

# Breast Metastasis from Primary Lung Adenocarcinoma: A Rare Occurrence with Diagnostic Challenges and Treatment Implications

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## ABSTRACT

Breast metastasis from non-mammary sites is a rare occurrence with a prevalence ranging from 0.5 to 3%. Accurate diagnosis is crucial as it influences treatment planning and management. Distinguishing primary breast cancer from metastatic disease can be challenging, and an incorrect diagnosis can result in unnecessary surgical interventions. Immunohistochemistry plays a crucial role in identifying the primary tumor origin, especially when cytological patterns appear atypical. Here we present a case of a 53-year-old female patient with breast metastases from a primary lung adenocarcinoma. Pathology from the lung biopsy revealed a well to moderately differentiated adenocarcinoma with epidermal growth factor receptor mutation. Immunohistochemical analysis using specific markers such as TTF-1 and GATA-3 was instrumental in determining the malignant cell origin and formulating a treatment plan. This report highlights the importance of early diagnosis, thorough investigation and the role of immunohistochemical markers in managing this rare occurrence.

**Keywords:** Breast metastasis, lung cancer, core biopsy, EGFR mutation

## INTRODUCTION

Breast metastasis from non-mammary sites is a rare occurrence, with an incidence of 0.5% to 3%. Accurate diagnosis is crucial as it influences treatment planning and management. Distinguishing between primary breast cancer and metastatic disease can present diagnostic challenges, potentially leading to unnecessary surgical interventions. The distinction becomes even more critical when cytological patterns appear atypical, necessitating the use of complementary diagnostic tools. Metastasis to the breast from extra mammary malignancies, such as lung adenocarcinoma, is an unexpected finding due to the relatively uncommon nature of such events. Lung neoplasms can metastasize through hematologic and lymphatic routes with distant metastases most commonly affecting organs such as the liver, adrenal glands, bones, and brain. However, the breast involvement remains rare, making its diagnosis particularly challenging. In this context, we present a case report of a 53-year-old female patient with breast metastases from a primary lung adenocarcinoma. Our aim is to emphasize the clinical significance of early and accurate diagnosis and the challenges associated with differentiating primary breast cancer

from metastatic disease. The role of immunohistochemistry (IHC) in assisting with the identification of malignant cell origin and the formulation of a tailored treatment plan will also be discussed.

## CASE PRESENTATION

A 53-year-old female patient was referred to the ENT station by the maxillofacial surgeon because of confirmed adenocarcinoma manifestations in the right occipital area. The primary tumor has not yet been found. Complaints regarding the shortness of breath, cough, hemoptysis, or B-symptomatic were denied. She had no pre-existing oncological disease. Only the patient's mother had a malignancy of the abdomen (uterus, not further specified), otherwise, she had no family history of known risk factors and no history of exposure to noxious agents. Computed tomography-thorax imaging with contrast medium revealed some pulmonary changes but not a clear tumor mass. It showed an unclear structure in the caudomedial area of the left breast. The patient underwent a bronchoscopy with EBUS and a lung biopsy. The histopathologic examination of biopsies and cytology materials indicated a well to moderately



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differentiated adenocarcinoma. In further molecular analyzes, an epidermal growth factor receptor mutation [c.2573T>G, p. Leu858Arg (27%, NM\_005228.5)] was detected in tumor cells. The tumor infiltration was primarily in the lingula area with the involvement of the distal and medial main bronchus on the left side.

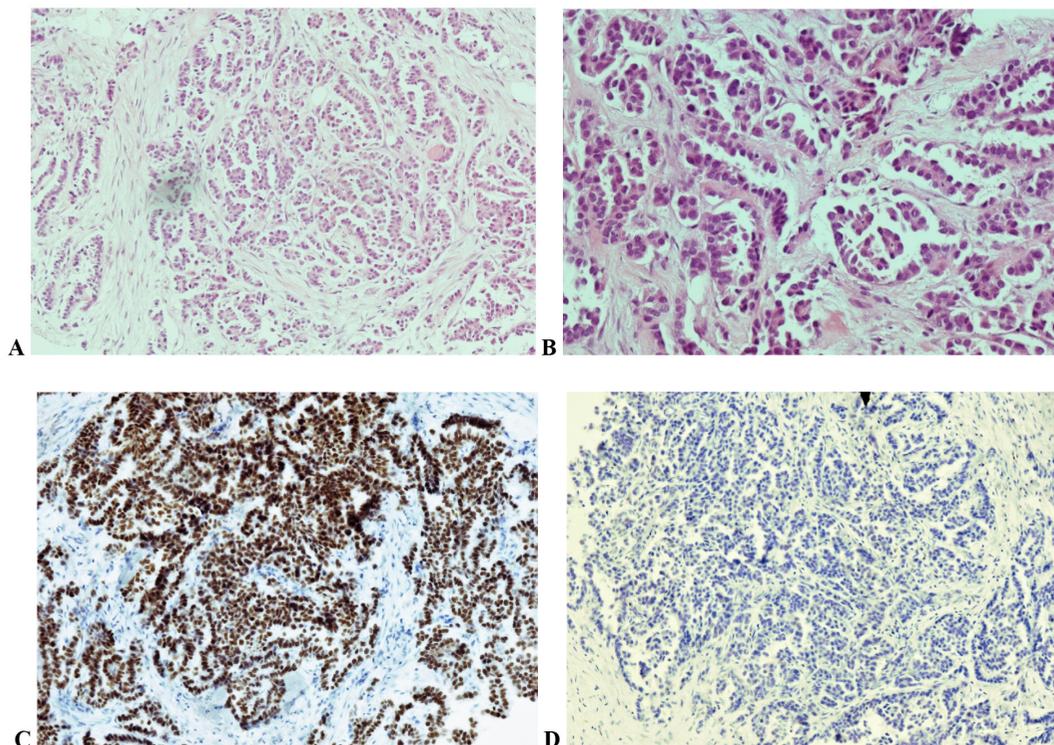
With suspicion of a second carcinoma in the breast tissue, a core biopsy of the breast mass was performed. Histopathological evaluation revealed adenocarcinoma with a predominantly tubulopapillary growth pattern. Primary immunohistochemical evaluations showed a triple negative adenocarcinoma (ER, PR, and Her2 negative). Considering the recently detected bronchial adenocarcinoma of the lung and the untypical histological image for a primary triple-negative breast carcinoma, a diagnosis of breast metastasis by tumor cells of bronchial carcinoma was considered. This assumption could be confirmed by additional immunohistochemical evaluations. The tumor cells in the breast biopsy were also negative for GATA-3 and mammaglobin. However, they were strongly positive for CK7 and TTF1 (Figure 1). The results of conventional histopathological and immunohistochemical evaluations confirmed breast metastasis by bronchial carcinoma.

Further imaging analyzes revealed meningiosis carcinomatosa with subarachnoid tumor nodes without any involvement of brain tissue. Magnetic resonance imaging of the spine also showed multifocal bone metastases with complete infiltration of thoracic vertebrae 11 and 4 with a suspected risk of fracture. In addition, larger metastases were detected near the baseplate in thoracic vertebra 12 and left in sacral vertebra 1 without evidence of a clear spread into the spinal canal.

## DISCUSSION

Lung adenocarcinoma is the most common subtype of non-small-cell lung cancer, accounting for approximately 40% of all lung cancer cases [1]. Metastatic disease of the breast is an uncommon occurrence with reported clinical cases ranging from 0.2% to 2.7% [2,3]. Metastatic cancer presenting as a breast mass is an unexpected finding in female patients because it is relatively uncommon due to the large area of fibrous tissue and poor blood supply in the breast [4]. According to a study by Riihimäki et al. [5], metastases from lung adenocarcinoma most frequently occur in the bone, liver, and brain, while metastases to the breast are relatively rare.

Accordingly, the presence of synchronous tumor masses in the lung and breast of a patient is more consistent with two distinct



**Figure 1.** (A, B) The biopsy of the breast shows a tubulopapillary epithelial growth of invasive adenocarcinoma (H and E,  $\times 100$ ;  $\times 200$ ); (C, D) immunohistochemical staining of the tumor shows widespread nuclear positivity for TTF-1 and negative for GATA-3 (H and E,  $\times 100$ )

H and E: Hematoxylin and eosin

and independent malignancies or breast carcinoma with lung metastasis than bronchial carcinoma with breast metastasis. In this context, the correct diagnosis of breast metastasis from bronchial carcinoma requires a high index of suspicion and the application of an appropriate profile of immunohistochemical findings. One of the key diagnostic features in this case was the histopathological appearance of the tumor in breast biopsy. The histologic appearance of carcinoma in the breast was not typical for triple-negative breast carcinoma (TNBC). TNBC accounts for approximately 10-20% of all breast cancer cases and is associated with a poor prognosis [1]. Except for specific triple-negative low-grade tumors of the breast (adenoid-cystic carcinoma of the breast and micro-glandular adenosis), most triple-negative breast cancers are high-grade tumors with necrosis, show aggressive biological behavior and have a higher rate of distant metastases compared to other subtypes of breast cancer [6-8]. In one study, 18% of TNBCs showed lung metastasis in 5-year follow-up, compared to 7% for non-TNBCs [9].

The clinical presentation of breast metastases from lung cancer can vary widely and may include palpable masses, nipple discharge, and skin changes. In some cases, breast metastases may be the first sign of underlying lung cancer. In most cases, metastatic disease of the breast occurs after the primary tumor has been diagnosed. However, in approximately 25% of patients, a breast mass is the initial mode of presentation [10]. Breast metastases from extramammary sites can often present as solitary breast masses and can be challenging to distinguish from primary breast malignancies or benign diseases. A potential list of usual sources of metastasis to the breast includes lung, ovarian, gastrointestinal, and soft tissue tumors [11,12].

The use of immunohistochemical staining in this case played a crucial role in confirming the diagnosis of metastatic lung adenocarcinoma. This finding is consistent with previous studies showing that the use of immunohistochemical markers can help differentiate between primary and metastatic tumors [1]. Several markers can be helpful in differentiating metastatic breast tumors from primary breast carcinoma. TTF-1 and napsin-A are helpful in identifying lung adenocarcinoma, whereas PAX-8 and CA-125 are useful for ovarian cancer. Gastrointestinal tumors can be identified using CK20, CDX-2, and villin, and soft tissue tumors can be identified using markers such as S-100, smooth muscle actin, and desmin [13,14].

In addition, molecular profiling using next-generation sequencing (NGS) can be useful in identifying the origin of metastatic tumors [15,16]. Overall, the use of IHC and NGS can aid in the diagnosis of metastatic breast tumors and help differentiate them from primary breast carcinoma, ultimately guiding appropriate treatment strategies.

In conclusion, breast metastasis from non-mammary sites is a rare occurrence that can pose diagnostic challenges for clinicians. Metastasis of lung adenocarcinoma to the breast represents a triple-negative carcinoma and should be considered in differential diagnosis by a pathologist, particularly when the histological findings are not completely typical for triple-negative breast carcinoma. Accurate diagnosis is important and helps prevent unnecessary breast surgery or additional tumor therapy.

### Ethics

**Informed Consent:** Informed consent was obtained from the patient.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: R.R., M.M., I.P., Concept: R.R., M.M., I.P., Data Collection or Processing: R.R., M.M., I.P., Analysis or Interpretation: R.R., M.M., I.P., Literature Search: R.R., M.M., I.P., Writing: R.R., M.M., I.P.

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