Lung Adenocarcinoma Metastasis to the Male Breast: A Case Report

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Summary: We report the case of a 60-year-old male patient who was diagnosed with metastasis from primary lung cancer to the breast. The patient presented with a mass in the right breast. Mammography, ultrasound, and magnetic-resonance imaging each suggested primary breast cancer. A core-needle biopsy of the right breast mass indicated poorly differentiated adenocarcinoma. A basic chest X-ray showed a shadow in the left upper lung. Thoraco-abdominal computed tomography revealed a mass with a diameter of 90 mm in the left superior region, the shape of which was indicative of primary lung cancer. A lung biopsy confirmed poorly differentiated adenocarcinoma. We diagnosed primary lung cancer with metastases to the bone, brain and right breast (cT2N3M1, stage IV) by imaging and histopathology. He was administered carboplatin (area under the curve 6 mg/ml) and paclitaxel (200 mg/m²) tri-weekly, and underwent gamma-knife treatment for the brain metastasis. The treatments reduced the primary tumor and the metastases. However, after completion of the fifth treatment cycle, he developed disseminated intravascular coagulation from septic shock, and died on the eleventh day after completing the fifth cycle of treatment. Although metastasis to the mammary gland is uncommon, especially among males, metastasis to the mammary gland should be considered when a mammary mass does not exhibit the typical characteristics of breast cancer. A correct diagnosis of metastasis to the mammary gland from lung cancer makes it possible to select the most appropriate treatment method.

Key words: lung cancer, male breast, metastasis

INTRODUCTION

The mammary gland is a rare site for the development of metastatic tumors, particularly in males. Here we report a case of a 60-year-old male patient who presented a mass in the right breast that had been detected through self-examination. After further detailed examinations, the patient was diagnosed with primary lung cancer that had metastasized to the right mammary gland.

CASE REPORT

A 60-year-old male presented with a mass in the right breast. He had a history of high blood pressure, bronchiectasis, and chronic renal failure due to chronic...
glomerulonephritis. He smoked 60 cigarettes a day and had a Brinkman Index (defined as the number of cigarettes smoked per day multiplied by the number of smoking years) of 1,500. The family medical history was unremarkable. On a routine out-patient visit, he complained of coughs, chills, and night sweats, and reported a mass in his right breast. He then underwent mammography, ultrasound imaging, and magnetic resonance imaging (MRI), which indicated the possibility of primary breast cancer. A core-needle biopsy of the lesion in the right breast indicated poorly differentiated adenocarcinoma. Chest X-ray revealed a shadow in the left upper lung, suggesting the possibility of lung cancer. He was subsequently admitted for further examinations.

On admission, he was 170 cm in height, 71.1 kg in weight, with a blood pressure of 145/89 mmHg, a heart rate of 100/min, body temperature of 36.6 °C, and a blood oxygen saturation (SpO₂) of 99%. His consciousness level was clear. A left supraclavicular lymph node was palpable. A red, swollen, movable tumor mass with a diameter of 3×4 cm was detected directly below the areola of the right breast (Fig. 1). He did not report any pain, and no other abnormality was observed in other parts of the body, including chest and abdominal regions. The patient had a serum creatinine level of 1.7 mg/dl, which indicated renal dysfunction due to chronic renal failure. His white blood-cell count was 16,000/μl and C-reactive protein (CRP) level was 14.9 mg/ml, indicating an elevated level of inflammation. His blood hemoglobin level was 8.4 g/dl, indicating anemia. Increased levels of tumor markers, including carcinoembryonic antigen (CEA; 34.7 ng/ml), cytokeratin 19 fragment (CYFRA; 39 ng/ml), and squamous cell carcinoma (SCC; 1.8 ng/ml) were also observed. Carbohydrate antigen15-3 (CA15-3) and Nation Cancer Center-Stomach-439 (NCC-ST-439) were within normal ranges.

A chest X-ray revealed a shadow in the left upper lobe (Fig. 2). Mammography showed a shadow (30×28 mm) with an irregular border in the right breast (Fig. 3). Breast ultrasound scanning detected an irregular-shaped hypoechoic mass (23×23×16 mm) with an uneven internal echo pattern below the right nipple, which had a rich blood flow suggesting malignancy. Breast MRI using the short TI inversion recovery (STIR) sequence produced a relatively uniform high signal, T1-weighted imaging (T1WI) showed similar signal intensity to the mammary glands, and diffusion-weighted imaging (DWI) gave a uniform high signal with strong intensity. A dynamic tumor was seen with a diameter of 30 mm, a clear border, and a slow- and pale-staining interior (Fig. 4). The patient’s MRI pattern thus differed from the typical pattern seen in breast cancer. Thoraco-abdominal computed tomography (CT) scanning revealed a shadow with a diameter of 90 mm between the origin of the left upper lobe and the apical portion of the left lung; its shape suggested primary lung cancer (Fig. 5). Enlargement in multiple lymph nodes was confirmed in the left clavicular and the hilar lymph nodes. CT scanning also revealed a tumor (30×40 mm) with an irregular border in the right breast (Fig. 5). No clear abnormalities were detected in the abdominal area, except for marked atrophy in the left kidney. A brain CT scan revealed a 12 mm-diameter lesion in the left frontal lobe; the lesion

Fig. 1. Physical findings of the chest. A palpable lesion 3×4 cm in diameter with red swelling is seen directly below the areola of the right breast.

Fig. 2. Basic chest X-ray. A shadow can be seen in the left upper lung.
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contained a fluid–fluid level, and the surrounding area showed edema formation. These findings suggested brain metastasis. Bone scintigraphy showed accumulation in the seventh through eleventh thoracic vertebra, which indicated bone metastasis. Core-needle biopsy of the tumor mass in the mammary glands showed many atypical large round cells with irregular nuclei, and a diagnosis of poorly differentiated adenocarcinoma was confirmed by hematoxylin and eosin (HE)-staining (Fig. 6). The tumor was estrogen-receptor (ER) negative (−), progesterone-receptor (PgR) negative (−), and human epidermal growth factor (HER2) receptor negative (−).

Although male breast cancer was initially suspected, the examination results did not rule out the possibility that primary lung cancer had metastasized to the mammary glands. In order to establish a definitive diagnosis, transbronchial lung biopsy (TBLB) was performed after the patient had been admitted to hospital. The results showed that the superior lobe bronchus exhibited overall marked reddening and swelling, and HE-staining showed that atypical large round cells were growing while forming a papillary or glandular structure. Thus, a diagnosis of poorly differentiated adenocarcinoma was established, and the findings were very similar to the breast core-needle biopsy (Fig. 6). Thyroid transcription factor-1 (TTF-1),

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![Fig. 3. Mammography. A shadow (30×28 mm) with an irregular boundary can be seen in the right E section.](image)

![Fig. 4. Breast MRI (dynamic view). A well-defined lesion (30 mm in diameter) can be seen with a slow-and pale-stained interior and clear boundary.](image)

![Fig. 5. Thoraco-abdominal CT scan. A shadow (90 mm in diameter) can be seen between the origin of the left upper lobe and the apical portion of the left lung. CT scanning also shows the lesion (30×40 mm) with an irregular border in the right breast.](image)
Napsin-A, surfactant protein-A (SP-A), ER, PgR and gross cystic disease fluid protein-15 (G-CDFP15) immunostainings were used to determine whether the lung mass was primary lung cancer or metastasis from cancer in other organs. However, all showed negative expression in the lung or breast tumor cells. Although it was not a typical case of primary lung cancer metastasized to the right mammary glands on immunohistochemical findings, we diagnosed the breast lesion as lung adenocarcinoma metastasis to the breast (cT2N3M1, stage IV), because the lung tumor suggested primary lung cancer by thoraco-abdominal CT; the MRI of the breast lesion was different from the typical pattern of breast cancer; the finding of TBLB in HE-staining was very similar to that of the breast biopsy; and G-CDFP15 was negative in the lung tumor and in the breast lesion.

In accordance with the guidelines for treating lung cancer, we selected a regimen of carboplatin (area under the curve [AUC] 6 mg/ml) and paclitaxel (200 mg/m²) tri-weekly (hereafter referred to as CBDCA+PTX). However, after being admitted to hospital, the patient’s speech became slurred, and treatment for the brain metastasis was prioritized. Upon completion of the first cycle of CBDCA+PTX, the patient was treated by internal decompression of the brain, and gamma (γ)-knife treatment was performed at another hospital. He subsequently exhibited symptoms that typically accompany cerebral edema, including vomiting, slurred speech, and facial nerve paralysis, although these gradually lessened. He continued CBDCA+PTX treatment as an out-patient. After completion of the fifth cycle of CBDCA+PTX, he experienced general malaise and loss in appetite. At 5 days later, he was admitted to our...
hospital complaining of respiratory discomfort at night. At the time of admission, he was in a state of shock with a heart rate of 130 /min, a systolic arterial pressure of 90 mmHg, and SpO_2 of around 80%. A chest X-ray and CT scan indicated the possibility of bacterial pneumonia in the left and right upper lung zones. Chemotherapy reduced in diameter of the primary tumor in the lung by 41% (to 80×60 mm). The metastatic tumors in the mammary glands and the lymph node below the left collar bone had shrunk to negligible size. CBDCA+PTX treatment thus yielded a partial response (PR) and was judged to be effective. However, laboratory data showed pancytopenia, an elevated CRP level, and worsening renal dysfunction; we therefore concluded that the patient had developed severe infection. The patient experienced septic shock and was treated by massive transfusion and administration of catecholamine. Despite additional treatments for septic shock and disseminated intravascular coagulation (DIC), and mechanical ventilation, the patient’s general condition did not improve, and he died on the eleventh day after completion of the fifth cycle of CBDCA+PTX.

**DISCUSSION**

Malignant tumors metastasizing to the mammary gland comprise only 0.2-1.3% of all clinical cases and 2-7% of autopsy cases [1]. Most cases of metastasis to the mammary gland are caused by contralateral breast cancer [2]. Other causes include blood disorders, malignant melanoma, and cancer in the lung, ovaries, prostate, kidney, or stomach [3]. They are mainly observed among females, and are extremely rare among males [2]. To our knowledge, only 7 cases of male breast metastasis from lung cancer have been reported.
to date (Table 1) [4-10]. Their average age was 61.1 years, and included 6 cases of non-small cell lung carcinoma (NSCLC) and 1 case of small cell lung carcinoma (SCLC).

Previous studies have shown that metastasis to the breast mass can be hematogenous or lymphogenous [11]. The current case showed metastasis to the brain and bone, suggesting that primary lung cancer had spread by hematogenous metastasis to the breast, and by direct lymphogenous metastasis to the lymph node below the clavicular and the hilar area.

During initial consultation, the patient should be investigated closely to determine whether they have any pre-established malignant tumor. Metastasis in the mammary gland typically comprises a single tumor without pain or nipple discharge, and tends to be located relatively close to the surface [12]. The patient in the present case had few mammary glands and exhibited redness and swelling, obscuring the location of the tumor. In addition, mammography of a metastatic tumor in the mammary gland normally reveals a circular shadow with a clear or unclear boundary, and does not show spiculation or calcification [13,14]. In our patient, mammography showed a tumor shadow with an unclear boundary and no spiculation or calcification. Metastasis in the mammary gland has also been reported to be hypoechoic without acoustic shadows on ultrasound images [15,16], but ultrasound in our patient showed a hypoechoic tumor with an irregular shape and an uneven internal echo pattern. Furthermore, MRI of the breast showed a dynamic tumor mass with a well-defined boundary, and a slow- and pale-staining interior. This MRI pattern differed from that typically observed in cases of primary breast cancer, and suggested a metastatic mammary gland tumor. However, standard MRI protocols for detecting metastatic mammary gland tumors have not yet been established. The histological findings from the HE-stained breast core-needle biopsy showed significant atypical large tumor cell growth, suggesting poorly differentiated adenocarcinoma, and these findings were very similar to those from the TBLB sample. Differential diagnosis between primary breast cancer and metastasis to the mammary gland is often difficult when the histological form of the lesion in the mammary gland, or the site of metastasis, is confirmed as adenocarcinoma, as in the present case. Such tumors are often diagnosed as primary breast cancers rather than metastasis from adenocarcinoma of the lung. To determine whether the lesions in the lung and the breast were primary or metastatic, the biomarker of TTF-1, Napsin-A, SP-A and G-CDFP15 was used. The TTF-1, Napsin-A and SP-A is considered to be a reliable marker for primary adenocarcinoma of the lung, and G-CDFP15 is a marker for breast metastasis [17-21]. However, all showed negative expression in the lung tumor and in the breast lesion cells. In large cell carcinoma of the lung, it was reported that TTF-1 was positive in 50%, SP-A in 25%, and Napsin-A in 0% [17,22]. In our case, large round cells were seen on HE-staining in the specimens of the lung and the breast biopsy, suggesting this case had the character of large cell carcinoma. This could be the reason for the TTF-1, SP-A and Napsin-A being negative. Although this case was not a typical case of primary lung cancer metastasized to the right breast, on immunohistochemical findings, we finally diagnosed this case as lung cancer metastasis to the right breast, because the lung tumor suggested primary lung cancer by thoraco-abdominal CT; the MRI of the breast lesion was different from the typical pattern of breast cancer; the finding of TBLB in HE-staining was very similar to that of the breast biopsy; and G-CDFP15 was negative in the lung tumor and in the breast lesion.

The NSCLC Meta Analyses Collaborative Group states that chemotherapy in a supportive care setting demonstrates conclusively that chemotherapy improves overall survival in all patients with advanced NSCLC. The clinical guidelines set by the Japan Lung Cancer Society also suggest chemotherapy for cases with a level-A recommendation [23,24]. A combination of platinating agents and third-generation anticancer drugs is recommended as the treatment regimen. When there are concerns about the toxicity of the combined treatment, administration of third-generation basic anticancer drugs is recommended [24]. Our patient was relatively young at 60 years of age, and in good general health with a high performance status (PS0); he was therefore treated with a combination of platinating agents and PTX. He exhibited mild renal failure due to chronic renal dysfunction, so we selected CBDCA, which causes fewer renal disorders than cisplatin (CDDP), for the platinating agent [25]. γ-knife treatment for brain metastasis reduced the related symptoms. PR was observed with chemotherapy, and the treatment for primary lung cancer was effective. Although great care was taken while administering chemotherapy, the patient presented worsening renal dysfunction, severe infection, and septic shock, and he died after completion of the fifth cycle of treatment. Cases of metastasis to the mammary gland often have a poor prognosis, due to late diagnosis [1], as in the present case.

Our patient illustrates that the possibility of metas-
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Metastasis from primary lung cancer should not be ruled out for a lesion that does not show the typical characteristics of breast cancer. It is important to determine whether the tumor in the mammary gland is metastatic, to avoid unnecessary surgical procedures such as mastectomy, and to select a systemic treatment for the lung cancer.

REFERENCES