

## **Breast and Axillary Lymph Node Metastases from Advanced Non-small Cell Lung Carcinoma**

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*Abstract.* Lung cancer metastasizing to the breast is rare. Only few published case reports can be found in the literature. Metastatic lung cancer to the breast and its ipsilateral axillary lymph node is extremely unusual. No awareness of any prior case reports of lung cancer with such a presentation is known. Herein, this study reports an unusual case of a middle aged Saudi female with non-small cell lung cancer that has metastasized, not only to the lungs and the breast, but also to the ipsilateral axillary lymph nodes. It is important for the oncologists to be mindful of rare presentations for such a common malignancy as lung cancer.

*Keywords:* Breast, Lung, Carcinoma, Axillary lymph node metastases, Non-small cell.

### **Introduction**

Up to 40% of newly diagnosed non-small cell lung cancer presents with metastatic disease. Major sites of metastases include the liver (33% to 40%), adrenal glands (18% to 38%), brain (15% to 43%), bone (19% to 33%), kidney (16% to 23%), and abdominal lymph nodes (29%)<sup>[1-3]</sup>. Breast cancer is the most common cancer in women, yet metastatic

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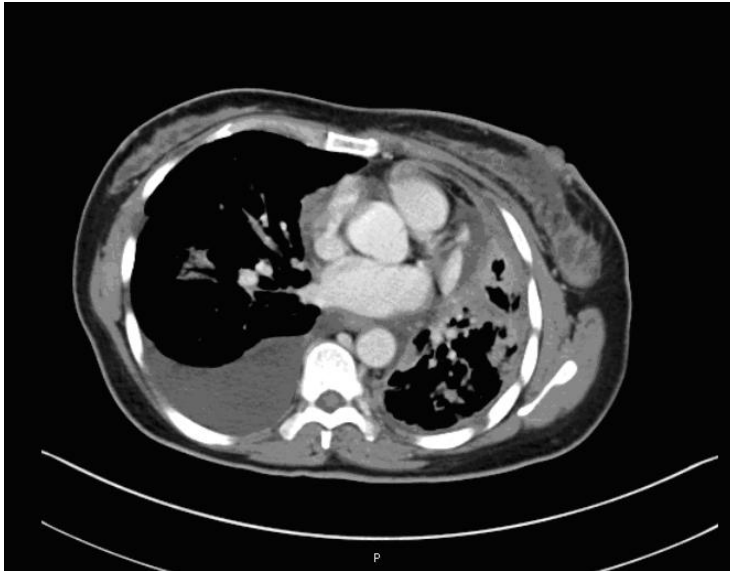
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tumors to the breast from extra mammary malignancies are rare which accounts for 1.2% to 2% of cancers in the breast<sup>[3,4]</sup>. The presence of breast mass in association with pathologically enlarged axillary lymph nodes usually triggers the working diagnosis of a locally advanced breast cancer. When this presentation is combined with a lung mass, not an uncommon presentation, the clinical scenario suggests two main possibilities. The first possibility is that the lung mass is metastatic spread from primary breast cancer and the second possibility is that the lung mass represents a second primary. The presence of a primary lung cancer metastasizing both to the breast and its ipsilateral axillary nodes is extremely rare. There are few reported cases of lung cancer with axillary lymph nodes metastases; however, none of them were associated with breast involvement<sup>[5,6]</sup>. It is less likely to be considered in the list of differential diagnosis. This study reports a case of a middle aged Saudi female with non-small cell lung carcinoma (NSCLC), and metastatic spread not only to the left breast but also to the ipsilateral axillary nodes.

### **Case Report**

A 44-years-old woman, non smoker and with no family history of cancer was presented with shortness of breath, and a productive cough with blood streaked sputum for several months.

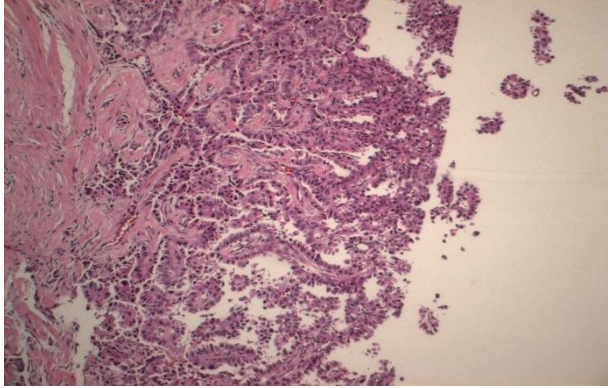
Physical examination revealed a middle aged female in mild respiratory distress. Chest examination revealed diminished air entry to left lung base. The rest of her physical examination is remarkable for an ill-defined left breast mass and a 3 cm left axillary mass, which was mobile and hard in consistency. Patient's blood work was unremarkable. The mammogram reported the left breast with evidence of skin thickening; however, no obvious masses, distortion of tissue architecture or suspicious microcalcifications to suggest the presence of malignancy. An ultrasound of the breast showed an ill-defined mass in the left periareolar region and a 2.7 cm hypoechoic left axillary node. CT scan of the chest showed a left upper lobe lung mass with associated consolidation/atelectasis of the left lower lobe. Additionally, an ill defined mass was noted in the left breast (Fig. 1 and 2). She underwent video-assisted thoracotomy with therapeutic thococentesis and biopsy from a pleural-based mass. Pathological examination showed a malignant neoplasm that was composed of glands and papillae (Fig. 3a).



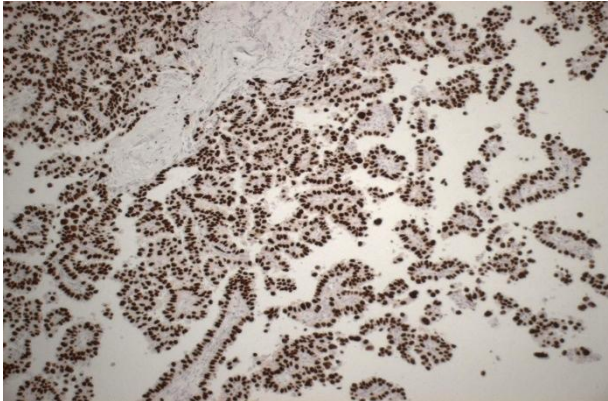
**Fig. 1.** CT mediastinal window showing ill defined left breast mass and atelectasis/consolidation to the left lung.



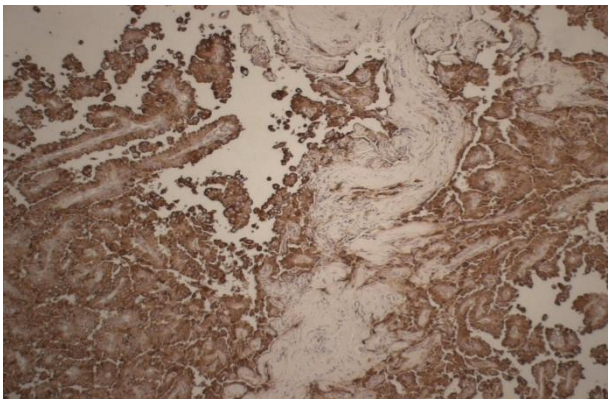
**Fig. 2.** CT coronal view showing the left upper lung mass with associated consolidation of the left lower lobe and left side pleural effusion.



**Fig. 3A.** Section from the pleural biopsy reveals a papillary neoplasm composed of cuboidal to columnar cells (Hematoxylin and Eosin stain, x 100).



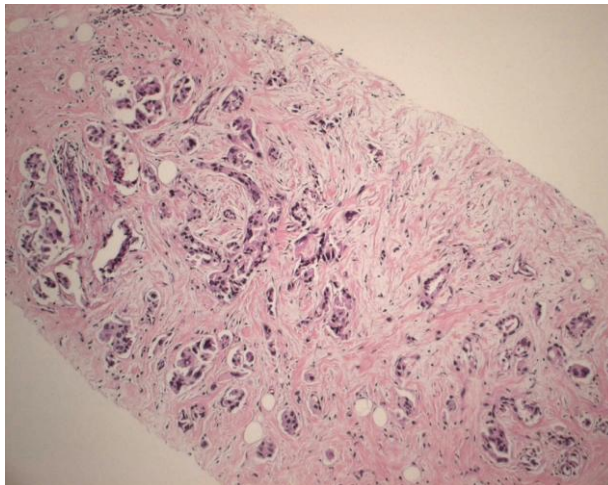
**Fig. 3B.** Immunohistochemistry stain for TTF-1 shows strong positive nuclear staining of the tumor cells.



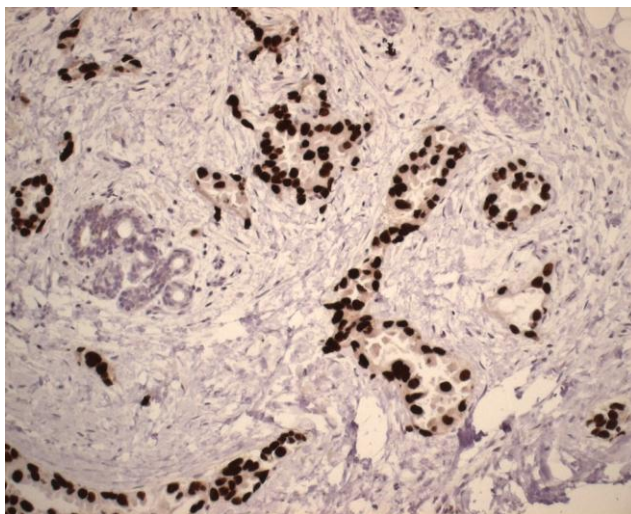
**Fig. 3C.** Immunohistochemistry stain for CEA shows positive staining of the tumor cells.

Immunohistochemistry evaluation revealed that the tumor cells were positive for CK7, TTF-1 (Fig. 3b), BerEP4, and CEA (Fig. 3c). They were negative for calretinin and CK5/6. The overall immunohistochemical findings were consistent with adenocarcinoma of the lung. Because the clinical picture was highly suggestive of metastatic breast cancer, it was decided to biopsy the left breast and the left axillary lymph node. Needle core biopsy from the left breast mass and fine needle aspiration cytology were performed. Pathological examination of the breast biopsy showed a malignant neoplasm that is composed of variable sized glands (Fig. 4a). Immunohistochemistry evaluation also revealed that the tumor cells were positive for CK7 and TTF-1 (Fig. 4b). They were negative for CK20, Thymoglobulin, ER and PR, Her-2 and CK5/6. The overall immunohistochemical findings were consistent with involvement of the left breast by metastatic adenocarcinoma consistent with primary lung origin. FNA of the left axillary lymph node showed malignant cells consistent with metastatic adenocarcinoma. The pathology was compared again with left pleural biopsy, which showed similar morphological and immunohistochemical profile.

The patient was treated with palliative chemotherapy. Five months after the initiation of chemotherapy, she was presented with seizure. She was found to have brain metastasis and died in a very short period of time.



**Fig. 4A.** Section from the breast biopsy reveals a malignant neoplasm that is composed of glands/ducts (hematoxylin and eosin, x 100).



**Fig. 4B.** Immunohistochemistry stain for TTF-1 shows strong positive nuclear staining of the tumor cells. The native mammary lobules are negative.

## Discussion

Up to 40% of newly diagnosed non-small cell lung cancer presents with metastatic disease. Major sites of metastases include liver, adrenal glands, brain, bone, kidney, and abdominal lymph nodes<sup>[1,2]</sup>. In a study by Quint *et al.* the frequencies of M1 disease at presentation was reported as 21%. Additionally, metastases to individual organs were seen in the following frequencies (expressed as a percentage of all patients): brain, 10%; bone, 7%; liver, 5%; adrenal glands, 3%; body wall, 3%; lung, 2%; spleen, 1%; abdominal lymph nodes, 1%; and axillary lymph nodes, spinal canal, and pancreas, less than 1% each<sup>[7]</sup>. The incidence of metastatic cancers to the breast is approximately 1.2-2%<sup>[8,9]</sup>. The first reported case of metastasis to the breast was in 1903 by Trevithick who reported a reticulum cell sarcoma metastasis to the breast<sup>[8]</sup>. Metastasis to the breast from other sites, though it is very rare, has been reported in the literature as case reports series<sup>[10-13]</sup>. Examples of extramammary cancers was reported with metastasis to the breast included hematopoietic, genitourinary and gastrointestinal tracts malignancies, rhabdomyosarcoma<sup>[4,14]</sup> and small cell lung cancer<sup>[15]</sup>. In adults, the most frequent types of tumors metastasizing in the breast are malignant melanoma and neuroendocrine-like tumors, especially small cell



carcinoma and carcinoid<sup>[9]</sup>. The incidence of metastatic non-small cell lung cancer to the breast is very low (< 0.5% of all metastatic disease)<sup>[3,4]</sup>. To our knowledge, none of the cases were presented with both biopsy proven breast and axillary lymph node metastases. Our case is considered extremely rare among metastatic cancers to the breast. Such a case may significantly improve our understanding of the mechanisms associated with the advancement of the metastatic processes in lung cancer.

TTF-1 immunoreactivity is a very sensitive and highly specific marker in the differential diagnosis of lung adenocarcinoma and other non-pulmonary carcinoma and highly recommended to be used in regular clinical practice for this purpose<sup>[16]</sup>. TTF-1 expressed in about 90% of bronchogenic adenocarcinoma. Apart from thyroid carcinoma, all non pulmonary adenocarcinomas classically lacked TTF-1 staining<sup>[17,18]</sup>. Yang *et al.*<sup>[18]</sup> tested TTF-1 expression in 115 invasive mammary carcinomas (91 ductal, 24 lobular type) and all of them turned to be negative. Thymoglobulin stain was negative in our case which was against thyroid carcinoma that usually shares with lung adenocarcinoma the TTF-1 expression.

Usually, the histological pattern and the clinical picture lead to the conclusive diagnosis. In this case study, it is mainly relied on the histological features and immunohistochemistry to reach this rare diagnosis.

### Conclusion

This is a case report of a middle aged Saudi lady presented with a lung mass with metastatic spread to the left lung, the breast, and its ipsilateral nodes. The pathological evaluation, including immunohistochemistry, is crucial for the correct diagnosis of the primary source. Extramammary tumors should be distinguished from the primary breast tumors as treatment and prognosis may differ significantly. This case report emphasizes the fact that the presence of breast mass with an enlarged axillary node is not synonymous with primary breast cancer. In the presence of another primary, the rare possibility of metastatic disease to the breast and axillary node should be considered because of its potential to impact the treatment plan and the patient's prognosis.

As one might expect, this presentation created a diagnostic dilemma and a clinical management challenge since treatment strategies and prognosis differ according to the primary. This case underscores the fact that the presence of metastatic axillary lymph nodes in patients with breast mass is not synonymous with breast cancer. Metastatic carcinoma to the breast from an extra mammary site usually denotes wide spread dissemination and signals poor prognosis.

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## سرطان الرئة غير ذي الخلية الصغيرة المنتشر الى الثدي والعقد اللمفاوية في الإبطين

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المستخلص. سرطان الرئة المتفاقمة في الثدي أمر نادر الحدوث. يمكن العثور على عدد قليل من التقارير التي نشرت. سرطان الرئة المنتشر في الثدي والغدد اللمفاوية في الإبطين المماثل نادرة للغاية. نحن لسنا على علم بأي تقارير عن حالات الإصابة بسرطان الرئة مع هذا الانتشار من هذا القبيل. ونحن هنا نقرر حالة غير عادية لامرأة سعودية في منتصف العمر، مصابة بسرطان الرئة من الخلايا غير الصغيرة، الذي انتشر ليس فقط إلى الثدي، ولكن أيضًا إلى العقد اللمفاوية في الجهة المماثلة. من المهم لأطباء الأورام أن يضعوا في اعتبارهم مثل هذا الورم.