

Case Report
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Non-Small Cell Lung Cancer Metastases to Breast, Colon and Skin: A Case Report

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ABSTRACT

Bronchogenic carcinoma is a leading cause of cancer mortality worldwide. Of lung cancer cases overall, 50% have metastasis at presentation, mostly to the brain, bone, liver, the adrenal glands, thoracic cavity and non-regional lymph nodes. This case report presents a female patient with three rare sites of lung cancer metastasis: breast, colon, and skin. Her initial presentation was a several-month history of a mass in the left breast and in the upper abdominal wall, dyspepsia, weight loss, and intermittent per rectal bleeding. Diagnosis of this case was difficult because of the challenge to differentiate between primary breast cancer and metastasis. However, the diagnosis was made by the interpretation of images and immunohistochemistry.

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Introduction

Bronchogenic carcinoma is one of the significant causes of cancer-associated death. About 50% of these patients have a metastatic disease on presentation, mostly to bone, contra lateral lung, liver, adrenal glands, or brain. Of malignant breast tumors, approximately 0.4% to 1.3% of cases are metastasized from various sites, including renal cell carcinoma, malignant melanoma, and ovarian, thyroid, gastrointestinal, and hematologic malignancies, and as well as lung cancer [1-4].

Several cases of primary lung cancer metastasized to the breast have been published. Gastrointestinal metastasis from primary lung cancer was found in about 0.2%–11.9% of cases at autopsy, indicating that the rate of metastasis of primary lung cancer to the gastrointestinal tract is higher than expected because most of the cases are asymptomatic. Of these cases, the small bowel is the dominant site of metastasis, and the large bowel is a very rare site. Compared with other cancers, lung cancer is the fastest to metastasize to the skin. In women with lung cancer, metastasis to the skin accounts for about 4% of cases, followed in decreasing frequency by breast cancer, colorectal malignant melanoma, and ovarian cancer [5-17].

Case History

Patient Information

This case report presents a 52-year-old female patient with breast metastasis from pulmonary adenocarcinoma, in addition to colonic and skin metastasis. The patient is a non-smoker widowed with nonsignificant past medical, surgical and family history. She was referred from Asir Central Hospital to King Fahad Medical City on October 2018 with the diagnosis of carcinoma of unknown primary.

Clinical Findings

The patient's initial presentation to the referring institution on July 2018 was a 4-month history of vague abdominal pain, dyspepsia, and weight loss. She also had intermittent episodes of rectal bleeding. One month after her initial presentation, the patient notified masses in the right abdominal wall, left breast, and left axillary lymph node.

Diagnostic Assessment

Computed tomography (CT) scans of the chest, abdomen, and pelvis done on September 2018 revealed extensive lymphadenopathy and masses in the left lower lung lobe, colon, and right abdominal wall. Biopsy from the abdominal wall mass reveals poorly differentiated adenocarcinoma (Figure 1). On October 2018 was first evaluation in the outpatient clinic, a plan was made for a positron emission tomography (PET) CT scan

(Figure 2), mammography, and left breast biopsy. Two days after scheduling the PET CT, the patient was admitted to the hospital with symptoms and signs of pulmonary embolism, which was subsequently confirmed by the pulmonary angiography scan. The patient was started on therapeutic low-molecular-weight heparin (LMH), which led to fresh rectal bleeding. In response, the LMH was held while the patient received 4 units of red blood cell and intravenous tranexamic acid 5 days later the LMH was resumed after she stabilized.

Upper and lower gastrointestinal endoscopy revealed a sigmoid mass semi-obstructing the lumen of the colon. Biopsy and pathology also confirmed adenocarcinoma (Figure 1) of lung origin. The PET CT scan on October 29 2018 revealed widespread

metastatic disease, which suggested either lung or breast as the primary cancer, with the possibility of double primary cancer (lung and breast) (Figure 2). Mammography on October 30.2018 revealed a left breast mass, which was biopsied. In the upper outer quadrant, axillary nodes showed no microcalcification, and the breast mass pathology was first reported as invasive ductal carcinoma. However, subsequent immunohistochemical analysis showed pathology was consistent with metastatic adenocarcinoma of lung origin. Tumor marker data were as follows: cancer antigen (CA) 15-3, 274.6 U/mL; CA 125, 258.6 U/mL; CA 19-9, 747.7 U/mL; and carcinoembryonic antigen, 13.9 ng/mL. Next generation sequencing results were negative for ALK, BRAF, EGFR, ERBB2, K-RAS, MAP2KI, MET, N-RAS, PIK3CA, ROS1, and TP53.

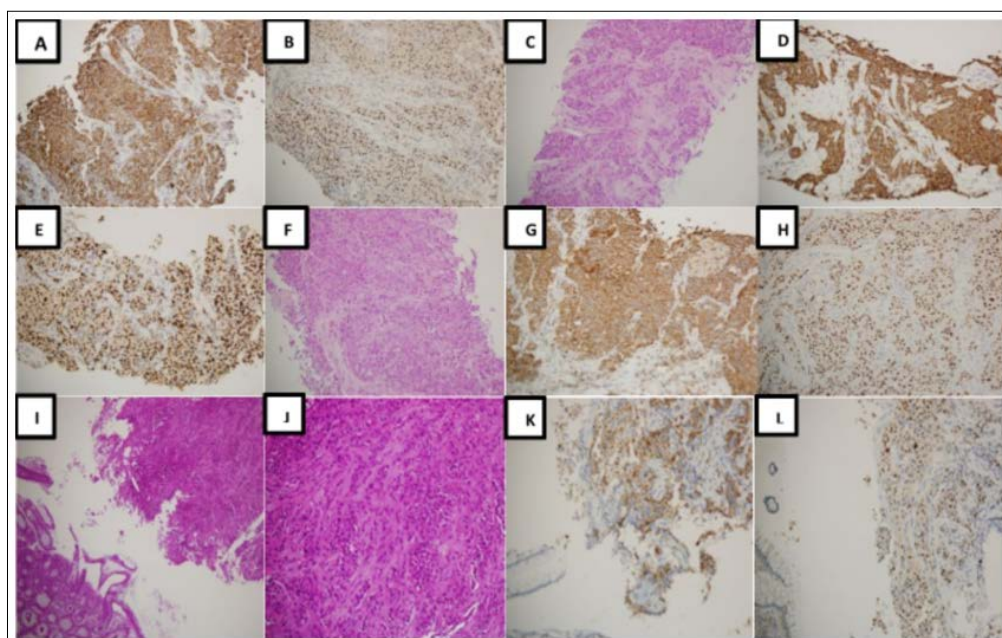


Figure 1: Tissue biopsies for the case patient: A) abdominal wall napsin A immune stain; B) abdominal wall TTF1; C) left axilla hematoxylin and eosin (H&E) stain; D) left axilla napsin A; E) left axilla TTF1; F) left breast H&E stain; G) left breast napsin A; H) left breast TTF1; I) sigmoid mass H&E stain 1; J) sigmoid mass H&E hyperplastic ; K) sigmoid mass breast napsin A; L) sigmoid mass TTF1.

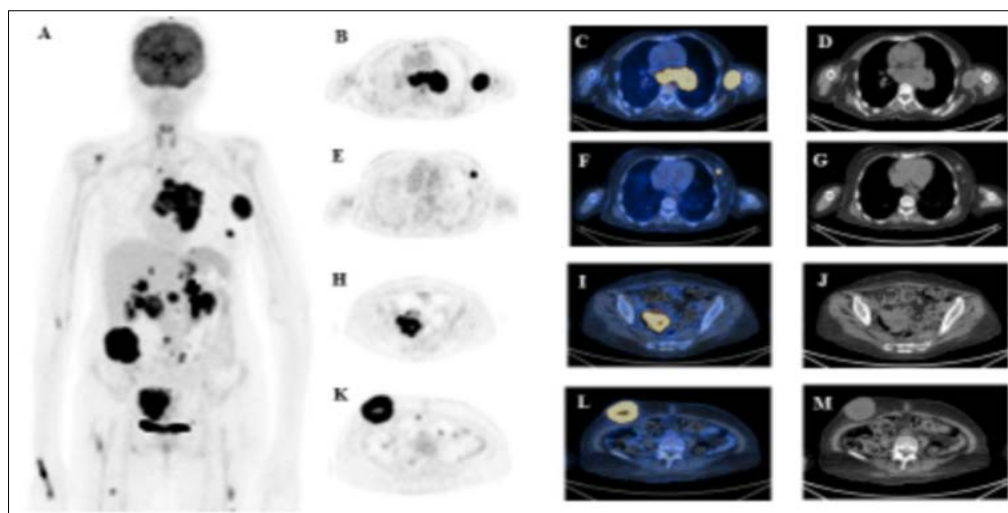


Figure 2: Whole body scan (F18-fluorodeoxyglucose, maximum intensity projection mode) image demonstrates intensely hypometabolic primary left hilar lung mass (A), which extends medially toward the posterior mediastinum (B, C, D). The mass metastasized to the left breast (E, F, G), cecum (H, I, K) and right anterior abdominal wall (K, L, M).

therapeutic Intervention, Follow-up and Outcomes

The patient was started on the platinum and pemetrexed protocol, which was continued as treatment after the next generation sequencing results were available. The patient received 6 treatment cycles of pemetrexed and carboplatin followed by maintenance pemetrexed lasted on August 2019, with good tolerability and improvement in her symptoms and signs, although her baseline performance status was poor at Eastern Cooperative Oncology Group (ECOG) performance status grade 3. After completion of 6 cycles, the patient was ambulatory with no pain; her ECOG performance status was grade 1; and interim PET CT on December 14, 2018 revealed partial radiologic response. The current management plan is to continue her chemotherapy holiday.

Discussion

Distinguishing breast metastasis from primary mammary adenocarcinoma based on mammographic findings may be very difficult because of the wide range of manifestations of metastatic lesions on imaging. Metastasis to the breast can mimic a primary malignancy or even a benign breast tumor. Mammography in the case of the metastatic disease most commonly shows a well-defined rounded mass; however, multiple well-circumscribed lesions with smooth margins may also be present. Calcification is rare in breast metastases, which is a finding compatible with this case report. The distinction between metastases from lung adenocarcinoma and primary mammary adenocarcinoma may cause a significant diagnostic dilemma.

As such, the contribution of immunohistochemistry is crucial for a correct diagnosis. For example, TTF1 is a useful marker of pulmonary adenocarcinoma with a reported frequency of 68%–80%; however, no stains have been positively detected in breast carcinoma, except a single case in the literature [18]. A detailed examination of the breast mass and specific immunohistochemical analysis is necessary to distinguish primary breast cancer from metastasis to the breast, which is critical to avoid unnecessary mastectomy and to provide appropriate systemic treatment. This point must absolutely be emphasized because the recommended therapy differs between primary breast cancer and metastasis to the breast with considerably varying outcomes as seen in this case. The patient's first diagnosis was primary breast invasive ductal carcinoma; however, after appropriate immunohistochemical analysis, this diagnosis was corrected to metastatic adenocarcinoma of lung origin.

Rossi et al. stated that gastrointestinal metastasis from lung cancer has been underdiagnosed in living patients because it is often seen as part of a generalized metastatic disease or gastrointestinal lesions considered to be an adverse effect of chemotherapy, such as ulcers, enteritis, or colitis [19]. Metastatic small bowel tumors are likely to present with serious clinical complications such as perforation, blockage, or bleeding. Therefore, some clinical cases of small intestine metastasis from lung cancer have been reported, whereas clinical cases of colon metastases have been reported rarely.

For preoperative diagnosis, it is difficult to diagnose the origin of a gastrointestinal tumor correctly by CT scan, and also on endoscopy, because lung cancer involving the gastrointestinal tract has no particular features, thus mimicking a primary gastrointestinal tumor. Therefore, the histologic examination is the only means to diagnose metastatic tumors to the gastrointestinal tract. Immunostaining with TTF-1, CDX2, cytokeratin (CK) 7, and CK20 is also supportive of distinguishing primary gastrointestinal carcinoma from metastasis of lung carcinoma [19]. For the current case patient, if preoperative immunohistochemical examination had

been performed, the correct diagnosis may have been made earlier. The PET CT scan may also play an important role in the early diagnosis of lung cancer metastasis to the colon. Gastrointestinal symptoms should be observed in lung cancer patients to avoid underdiagnosis or over-searching for colon metastasis from lung cancer and to support early detection by these methods.

All histologic types of lung cancer may develop metastases in the skin. In literature, various data are reported related to the frequency of skin metastases of different histologic types of lung cancer. Some studies demonstrate that adenocarcinoma is the most common type of lung cancer that develops skin metastases. As observed in this current case, most tumor markers were elevated, which was not relevant for diagnosis and aligns with the fact that the tumor marker is not used as a diagnostic tool [20].

Conclusions

Breast metastasis for extramammary sites is rare and difficult to diagnose by pathology alone. Immunohistochemical analysis is necessary to differentiate metastasis from primary breast cancer. Colonic metastasis from a lung origin is very rare, but it may be underdiagnosed. Although the prognosis is very poor, some cases may benefit from early detection of the primary site. Skin metastasis may be the first presentation of lung cancer, so a detailed history and examination with good pathologic and immunohistochemical analysis can guide the clinicians to an accurate diagnosis. Tumor markers are misleading in some cases if they are used to provide diagnosis guidance.

Declaration of Conflict of Interest: The authors report no conflicts of interest.

Ethical Approval: Consent was given by the patient.

Acknowledgments: For patient and her family

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