinoma: a case report. Anticancer Res 2003;23:1825–1826.
4 Liu W, Palma-Diaz F, Alasio TM: Primary small cell carcinoma of the lung initially presenting as a breast mass: a fine-needle aspiration diagnosis. Diagn Cytopathol 2009;37:208–212.
5 Sousaris N, Mendelsohn G, Barr RG: Lung cancer metastatic to breast: case report and review of the literature. Ultrasound Q 2013;29:205–209.
6 Lv N, Xie X, Ge Q, Lin S, Wang X, Kong Y, Shi H, Xie X, Wei W: Epidermal growth factor receptor in breast carcinoma: association between gene copy number and mutations. Diagn Pathol 2011;6:118.
7 Teng YH, Tan WJ, Thike AA, Cheok PY, Tse GM, Wong NS, Yip GW, Bay BH, Tan PH: Mutations in the epidermal growth factor receptor (EGFR) gene in triple negative breast cancer: possible implications for targeted therapy. Breast Cancer Res 2011;13:R35.
8 Jacot W, Lopez-Crapez E, Thezenas S, Senal R, Fina F, Bibeau F, Romieu G, Lamy PJ: Lack of EGFR-activating mutations in European patients with triple-negative breast cancer could emphasise geographic and ethnic variations in breast cancer mutation profiles. Breast Cancer Res 2011;13:R133.
9 Mirrielees JA, Kapur JH, Szalkucki LM, Harter JM, Salkowski LR, Strigel RM, Traynor AM, Wilke LG: Metastasis of primary lung carcinoma to the breast: a systematic review of the literature. J Surg Res 2014;188:419–431.
10 Sequist LV, Yang JC, Yamamoto N, O'Byrne K, Hirsh V, Mok T, Geater SL, Orlov S, Tsai CM, Boyer M, Su WC, Bennouna J, Kato T, Gorbunova V, Lee KH, Shah R, Massey D, Zazulina V, Shahidi M, Schuler M: Phase III study of afatinib or cisplatin plus pemetrexed in patients with metastatic lung adenocarcinoma with EGFR mutations. J Clin Oncol 2013;31:3327–3334.
11 Fukumoto K, Usami N, Okasaka T, Kawaguchi K, Okagawa T, Suzuki H, Yokoi K: Late breast metastasis from resected lung cancer diagnosed by epidermal growth factor receptor gene mutation. Lung Cancer 2011;74:352–353.
12 Sato K, Takeyama Y, Yoshihara M, Kato T, Hashimoto H, Fukui Y, Gonda H, Suzuki R: CBDCA + pemetrexed + bevacizumab and its maintenance chemotherapy in a case of solitary breast metastasis from a lung adenocarcinoma resistant to gefitinib. Case Rep Oncol 2012;5:546–553.

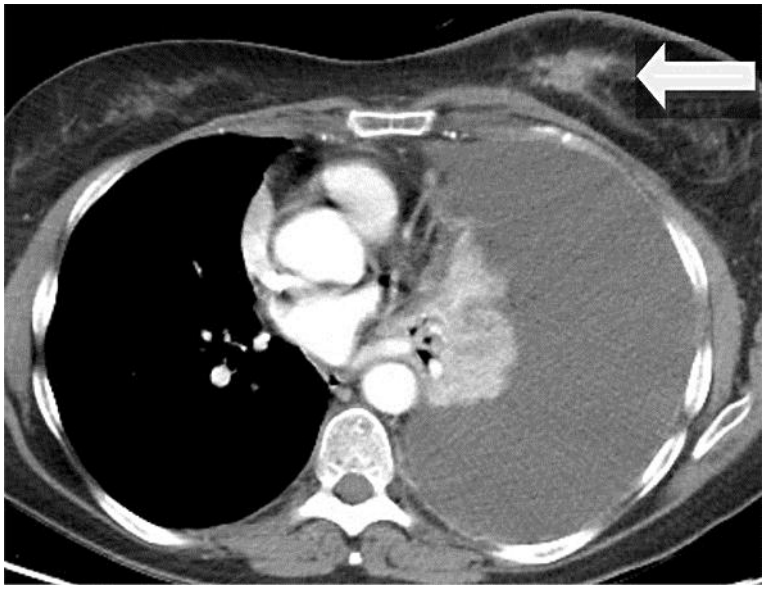

Fig. 1. Chest CT scan. Massive pleural effusion and left breast mass (arrow).

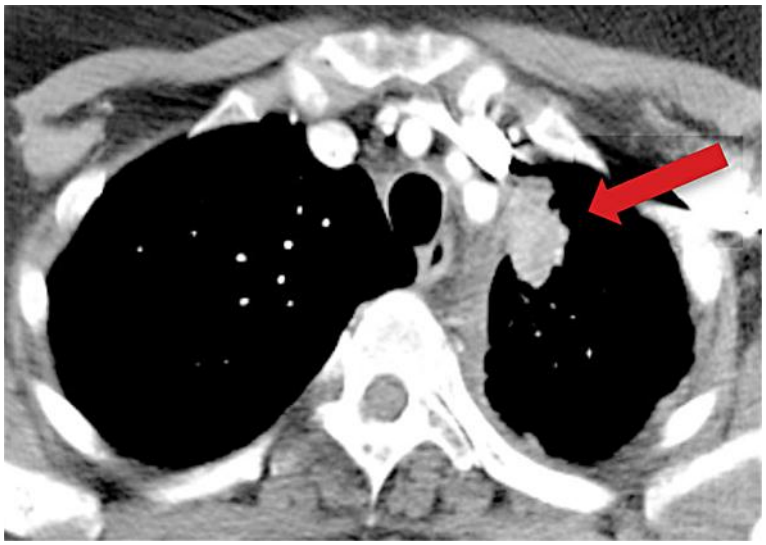

Fig. 2. Chest CT scan. Primary lung cancer in the left upper lobe (arrow).

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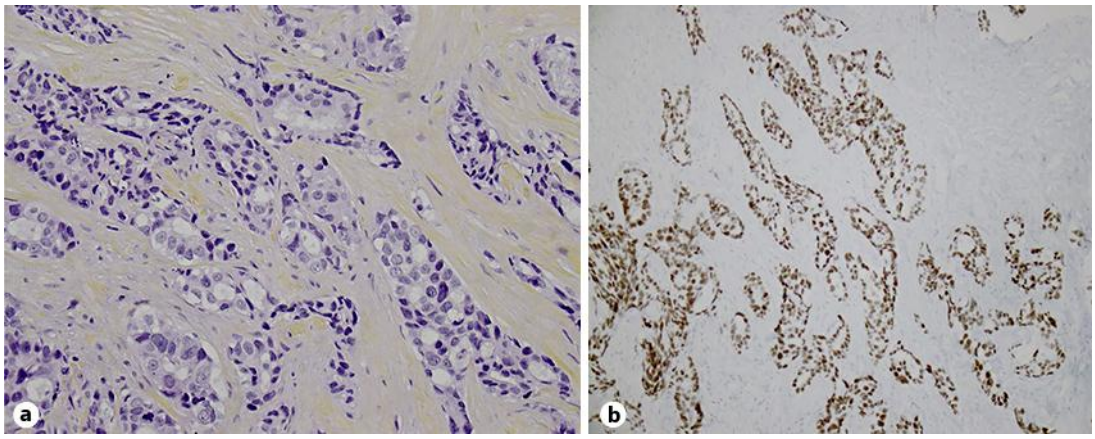

Fig. 3. Breast biopsy. Histology features (**a**) and TTF1-positive immunostaining profile (**b**) for breast metastasis of the lung adenocarcinoma.

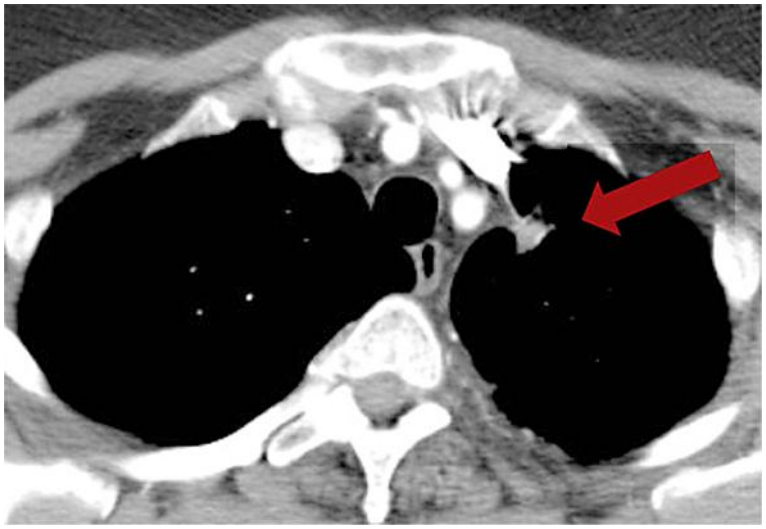

Fig. 4. Chest CT scan. Objective response after 2 months of afatinib (arrow; see fig. 2 for baseline).