〈Case Report〉

A Case of Takotsubo syndrome after Surgery for Papillary Thyroid Cancer

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ABSTRACT The patient was an 82-year-old woman undergoing treatment for bronchial asthma. In December 200X, she visited her former doctor because of a left cervical mass and pain, and was referred to our hospital for detailed examination. A 19-mm mass was found in the left lobe of the thyroid gland and there were many swollen lymph nodes on both sides of her neck. Fine-needle aspiration cytology revealed malignant and papillary cancer in both the left lobe and left cervical lymph node, but no lung metastasis was found in chest CT, and it was judged to be T1bN1bM0 Stage IVa. Total thyroidectomy + bilateral cervival lymphnode dissection was performed. The left lobe mass of the thyroid gland invaded the sterno-thyroid muscle, but no infiltration to other organs, including the lymph nodes on both sides, was observed. On the night of the operation, wheezing, dyspnea, lower mandibular breathing, and impaired consciousness suddenly developed, and the oxygen saturation of peripheral artery (SpO2) decreased to 60%. No postoperative bleeding was observed. Chest CT demonstrated no signs of heart failure, but based on thickening of the bronchial wall, the cause of hypoxemia was considered to be bronchial asthma. Steroids and oxygen (high-dose, 15 L/min) were administered, but respiratory acidosis developed and non-invasive positive pressure ventilation (NIPPV) was started. The respiratory condition gradually improved thereafter. Acute coronary syndrome (ACS) was suspected based on symptoms, increased troponin T, and ST elevation on ECG. Echocardiography revealed akinesis and left ventricular apical and basal hypercontractility. No coronary arterial stenosis was noted on coronary angiography and left ventriculography demonstrated Takotsubo-like wall movement (hypercontraction of the base and contraction failure of the apex), leading to a diagnosis of Takotsubo syndrome (TS). The

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subsequent course was good and she was discharged on the 10th postoperative day.

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INTRODUCTION

Takotsubo syndrome (TS) is generally characterized by transient and reversible ventricular wall dyskinesias caused by physical or mental stress [1, 2]. TS causes symptoms and ECG findings similar to acute coronary syndrome (ACS); therefore, an accurate diagnosis is essential [3, 4]. As there are few reports of TS associated with thyroid cancer, we report a case of TS after postoperative papillary thyroid cancer.

CASE REPORT

[Patient] 82-year-old woman

[Chief complaint] Left cervical mass

[Present illness] In 201X, she noted a left cervical mass and visited a neighborhood hospital. Based on detailed examination, she was diagnosed with papillary thyroid cancer and referred to our department for consultation.

[Past history] Bronchial asthma and postoperative cataract

[Family history] Not contributory

[Physical findings] A tumor of approximately 20 mm was observed in the left lobe of the thyroid gland and the 15-mm left cervical lymph node was palpable.

[Image findings]

Ultrasonography:

A 19 × 18 × 18-mm hypoechoic mass was found in the middle left lobe of the thyroid gland. The mass had a rough boundary and heterogeneous internal structure (Fig. 1a), and the internal blood flow was abundant (Fig. 1d). Left deep cervical lymph node: Lymphadenopathy was observed and

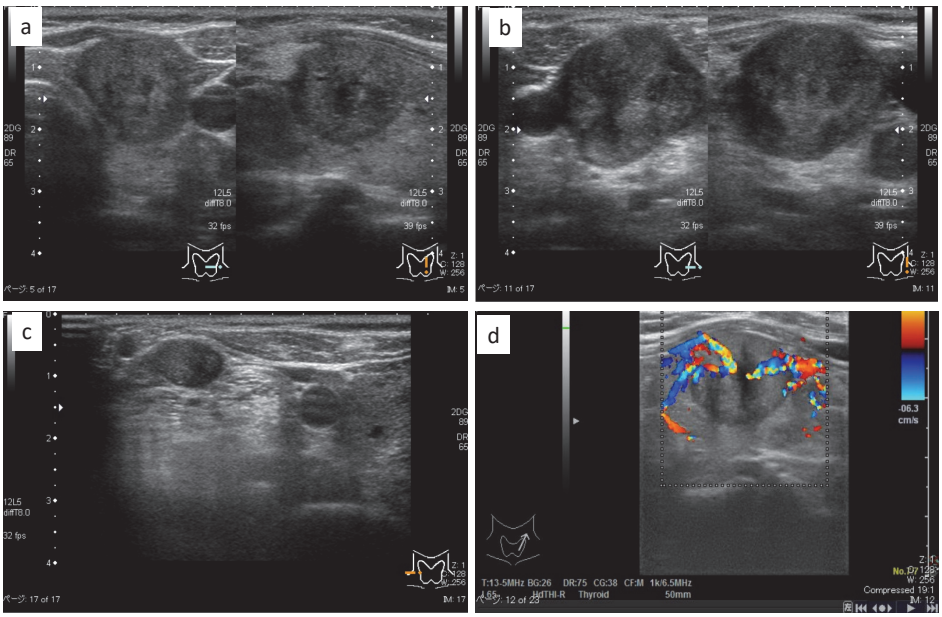

Fig. 1. Ultrasonographic findings: Lt. lobe mass (a). Lt. cervical lymph node (b). Rt. cervical lymph node (c). Color Doppler (d).

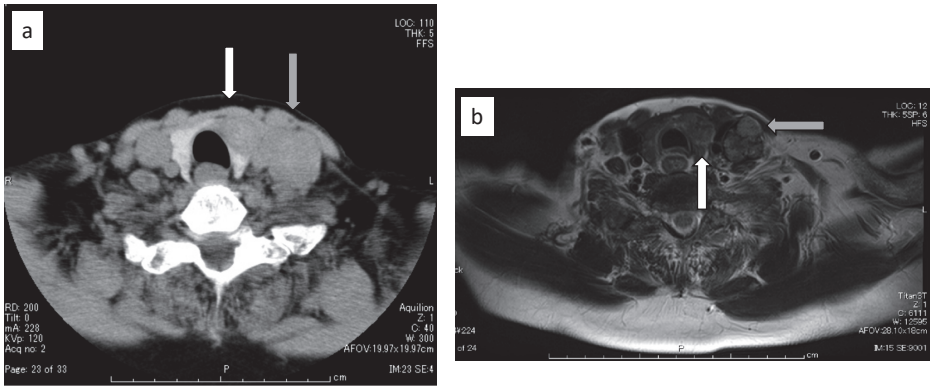

Fig. 2. CT (a) and MRI (b) showing a lt. lobe mass (white arrow) and a lt. cervical lymph node (gray arrow).

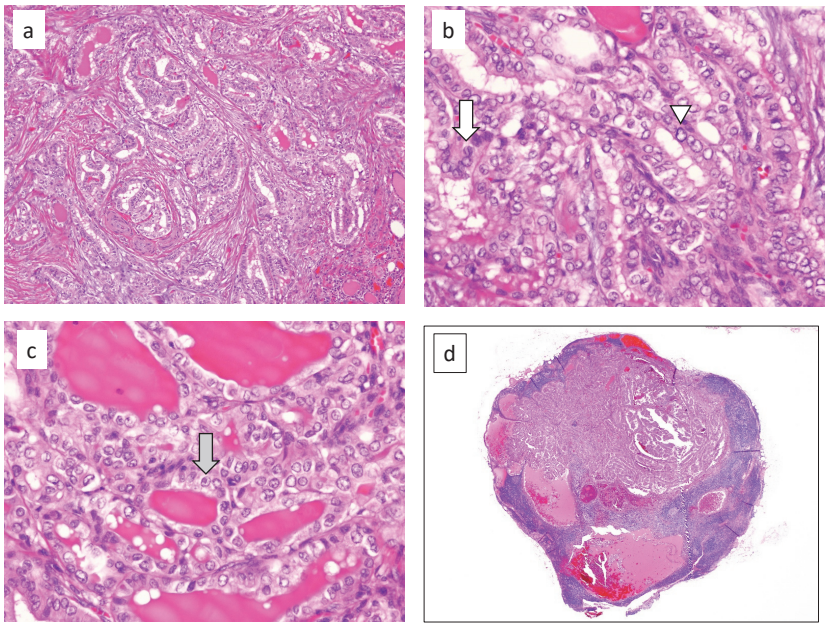

Fig. 3. Histopathological examination of the resected specimen: Papillary cell proliferation was observed (a), and ground glass-like nuclei (arrowhead), nuclear grooves (white arrow), and intranuclear cytoplasmic inclusion bodies (gray arrow) were noted (b, c). Lymph node metastases (d) were widespread.

the maximum diameter was 25 mm, suggesting metastasis (Fig. 1b). It was in contact with the internal jugular vein and infiltration was suspected. Right deep cervical lymph node: At least two sites of lymphadenopathy were found, also suggesting metastasis (Fig. 1c).

CT (Fig. 2a), MRI (Fig. 2b):

No notable tracheal infiltration of the tumor was observed. The tumor may have invaded the left internal jugular vein. No lung metastasis was found.

[Fine-needle aspiration cytology]

Malignant and papillary cancer in both the left lobe mass and left cervical lymph node

[Blood test at first visit]

Thyroid function was normal. The thyroglobulin level was high at 313 ng/mL, but anti-thyroglobulin antibody was negative. There were no other abnormal findings.

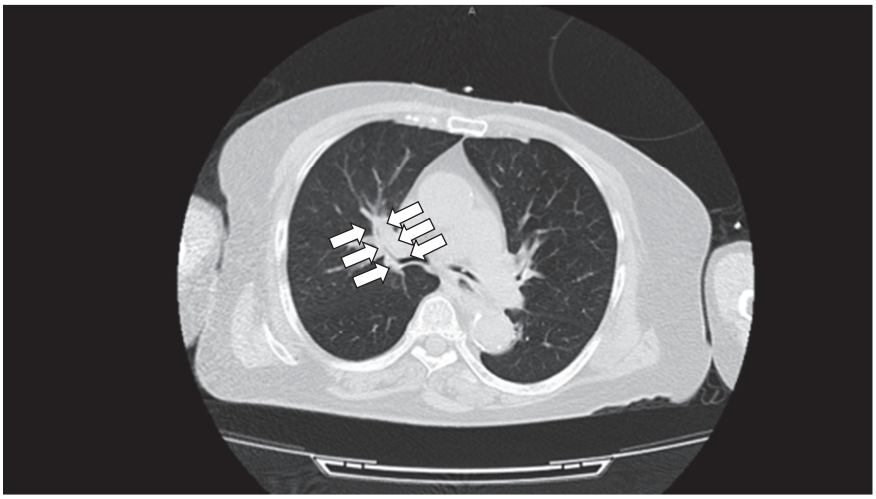

Fig. 4. Chest CT: Thickening of the tracheal wall was observed (white arrow).

[Operation]

Total thyroidectomy + bilateral cervical lymphnode dissection was performed. The left lobe mass of the thyroid gland invaded the sterno-thyroid muscle, many sites of bilateral cervical lymphadenopathy were noted, but there was no infiltration into the internal jugular vein.

[Histopathological examination]

Papillary cell proliferation was observed (Fig. 3a), and ground glass-like nuclei, nuclear grooves, and intranuclear cytoplasmic inclusion bodies were noted (Fig. 3b, 3c), leading to a diagnosis of papillary thyroid cancer (PTC). PTC of the thyroid gland infiltrated the surrounding muscles and adipose tissue, but the surgical margin was negative. Lymph node metastases (Fig. 3d) were widespread (maximum diameter of metastases 27 mm, a total of 12 metastatic lymphnodes).

[Postoperative course]

On the night of the operation, the patient suddenly developed wheezing, respiratory distress, mandibular breathing, and impaired consciousness, and the oxygen saturation of peripheral artery (SpO2) decreased to 60% at room air. No postoperative bleeding was observed. Chest CT was performed to search for the cause of hypoxemia. There was no evidence of heart failure, but based on thickening of the bronchial wall (Fig. 4), the cause of hypoxemia was considered to be bronchial asthma.

Although steroids and oxygen (high-dose, 15 L/min) were administered, respiratory acidosis (pH 6.978, pCO2 106.1 mmHg, pO2 138.5 mmHg, BE -10.0 mEq/L) was confirmed on blood gas analysis and non-invasive positive pressure ventilation (NIPPV) was started. The respiratory condition gradually improved thereafter.

Blood tests demonstrated an increased troponin T level (0.232 ng/ml). ST elevation in leads V1-V3 and aVR was noted on ECG (Fig. 5b, Fig. 5a shows ECG on admission). Echocardiography demonstrated akinesis of left ventricular apex, and basal hypercontractility. Therefore, the differential diagnosis included TS and ACS. Because the regional wall motion abnormalities extend beyond a single epicardial vascular distribution, TS was strongly suspected.

16 hours later after onset, the patient underwent coronary angiography to differentiate acute coronary syndrome (ACS) from stress cardiomyopathy.

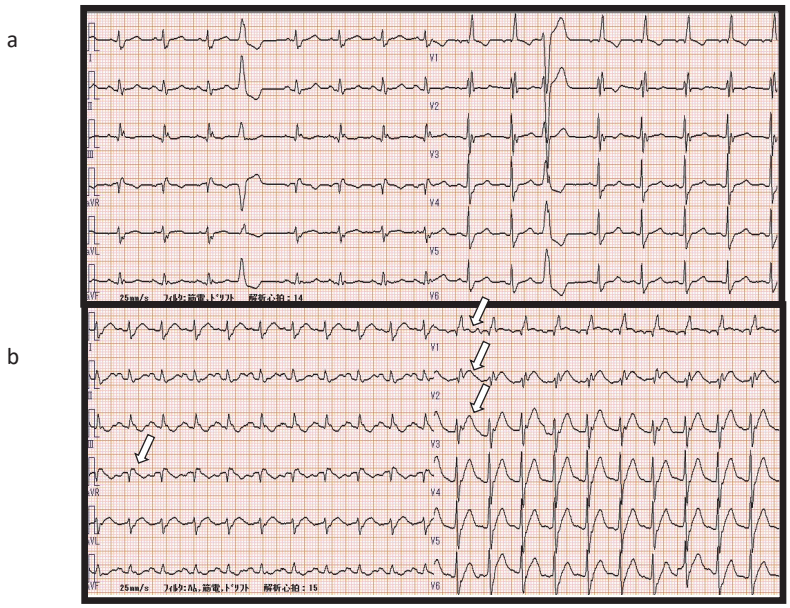

Fig. 5. ECG: On admission (a). At sudden change (b).ST elevation was noted in leads V1-V3 and aVR (white arrow).

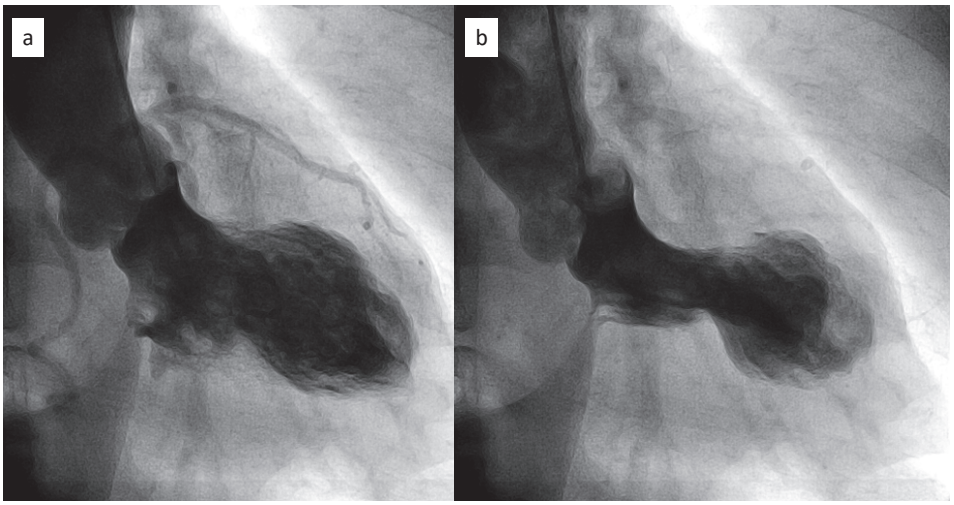

Fig. 6. Left ventriculography: Diastolic phase (a). Systolic phase (b).

No coronary arterial stenosis was present and left ventriculography (Fig. 6) revealed Takotsubo-like wall movement (hypercontraction of the base and contraction failure of the apex), leading to a diagnosis of TS.

The subsequent course was good. Although she had reduced left ventricular systolic function on echocardiography, she was discharged on her own on the 10th postoperative day.

DISCUSSION

Takotsubo Cardiomyopathy was first described in Japan in 1990 by Dote and colleagues[5]. The name "Takotsubo" was used to describe the

cardiomyopathy due to the characteristic apical ballooning on left ventriculography, which was similar in shape to a Japanese octopus trap. It is also referred to as "broken heart", "apical ballooning syndrome", "myocardial stunning", or "stress cardiomyopathy"[6], however "Takotsubo syndrome" is common internationally that causes contraction disorders in the heart associated with various pathological conditions..

TS is a reversible disease commonly affecting postmenopausal women, characterized by transient ventricular wall motion abnormalities mediated by physical or mental stress[1, 2]. The well-accepted catecholamine hypothesis suggests that stress-induced release of epinephrine and norepinephrine adversely affects cardiac and microvasculature functions, leading to myocardial stunning[7].

In this case, the cause of TS may have been related to postoperative bronchial asthma attack in addition to the stress caused by thyroid cancer surgery.

The symptoms of TS mimics those of ACS, as patients often present with chest pain, dyspnea, and hypotensive shock[4], in addition to ECG manifestations akin to those of myocardial infarction[5]. In this case, ACS was suspected based on symptoms, increased troponin T level, and ECG findings. However, Mayo Clinic criteria for TS described "Transient hypokinesis, akinesis, or dyskinesis of the left ventricular midsegments with or without apical involvement; the regional wall motion abnormalities extend beyond a single epicardial vascular distribution"[8]. In this case, Echocardiography showed similar findings, so TS was strongly suspected. After that, we were able to make a definitive diagnosis by coronary angiography and left ventriculography.

TS has a favorable long-term prognosis because supportive treatment leads to spontaneous rapid recovery in nearly all patients[9]. In this case, the patient was treated with supportive treatment and her general condition recovered. And then she was discharged on the 10th postoperative day.

Cancer is a chronic condition that induces significant emotional and physical stress, increasing the risk of stress cardiomyopathy. The potential triggers of TS in cancer patients include the emotional turmoil of the diagnosis, the inflammatory state of cancer, and the physical stress of cancer treatments, including chemotherapy[10, 11].

In a recent International Takotsubo Registry (InterTAK)[12], malignancy was found in 16.6% of 1,604 TS patients. The most frequent type of malignancy was breast cancer, followed by tumors of the gastrointestinal system, respiratory tract, and internal sex organs. Long-term mortality was higher in TS patients with malignancy[13].

Only two cases of TS associated with thyroid cancer have been reported, one that developed during lenvatinib treatment[14] and one that developed postoperatively[15].

Hayashi *et al.*[15] reported a case of TS that developed after surgery for thyroid cancer.

A 72-year-old woman developed sudden dyspnea and arrhythmia on the 3rd day after surgery, and a negative T wave was observed on ECG. However, she did not exhibit significant stenosis on coronary angiography and there was no contraction of the apex of the heart on left ventricular angiography, but she was diagnosed with TS. She had a good course and was discharged 11 days after surgery[15].

If cardiovascular complications are observed during the perioperative period for thyroid gland surgery, TS should be kept in mind.

CONCLUSIONS

We reported a case of TS after surgery for papillary thyroid cancer

CONFLICTS OF INTEREST

JK received advisory/consultation fees and research funding from Takeda Pharmaceutical Co. JK also received research funding from Eisai Co.

The other authors declare that they have no conflicts of interest.

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