A Patient with Lung Squamous Cell Carcinoma Presenting with Severe Cardiac Dysfunction Similar to Dilated Cardiomyopathy with Left Bundle Branch Block Induced by Myocardial Metastasis

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Abstract

A patient with severe cardiac dysfunction similar to dilated cardiomyopathy expired because of lung squamous cell carcinoma. He was admitted with respiratory failure and was diagnosed with congestive heart failure due to dilated cardiomyopathy based on the chest X-ray, electrocardiography, echocardiography, and coronary angiography. Chest computed tomography showed a mass shadow in the right lower lobe, and the patient was diagnosed with lung squamous cell carcinoma by bronchoscopy. The patient expired, and the autopsy revealed that a myocardial metastasis disrupted the cardiac-conduction system without dilated cardiomyopathy in myocytes. Left bundle branch block caused by myocardial metastasis presumably induced left cardiac dysfunction.

Key words: lung cancer, squamous cell carcinoma, myocardial metastasis, left bundle branch block, left cardiac dysfunction


Introduction

Cardiac metastasis is found at autopsy in up to 10% of patients with known malignancies (1). Lung cancer is reported to be the most common malignancy that causes cardiac metastasis followed by breast cancer and hematologic malignancies (1-6). In some cases, cardiac metastases, specifically epicardial and myocardial metastases, may result in a variety of life-threatening complications including cardiac conduction system disruption such as complete atrioventricular (AV) block or ventricular fibrillation. Epicardial and myocardial metastases exhibit ST and T-wave abnormalities on electrocardiography as well as elevated cardiac biomarkers such as acute coronary syndromes without coronary artery involvement. However, the pathophysiologic mechanisms of this phenomenon are not clear. We herein report a rare case of severe cardiac dysfunction similar to dilated cardiomyopathy, possibly due to left bundle branch block (LBBB) induced by myocardial metastasis, as a result of lung squamous cell carcinoma.

Case Report

A 69-year-old man visited our emergency room complaining of symptoms leading to the gradual development of dyspnea. Three months before the visit, he reported intermittent left chest pain. One week before, he experienced cough and dyspnea that gradually worsened. On the day of admission, he woke up with severe dyspnea before dawn and was taken to our hospital by ambulance.

The patient had a history of pneumothorax at 50 years of

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Computed tomography (CT) showed an enhanced mass 7 cm in diameter in the right lower lobe (Fig. 2), multiple enhanced nodules in both lungs, and right hilar lymphadenopathy. There was no evidence of pulmonary embolism. Moreover, thoracentesis revealed no evidence of malignancy. The patient’s respiratory failure improved as a result of the treatment for congestive heart failure (Fig. 3), and his oxygen saturation was almost 99% in room air condition. He was discharged on day 11 without the induction of home oxygen therapy. We did not see any difference in the electrocardiography which was taken after the improvement of congestion (data not shown).

Bronchoscopy was performed two weeks after discharge, and the results of the aspiration cytology from the S6 region were consistent with squamous cell carcinoma (Class 3b). No bone metastasis was detected by bone scintigraphy. However, two brain metastatic regions were detected by brain enhanced magnetic resonance imaging (MRI). The blood test revealed elevated serum cytokeratin 19 fragment (CYFRA) (69.8 ng/mL). Finally, we diagnosed the patient with lung squamous cell carcinoma with pleural effusion, lung metastasis and brain metastasis, cT4N1M1b stage 4. His performance status was 2 because of the dyspnea. Chemotherapy was not considered because of the patient’s poor performance status and left ventricular dysfunction. The patient’s respiratory failure worsened rapidly due to the lung metastasis, pleural effusion and carcinomatous lymphangiosis. The patient expired one month after his diagnosis.

The autopsy examination revealed poorly differentiated squamous cell carcinoma (6.2×6.3×11 cm) in the lower lobe of the right lung as well as metastatic regions in both lungs, the thoracic wall, heart (Fig. 4A, B), mediastinum, diaphragm, small intestine, dura mater, brain and lymph nodes. Interestingly, there was no pathological evidence of varying myocyte size or interstitial fibrosis indicative of dilated cardiomyopathy (Fig. 4C, D) or myocardial ischemia. However, metastatic tumors up to 0.6 cm in diameter were found in the interventricular septum, thus suggesting the metastatic

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**Table. Laboratory Data on Admission**

<table>
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<td>TSH</td>
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<tr>
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<td>BUN</td>
<td>NTproBNP</td>
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<td>Cr</td>
<td>TroponinT</td>
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<td>T-Bil</td>
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<tr>
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<td>UI/L</td>
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<td>ALT</td>
<td>Arterial blood gas analysis (FiO\textsubscript{2} 1.0)</td>
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<td>HbA1c</td>
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<td>mg/dL</td>
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</tbody>
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age and arteriosclerosis obliterans at 65 years of age, for which he had undergone surgical repair with a synthetic blood vessel. Regarding medications, he was taking cilostazol (200 mg), warfarin (2 mg), rosuvastatin (2.5 mg), and omeprazole (20 mg) daily. He smoked 30 cigarettes per day for 46 years and had no family history of malignancy.

Upon admission, the patient’s blood pressure was 146/87 mmHg, heart rate 129 beats/min, respiratory rate 25 breaths/min and oxygen saturation 90% on 10 L/min oxygen administration with a reservoir bag mask. On the physical examination, his lung sound was weakened on the right side and coarse crackles were audible on the right lower lung. The third and fourth heart sounds were also audible. The blood tests showed slightly elevated aspartate aminotransferase (AST), lactate dehydrogenase (LDH), creatine kinase (CK) and CK-MB isozyme levels; and the N-terminal pro-brain natriuretic peptide (NT-proBNP) level was 5,578 pg/mL. The arterial blood gas analysis showed severe hypoxemic respiratory failure. Bilateral pleural effusion and coarse crackles were audible on the right lower lung. His performance status was 2 because of the dyspnea.

The patient’s respiratory failure worsened rapidly due to the lung metastasis and brain metastasis, cT4N1M1b stage 4. His performance status was 2 because of the dyspnea. Chemotherapy was not considered because of the patient’s poor performance status and left ventricular dysfunction. The patient’s respiratory failure worsened rapidly due to the lung metastasis, pleural effusion and carcinomatous lymphangiosis. The patient expired one month after his diagnosis.
Discussion

We experienced a case of severe cardiac dysfunction in a 69-year-old man who expired due to lung squamous cell carcinoma. An autopsy examination showed myocardial metastasis in the intraventricular septum disrupted the cardiac conduction system, presumably causing observed cardiac dysfunction.

Myocardial metastasis is the second most common site of cardiac metastases and results in a variety of life-threatening complications including lethal arrhythmias due to the disruption of the cardiac conduction system. Cardiac dysfunction, such as acute coronary syndrome, can also be observed if the myocardium is replaced by tumor cells (1). In this case, the autopsy examination did not show myocyte degeneration, interstitial fibrosis or direct replacement of the myocar-
dium with tumor cells but revealed disruption of the cardiac conduction system due to myocardial metastasis. To our knowledge, this is the first case report of severe cardiac dysfunction similar to dilated cardiomyopathy presumably caused by LBBB induced by myocardial metastasis.

The results of coronary angiography and autopsy showed no evidence indicating myocardial ischemia or dilated cardiomyopathy. In the previous electrocardiography and echocardiography performed 4 years before admission, LBBB and cardiac dysfunction were not documented (Fig. 1D), suggesting that LBBB due to cardiac metastasis triggered the cardiac dysfunction. Recent clinical and pre-clinical studies showed evidence that LBBB itself induces cardiac dysfunction independently (termed LBBB-induced cardiomyopathy) (7). The pathophysiologic mechanisms of LBBB-induced cardiomyopathy are still not clear, however, LBBB-induced cardiomyopathy may have existed in this patient. Therefore, we speculate that the cardiac metastasis caused LBBB and LBBB-induced cardiomyopathy resulting in the severe cardiac dysfunction.

In this patient, the diameter of myocardial metastasis nodule was 6 mm in the autopsy examination. Hence, a metastatic nodule 2 to 3 mm in diameter and LBBB may have existed at least one year prior to admission [based on the tumor doubling time of lung cancer (60-220 days)] (8). Moreover, it is possible that LBBB-induced cardiomyopathy started forming a few years prior to admission, but it is difficult to accurately conclude the date of the onset from the data we obtained. We speculate that the cardiac metastasis or LBBB formed and progressed over a period of a few years, and resulted in symptomatic cardiac dysfunction one month prior to admission. Other factors may have attributed to the cardiac dysfunction, although we could not confirm them.

Cardiac resynchronization therapy (CRT) is typically the treatment for severe cardiac dysfunction with dyssynchrony (9). Moreover, LBBB-induced cardiomyopathy is thought to be reversible, and CRT is reported to resolve LBBB-induced cardiomyopathy (7). However, CRT was not considered in this case due to the patient’s poor prognosis with advanced lung cancer.

After the initial treatment, we saw improvement of the respiratory failure and heart enlargement in the chest X-ray (Fig. 3) despite no differences in the electrocardiogram between pre- and post-treatment of heart failure. Unfortunately, we did not perform a follow-up echocardiography after treatment of the heart failure, which was the major limitation of this report.

The incidence of cardiac metastasis is increasing as a result of advances in chemotherapy and radiotherapy (10).
However, in most cases cardiac metastasis is only diagnosed at autopsy. Several recent reports demonstrate the utility of imaging studies such as cardiac MRI, CT and $^{18}$F-fluorodeoxyglucose positron emission tomography/CT (FDG-PET/CT) to detect cardiac metastasis (11-14). However, we were unable to perform any of these tests in the present case. These imaging studies may have revealed the cardiac metastasis or the presence or absence of dilated cardiomyopathy.

Sato et al. (15) reported a case in which FDG-PET/CT was invaluable for the diagnosis of cardiac metastasis; moreover, chemotherapy improved the cardiac tumor and AV block. In the present case, we did not administer chemotherapy because of the patient’s performance status and left ventricular dysfunction. But chemotherapy may have improved the cardiac dysfunction caused by myocardial metastasis thereby positively affecting his performance status.

In summary, we admitted a patient with lung squamous cell carcinoma presenting with severe cardiac dysfunction with LBBB induced by myocardial metastasis. This case highlights the importance of examining cardiac metastasis in cancer patients who have cardiac dysfunction. Furthermore, treatment with chemotherapy should be considered in such cases.

The authors state that they have no Conflict of Interest (COI).

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References