Biologics: Targets and Therapy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

CASE REPORT

Tumor-to-Tumor Metastasis: Breast Cancer Metastasizing to EGFR Exon 19-Mutated Lung Adenocarcinoma with Long-Term Disease-Free Survival

Yana Zhang[1,2], Yang Hao[1,2], Han Yang[1,2], Xiangli Meng[1], Shanshan Yang[1], Jin Wang[1], Jinling Xie[1], Ping Lu[1,2,*], Yinghua Ji[1,2,*]

[1]Department of Oncology, The First Affiliated Hospital of Xinxiang Medical University, Xinxiang, Henan, 453100, People's Republic of China; [2]Department of Life Science Research Center, The First Affiliated Hospital of Xinxiang Medical University, Xinxiang, Henan, 453100, People's Republic of China

*These authors contributed equally to this work

Correspondence: Yinghua Ji; Ping Lu, Department of Oncology, The First Affiliated Hospital of Xinxiang Medical University, No. 88 Jiankang Road, Weihui, Xinxiang, Henan, 453100, People's Republic of China, Tel +86 0373 4402543; +86 0373 4402106, Email 54234317@qq.com; lupingdoctor@126.com

Biologics: Targets and Therapy downloaded from https://www.dovepress.com/
For personal use only.

Abstract: Tumor-to-tumor metastasis (TTM) is a rare phenomenon characterized by the metastasis of one malignant tumor into another histologically different tumor. While breast and lung cancers are prevalent among women globally, TTM involving breast cancer metastasizing to lung adenocarcinoma is exceptionally uncommon. Herein, we report a rare case of Luminal B breast cancer metastasizing to EGFR exon 19 deletion-mutated lung adenocarcinoma. The patient achieved prolonged disease-free survival following comprehensive treatment, including surgical resection, chemotherapy, EGFR-tyrosine kinase inhibitor (TKI) therapy, and endocrine therapy. This case highlights the importance of molecular profiling in guiding personalized therapeutic strategies for TTM, particularly when actionable mutations are present.

Keywords: tumor-to-tumor metastasis, breast cancer, lung cancer, EGFR mutation, targeted therapy

Introduction

Tumor-to-tumor metastasis (TTM) is an extremely rare phenomenon in which one metastatic tumor acts as a host for secondary metastases from another primary tumor. As of September 2023, only 685 cases of TTM have been documented. This condition involves at least two distinct tumors: a "donor" tumor (the source of metastatic cells) and a "recipient" tumor (the host). Common donor tumors include breast, lung, renal, colorectal, and prostate cancers, while meningiomas are recognized as the most frequent recipient lesions.[1] Mei et al[2] recently reviewed articles on TTM published between 2018 and 2023 and identified 68 cases. We have summarized the five documented cases involving breast cancer metastasis to pulmonary lesions thus far (see Table 1).

Due to its rarity, TTM has primarily been described through case reports without established management guidelines. Treatment is highly individualized, often combining surgery, radiotherapy, chemotherapy, immunotherapy, targeted therapy, or hormonal therapy based on tumor histology and stage.[2] Here, we report a unique case of Luminal B breast cancer metastasizing to EGFR exon 19 deletion-mutated lung adenocarcinoma in a 55-year-old woman. Notably, the patient achieved prolonged disease-free survival (DFS) with a multimodal treatment strategy, including EGFR-TKI therapy.

Received: 12 August 2025
Accepted: 11 November 2025
Published: 19 November 2025

© 2025 Zhang et al. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms.php and incorporate the Creative Commons Attribution – Non Commercial (unported, v4.0) License (http://creativecommons.org/licenses/by-nc/4.0/). By accessing the work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please see paragraphs 4.2 and 5 of our Terms (https://www.dovepress.com/terms.php).

Table 1 Summary of Clinical and Genomic Features of Breast-Lung Tumor-to-Tumor Metastasis (TTM) From Other Cases

Study	Age (y)	Gender	Smocking	Donor Site	Recipient Site	Lung Cancer Genomic Profile	Treatment of Breast Cancer	Treatment of Lung Cancer	Clinical Outcome
Sema Turker MD et al (2019)[3]	67	Female	NA	Breast carcinoma	Lung adenocarcinoma	NA	Surgery + hormonal therapy	Surgery+ chemotherapy (4 cycles of cisplatin and vinorelbine)	19m
Myoung Jae Kang et al (2020)[4,]	52	Female	NA	Breast carcinoma	Lung adenocarcinoma	NA	NA	NA	NA
Federico Piacentini et al (2011)[5]	75	Female	No	Breast carcinoma	Lung squamous cell carcinoma	NA	Surgery + FEC + Radiotherapy + hormonal therapy (Exemestane)	Surgery	24m (Ca15.3 was slightly increased)
Federico Piacentini et al (2011)[5]	59	Female	Yes	Breast carcinoma	Lung adenocarcinoma	Missense mutation of KRAS (G13C)	Surgery + FEC + Radiotherapy + hormonal therapy (Exemestane)	Surgery+ chemotherapy (carboplatin and gemcitabine)	24m (lost to follow-up)
Frank O. Velez-Cubian et al (2016)[6]	64	Female	NA	Breast carcinoma (solitary fibrous tumor admixed with metastatic invasive ductal breast carcinoma)	Lung adenocarcinoma	NA	Neoadjuvant chemotherapy (three cycles of doxorubicin and cyclophosphamide) +surgery+adjuvant chemotherapy (12 cycles of paclitaxel) + hormonal therapy (Letrozole) → hormonal therapy (exemestane and fulvestrant)	Sugery	NA

https://doi.org/10.2147/BTT.S558828

Case Presentation

A 55-year-old female non-smoker presented with a right-sided breast mass in December 2022. She had entered menopause at age 50. Ultrasonography revealed a 22×19 mm hypoechoic nodule in the right breast (BI-RADS 4B) (Figure 1A). A computed tomography (CT) scan of the chest on February 16, 2022, revealed a mass in the right breast (Figure 1B) and an irregular nodule measuring 2.3 cm in the right upper lung lobe. The nodule had irregular margins, with visible spiculation and pleural retraction (Figure 1C). Additionally, a ground-glass nodule approximately 0.7 cm in diameter was observed, and none of the lymph nodes were enlarged (all lymph nodes had a short axis of less than 1 cm). Morphologic features suggested a possible primary bronchogenic malignancy (Figure 1D). The right breast mass was confirmed to be invasive breast cancer by puncture biopsy. Brain CT showed no evidence of metastasis at that time. The multidisciplinary team (MDT) discussion concluded that surgical treatment should be preferred.

On December 20, 2022, the patient underwent a thoracoscopic right upper lung lobectomy combined with mediastinal lymph node dissection, as well as a modified radical mastectomy of the right breast. Three tumor foci were identified in the resected right upper lung lobe tissue. Lesion 1 was a 2.2×1.8×1.5 cm invasive lung adenocarcinoma (90% alveolar growth pattern, TTF-1+) (Figure 2A and B). Lesion 2 was a 0.8×0.6×0.5 cm microinvasive lung adenocarcinoma, with adjacent metastatic foci of invasive breast cancer (Figure 2C). Lesion 3 was a 1×0.7×0.4 cm invasive lung adenocarcinoma (alveolar growth pattern). 1/3 of the parabronchial lymph nodes showed metastases. Genomic testing (Lesion 1) confirmed an EGFR exon 19 deletion mutation in the lung adenocarcinoma. Breast pathology showed a 3×2×1.7 cm invasive carcinoma with metastasis in 1/1 sentinel lymph nodes (max diameter 15 mm) and 1/4 axillary lymph nodes. Immunohistochemistry (IHC) results were as follows: ER (90%), PR (10%), HER-2 (2+, no gene amplification), Ki-67 (5%), and GATA3 (+) (Figure 2D).

According to the postoperative pathologic findings, this patient was diagnosed with both lung adenocarcinoma (pT3N1M0 stage IIIA with EGFR exon 19 deletion mutation) and breast cancer (pT2N1M1 stage IV, Luminal B subtype). After the surgery, the patient received 6 cycles of chemotherapy (120 mg docetaxel and 0.9 g cyclophosphamide on day 1, with 21-day cycle intervals) from January 18 to May 13, 2023. Subsequent maintenance therapy included icotinib (125 mg orally thrice daily) for lung cancer and letrozole (2.5 mg orally daily) for breast cancer. No grade ≥2 adverse events occurred. As of December 26, 2024, follow-up CT showed no recurrence, with an estimated DFS of 27 months to April 1, 2025.

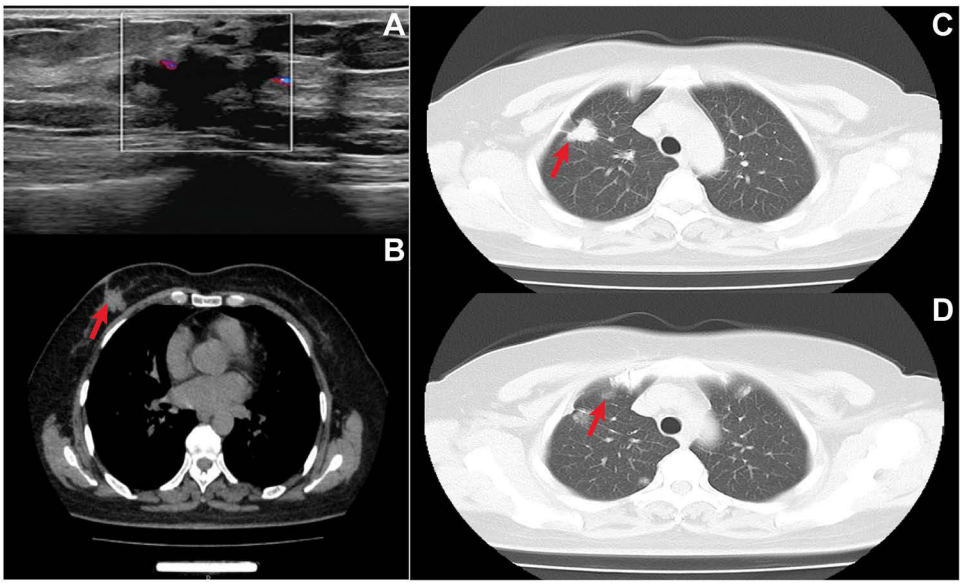

Figure 1 Pre-diagnostic imaging findings of the patient. (**A**) Breast ultrasound showing a breast mass (breast mass is indicated by the white box). (**B–D**) Chest computed tomography (CT) images, red arrows indicate the breast mass (**B**) and lung nodules (**C** and **D**).

https://doi.org/10.2147/BTT.S558828

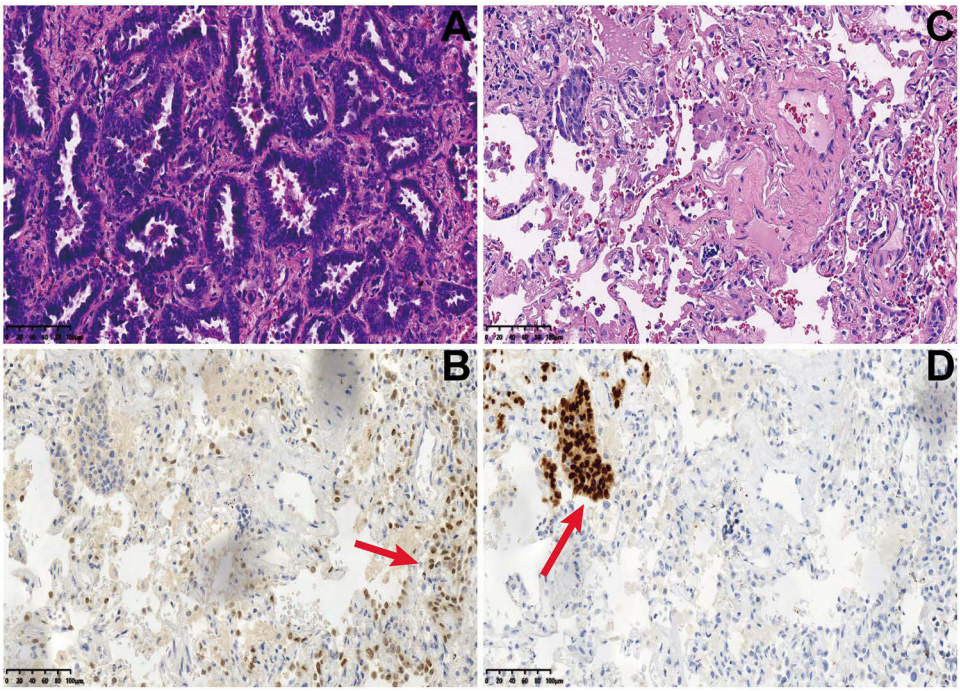

Figure 2 Pathological findings of surgical specimens. (**A**) Hematoxylin-eosin (HE) staining shows lung adenocarcinoma (200×; Lesion 1: Lung adenocarcinoma tissue morphology). (**B**) Immunohistochemical (IHC) staining shows malignant cells positive for TTF-1 (200×; red arrows indicate positively stained cells). (**C**) HE staining shows histological features of both lung adenocarcinoma and breast cancer (200×; Lesion 2: Tissue morphology of breast cancer metastasizing to lung adenocarcinoma). (**D**) IHC staining shows malignant cells positive for GATA3 (200×; red arrows indicate positively stained cells).

Discussion

TTM is a rare phenomenon, which was a primary malignant tumor migrated into a preexisting malignant tumor of another pathologic type by vascular or lymphatic pathways. The diagnostic criteria proposed by Dobbing and Campbell define TTM as follows:[7] (1) presence of two distinct primary malignancies; (2) the recipient is a genuine primary tumor; (3) confirmed metastasis within the recipient tumor (excluding lymphatic spread to lymphoma). The most common combination of tumor-to-tumor metastasis is breast cancer metastasis to meningioma. However, only five cases of breast cancer metastasis to lung cancer have been reported in the published literature.[3–6] Our case is the first to describe breast cancer metastasis to EGFR exon 19-mutated lung adenocarcinoma, with prolonged DFS under targeted therapy.

TTM is typically confirmed via histopathology, with two distinct tumor components in the same specimen. Previous cases of breast-to-lung TTM were initially misdiagnosed as simple breast cancer lung metastasis, with TTM confirmed only postoperatively.[3,4] This aligns with our case, as both patients were diagnosed TTM through surgery specimen. Tumor heterogeneity is a well-recognized phenomenon in cancer biology that may be missed by small sample biopsies.

EGFR mutations are one of the most common driver oncogene alterations in non-small cell lung cancer (NSCLC), particularly in never-smoking East Asian females with adenocarcinoma,[8] as seen in our case.

Patients with NSCLC harboring activating EGFR mutations, such as the exon 21 L858R mutation or exon 19 deletion, benefit from EGFR-TKI therapy, whereas patients with EGFR wild-type (WT) tumors do not. A meta-analysis showed that for patients with advanced EGFR-mutant NSCLC, exon 19 deletion was associated with longer PFS when treated with EGFR-TKI, compared to exon 21 L858R mutation. Both EGFR mutation status and EGFR mutation subtype are considered important predictors of the efficacy of EGFR-TKI therapy in NSCLC.[9] Therefore, it is important to detect mutations in lung adenocarcinoma, which provides a potential means for targeted therapy. For example, Turker et al treated a similar patient with cisplatin/vinorelbine without EGFR-TKI, achieving 19 months of survival.[3] In contrast, our patient's use of icotinib (a first-generation EGFR-TKI) likely contributed to her extended DFS (27 months), supporting the value of molecular profiling in TTM.

For stage IIIA NSCLC with EGFR mutations, adjuvant treatment with an EGFR-TKI has been shown to improve survival outcomes,[10] supporting the rationale for icotinib use in this case. With regard to breast cancer, postoperative adjuvant chemotherapy remains a standard treatment across all molecular subtypes following radical resection, with the primary goals of reducing the risk of micrometastasis and improving overall survival.[11] In the present case, the patient was diagnosed with stage IV Luminal B breast cancer and underwent radical mastectomy; thus, postoperative adjuvant therapy is particularly imperative. Additionally, in line with the recommendations of the MDT, letrozole was selected for subsequent maintenance therapy—it is an aromatase inhibitor specifically targeting estrogen receptor (ER)-positive tumors.

This case adds to the limited literature on breast-to-lung TTM and emphasizes the clinical utility of molecular testing in guiding therapeutic decisions. However, this is a single case, and larger studies are needed to validate treatment strategies.

Conclusions

This study is the first to report a case of breast cancer metastasizing to EGFR exon 19-mutated lung adenocarcinoma, in which the patient achieved long-term DFS via targeted therapy. It also confirms tumor heterogeneity and the limitations of small-sample biopsies, clarifies the definition and rarity of TTM, and verifies that comprehensive histopathological examination combined with molecular testing is key to precision diagnosis and treatment. Clinically, it helps doctors avoid misdiagnosis caused by incomplete testing and provides references for similar cases. In the future, it is necessary to explore its molecular mechanisms and optimize testing methods to improve the diagnosis and treatment system for TTM.

Ethics Approval and Informed Consent

The publication of case details has been approved by the Ethics Committee of the First Affiliated Hospital of Xinxiang Medical University. The patient has provided written informed consent for the publication of the case details and accompanying images.

Funding

This work was supported by the Henan Provincial Graduate Education Reform and Quality Improvement Project (grant number: YJS2023AL062) and Henan Medical Science and Technology Joint Construction Project (grant number: LHGJ20220624).

Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Kunc M, Skrzypkowska P, Peksa R, Biernat W. Tumor-to-tumor metastases: systematic review and meta-analysis of 685 reported cases. *Clin Exp Metastasis*. 2025;42(2):14. doi:10.1007/s10585-025-10332-7
2. Mei W, Zhang D. Unraveling Tumor-to-Tumor Metastasis: insights into Pathogenesis, Diagnostic Challenges, and Treatment Modalities. *Biologics*. 2025;19:43–58. doi:10.2147/BTT.S505950
3. Turker S, Cilbir E, Yilmaz KB, et al. Tumor-to-tumor metastasis: breast cancer metastasis to lung cancer. *Breast J*. 2020;26(3):534–535. doi:10.1111/tbj.13558
4. Kang MJ, An AR, Chung MJ, Kim KM. Tumor-to-tumor metastasis: metastatic invasive lobular carcinoma of the breast within adenocarcinoma of the lung. *J Pathol Transl Med*. 2020;54(2):188–191. doi:10.4132/jptm.2019.09.07
5. Piacentini F, Rossi G, Casali C, Cadioli A, Barbieri E, Guarneri V. Primary pulmonary cancer colliding with metastatic breast carcinoma: hitherto unreported cases of cancer-to-cancer metastasis focusing on clinical implications. *Lung Cancer*. 2011;74(1):145–148. doi:10.1016/j.lungcan.2011.06.008
6. Velez-Cubian FO, Gabordi RC, Smith PV, Toloza EM. Tumor-to-tumor metastasis: an unusual case of breast cancer metastatic to a solitary fibrous tumor. *J Thorac Dis*. 2016;8(6):E374–8. doi:10.21037/jtd.2016.03.79
7. Campbell LV, Gilbert E, Chamberlain CR, Watne AL. Metastases of cancer to cancer. *Cancer*. 1968;22(3):635–643. doi:10.1002/1097-0142-(196809)22:3<635::aid-cncr2820220320>3.0.co;2-o
8. Mitsudomi T, Kosaka T, Yatabe Y. Biological and clinical implications of EGFR mutations in lung cancer. *Int J Clin Oncol*. 2006;11(3):190–198. doi:10.1007/s10147-006-0583-4
9. Zhang Y, Sheng J, Kang S, et al. Patients with exon 19 deletion were associated with longer progression-free survival compared to those with L858R mutation after first-line EGFR-TKIs for advanced non-small cell lung cancer: a meta-analysis. *PLoS One*. 2014;9(9):e107161. doi:10.1371/journal.pone.0107161
10. Yang W, Gao Y, Li X, et al. Postoperative survival of EGFR-TKI-targeted therapy in non-small cell lung cancer patients with EGFR 19 or 21 mutations: a retrospective study. *World J Surg Oncol*. 2017;15(1):197. doi:10.1186/s12957-017-1251-z
11. Wang Y, Yin Q, Yu Q, et al. A retrospective study of breast cancer subtypes: the risk of relapse and the relations with treatments. *Breast Cancer Res Treat*. 2011;130(2):489–498. doi:10.1007/s10549-011-1709-6

Biologics: Targets and Therapy

Dovepress
Taylor & Francis Group

Publish your work in this journal

Biologics: Targets and Therapy is an international, peer-reviewed journal focusing on the patho-physiological rationale for and clinical application of Biologic agents in the management of autoimmune diseases, cancers or other pathologies where a molecular target can be identified. This journal is indexed on PubMed Central, CAS, EMBase, Scopus and the Elsevier Bibliographic databases. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/biologics-targets-and-therapy-journal