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Takotsubo Cardiomyopathy Developed After Two-stage Surgery for Double Primary Lung Cancer

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Abstract. *Takotsubo cardiomyopathy (TC) is a syndrome characterized by transient local systolic dysfunction of the left ventricle with no evidence of coronary artery disease or acute plaque rupture. We present the case of 71-year-old woman who developed TC after two-stage surgery for double primary lung cancer. On computed tomography, lung nodules were identified in the left upper and right middle lobes. Based on the diagnosis of double primary lung cancer, we performed two-stage surgery (left upper lobectomy followed by right middle lobectomy). One day after the second surgery, respiratory failure developed. Electrocardiography showed ST segment elevation, serum troponin levels were elevated, and chest x-ray showed acute pulmonary edema. Cardiac catheterization showed no coronary artery disease and apical akinesia. Based on these findings, we diagnosed TC and the patient recovered with supportive treatment.*

Takotsubo cardiomyopathy (TC) is a syndrome characterized by transient local systolic dysfunction of the left ventricle with no evidence of coronary artery disease or acute plaque rupture (1). TC is associated with physical or emotional stress, and more common in women than men (2). Most patients with TC recover with supportive treatment, but the risk of severe complications in TC is similar to that in acute coronary syndrome (2). Therefore, early detection and optimum treatment are important.

In the present report, we describe a case who developed TC after two-stage surgery for double primary lung cancer with a literature review.

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Case Report

A 71-year-old woman visited our Department for diagnosis and treatment of tumor at the right middle lobe (RML). The chest radiographs showed a nodular shadow in the RML field. Computed tomography (CT) showed 18 mm and 7 mm nodular shadows in the RML (Figure 1A and B), and a 10 mm nodular shadow in the left upper lobe (LUL; Figure 1C). Positron-emission tomography/CT (PET/CT) showed mild and avid uptake of fluorodeoxyglucose in tumors of the RML [maximum standardized uptake value (SUV_{max})=1.50] and LUL (SUV_{max}=8.49; Figure 1D). Additionally, a lymph node at the left hilum showed avid uptake of fluorodeoxyglucose (SUV_{max}=7.16) on PET/CT (Figure 1D). Thus, we suspected the nodule at LUL to be the primary cancer (cT1bN1M0, cStage IIB) and the nodules at RML to be secondary primary cancer (cT3N0M0, cStage IIB) or metastatic tumors from the tumor of the LUL.

In our treatment plan, left upper lobectomy was to be performed first, and surgery or radiation was planned for the nodules of the RML. The patient underwent left upper lobectomy and the clinical course after surgery was very good. The tumor size was 18×14×16 mm in size and diagnosed as adenocarcinoma which was composed of acinar and papillary pattern microscopically. After the first surgery, we performed a CT-guided biopsy for the nodules of the RML. Section of the nodules of the RML showed atypical columnar cells with cytoplasm arranged in acinar and lepidic pattern. Considering the difference in pathological findings, we diagnosed the nodules of the LUL and RML as double primary cancers. We then performed right middle lobectomy 108 days after the first operation. Pathological diagnosis of nodules of the RML was colloid adenocarcinoma with signet-ring features, and there was a small nodule which was considered to be pulmonary metastasis.

After the second surgery, on the first postoperative day, the patient developed respiratory failure. On electro-cardiogram (ECG), ST segments in leads V2 to V5 increased (Figure 2). The serum troponin level was elevated at 1.27 ng/ml and

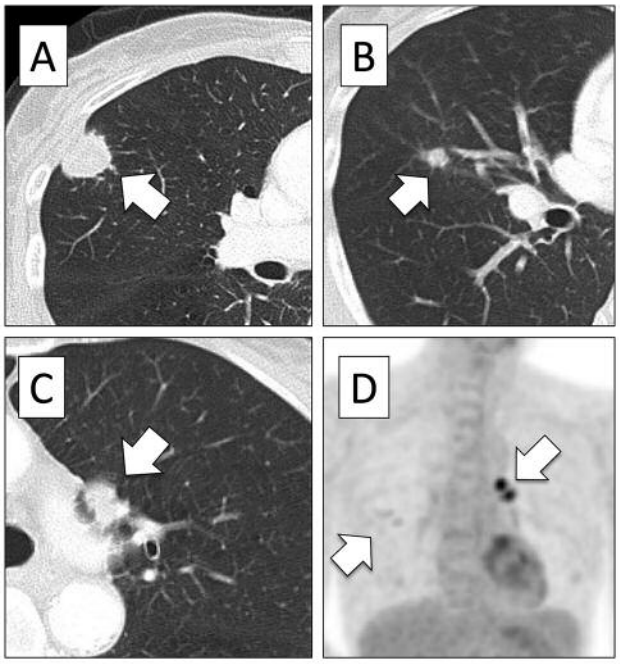

Figure 1. *Computed tomography (CT) showed a 18 mm tumor (A) and a 7 mm tumor (B) of the right middle lobe (RML). A 10 mm tumor was also determined in the left upper lobe (LUL). Positron-emission tomography/CT showed mild uptake of fluorodeoxyglucose at tumors of the RML (maximum standardized uptake value [SUV_{max}]=1.50) (C), and avid uptake at the LUL (SUV_{max}=8.49) and left hilar lymph node (SUV_{max}=7.16) (D).*

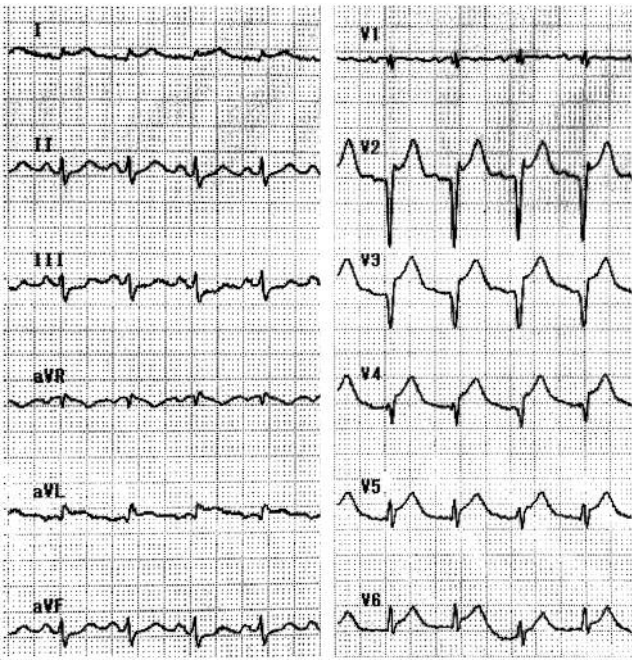

Figure 2. *Electro-cardiogram showed ST segments elevation in leads V2 to V5.*

chest X-ray showed acute pulmonary edema. We suspected that she developed acute heart failure from acute coronary syndrome (ACS) or TC. We began supportive treatment using non-invasive positive ventilation (NPPV), catecholamine and diuretics. On postoperative day 2, cardiac catheterization was performed, and it showed no coronary artery disease but did reveal apical akinesia (Figure 3). We therefore diagnosed TC and continued supportive treatment. The patient gradually recovered, and became free from NPPV, catecholamine and diuretics at postoperative days 4, 15 and 22. Additionally, on postoperative day 11, she underwent a mental health examination. She was diagnosed with depression, and treatment with selective serotonin reuptake inhibitor was started. She was transferred to another hospital for rehabilitation on postoperative day 30.

Discussion

TC was first used as a term in 1990 from Japan and was defined as a syndrome that is transient local (particularly in apex) systolic dysfunction of the left ventricle without obstructive coronary artery disease or acute plaque rupture (1). While it is well known that TC is associated with physical or emotional stress, and more common in women than men (2), the pathogenesis of TC has not been fully elucidated and various research studies on TC have been performed. Patients with TC were reported to have a significantly higher plasma level of epinephrine than patients with ACS, and epinephrine stimulates β2-adrenoreceptor that is rich in the apex and switches its signals from canonical cardiostimulant to cardiodepressant pathways (3). Furthermore, TC is frequently observed in postmenopausal woman, and a relationship between estrogen and TC has been suggested (4). Our patient was an elderly woman, and psychiatric disorder was identified during hospitalization. The physical and emotional stress of repeated surgery might affect the development of TC.

Mayo criteria have been established for diagnosis of TC: transient left ventricular systolic dysfunction, absence of obstructive coronary disease or angiographic evidence of acute plaque rupture, new abnormalities in ECG (either ST segment elevation or T-wave inversion) or modest elevation in serum cardiac troponin, and absence of pheochromocytoma or myocarditis (5). These four criteria are required for the diagnosis of TC. In the current case, ST segment elevation in ECG and elevation of cardiac troponin were found; however, these findings do not suffice to differentiate TC from ACS. Apical akinesia without coronary arterial disease on cardiac catheterization was decisive for the diagnosis of TC. Although

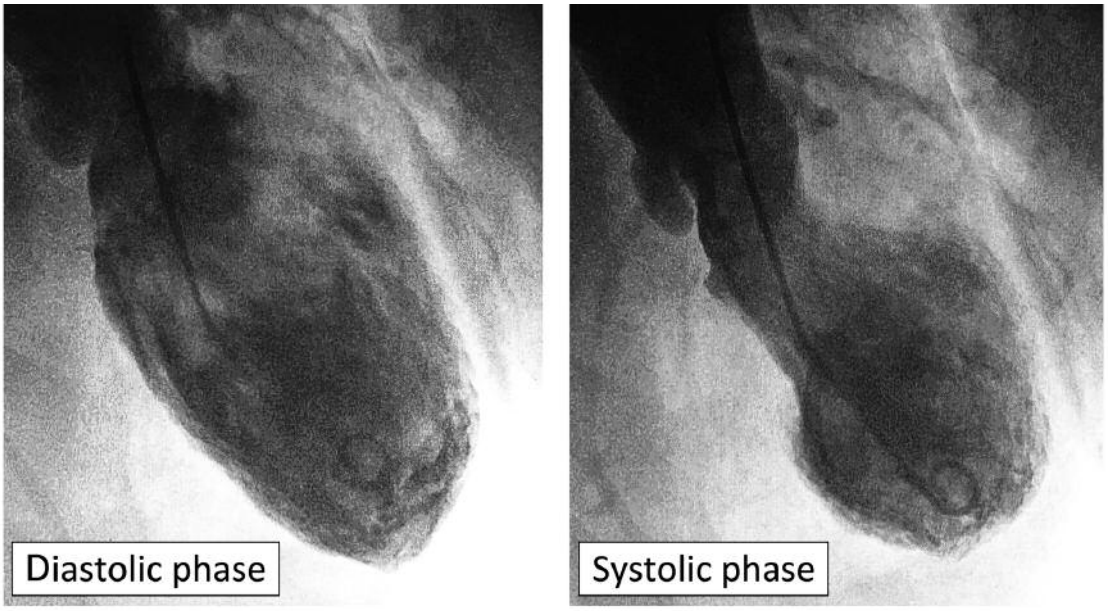

Figure 3. *Left ventricular angiography showed systolic dysfunction of the left ventricle at the apex.*

we did not perform additional examinations for exclusion of pheochromocytoma and myocarditis, based on the fact that that the patient had no history of heart disease or hypertension, we excluded the possibility of pheochromocytoma and myocarditis.

The common clinical manifestations of TC are chest pain, dyspnea, and syncope. These clinical manifestations and the test results of ECG and serum cardiac troponin are practically similar to those of ACS, and cardiac catheterization is often needed to accurately differentiate TC from ACS.

In an international statistical analysis of TC, most patients with TC were reported to recover with supportive treatment, but the risk of severe complications was similar to that in patients with ACS. The rates of severe complications of TC, such as cardiac shock, ventricular tachycardia, ventricular thrombus, and ventricular rupture, were 9.9%, 0.3%, 1.3%, and 0.2% and the mortality of TC was 4.1% (2).

There exist few reports that describe a relationship between TC and lung cancer. Toyooka *et al*. (6) and Lee *et al*. (7) reported cases with TC after or during pulmonary resection. In addition to surgery, chemotherapy (8) and cancer-related pain (9) were also reported to possibly trigger TC. In the surgical case, epidural anesthesia made typical chest pain unclear and early diagnosis difficult (6), and our case was also without chest pain. Therefore, ECG monitoring is especially important for early diagnosis of TC after surgery.

Patients with TC sometimes have a fatal course and lung cancer is related to the development of TC. Therefore, clinicians should be aware of TC in the treatment of lung cancer.

Conclusion

We reported a case of TC after two-stage surgery for double primary lung cancer. TC sometimes proves fatal, and early diagnosis and treatment are imperative.

Conflicts of Interest

The Authors have no conflicts of interest to declare.

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