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# 'Takotsubo' Cardiomyopathy Developing Immediately after Surgery for Esophageal Cancer

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## Introduction

'Takotsubo' cardiomyopathy is a type of cardiomyopathy similar to acute myocardial infarction[1,2]. It is often called 'takotsubo' because the left ventricular wall systolic pathomorphism resembles the shape of an octopus trap (takotsubo in Japanese)[3~5]. Most reports describing 'takotsubo' cardiomyopathy are from Japan although a similar condition, also referred to as ampulla cardiomypathy, has been reported in other countries. In this report, we describe a case that we suspected, at surgery, to be acute heart failure or myocardial infarction. Echocardiography confirmed that this was a very interesting case of 'takotsubo' cardiomyopathy.

**Key Words**: 'Takotsubo' cardiomyopathy, echo cardiography hyper catecholaminemia, post surgery state

## Case Report

The patient was a 75 -year-old man who was 160 cm tall and 45 kg in weight.At the age of 30 years, the patient underwent a left upper lobectomy for pulmonary tuberculosis. At 40 years a renal calculus developed, and at 69 years cataracts were diagnosed. At 75 years he had cervical spondylosis.

## Present illness

In August 2000, the patient experienced weight loss (4 kg/ 8 months) and was found to have esophageal cancer in the upper gastrointestinal tract by endoscopic examination. The patient was scheduled to undergo thoracoscopic resection of the esophagus with retrosternal reconstruction of the stomach canal in November of the same year.

## Preoperative findings and results of examinations

Lung function testing revealed restrictive impairment (percent vital capacity: 50%), and an electrocardiogram (ECG) showed complete right bundle block. An exercise ECG (Master double), however, revealed no abnormalities.

## Anesthetic course

Preanesthetic treatment was not given. After arrival at the operating room, an epidural catheter was inserted to the level of Th9/10. Anesthesia was induced with 150 mg of thiamylal, 0.1 mg of fentanyl, and 5 mg of vecuronium. To maintain anesthesia, 0.4% to 0.8% of sevoflurane and oxygen ($F_{IO_2}$ 0.3), and nitrous oxide were given with continuous epidural anesthesia (1.0% mepivacaine, 5 $ml \cdot hr^{-1}$). When appropriate, fentanyl (total dose, 0.2 mg) and vecuronium (total dose, 19 mg) were added. Blood gas analysis revealed no abnormalities; $P_{aO_2}$ was 140 to 170 mmHg and $P_{aCO_2}$ was 35 to 44 mmHg at $F_{IO_2}$ 0.33.

However, from the start of surgery no pulse oximetry wave was detected perhaps due to the peripheral circulatory procedure. Because of cardiac compression arising from the surgical procedure, systolic blood pressure was between 50 and 60 mmHg,

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and heart rate (HR) fell to 40 beats/min. An infusion loading of dopamine (3-8 $\mu g \cdot kg^{-1} \cdot min^{-1}$) were administered, and systolic blood pressure was maintained at about 100 mmHg. The ECG (leads II and V5) revealed no marked ST-T changes during surgery. The does of dopamine was decreased as the operation was completed. During surgery, the patient lost 2,590 ml of blood and was given 1,800 ml of concentrated red blood cells, 800 ml of fresh frozen plasma, and 1,250 ml of plasma substitute. As for the water balance, the urinary volume was 600 ml, and the patient received 3,300 ml of infusion. Surgery required 9 hr 25 min, and the duration of anesthesia was 10 hr 55 min. After surgery the patient was transferred to the ICU without removing the tracheal tube.

**The time course of the ICU**

On transfer to the ICU, the blood pressure was 140/75 mmHg and the HR was 80 beats $\cdot min^{-1}$. The patient presented with severe cyanosis in the limbs, with severe coldness of the limbs and extremely poor peripheral circulation. The ECG showed ST-T elevation of 1-7 mm in leads II, III, aVF, and V2-6 (Fig.1). Because acute myocardial infarction was suspected, the patient was immediately given 1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of isosorbide dinitrate. To stabilize hemodynamics, a continuous infusion of dobutamine (5 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was started. On transthoracic echocardiography, the left ventricular wall was extremely hypokinetic at the apex of the heart, with systolic accentuation at the base (Fig.2). The result of a troponin T test was negative, indicating that a myocardial infarction was unlikely. 'Takotsubo' cardiomyopathy was therefore suspected. The patient was given a continuous infusion of 2 mg $\cdot hr^{-1}$ of diltiazem. To monitor cardiac function, a Swan-Gantz pulmonary catheter was inserted via the right internal jugular vein. On insertion of the catheter, cardiac output was 3.1 $l \cdot min^{-1}$, cardiac index 2.1 $l \cdot min^{-1} \cdot m^{-2}$, HR 120 beats $\cdot min^{-1}$, right atrial pressure 4 mmHg, pulmonary arterial pressure 20/8 mmHg, pulmonary capillary wedge pressure 9 mmHg, and the systemic vascular resistance index 2,857 dynes $\cdot sec^{-1} \cdot cm^{-5} \cdot m^{-2}$.

Serum chemical analyses on admission to the ICU revealed the following: aspartate aminotransferase level(AST), 83 U/l; lactate dehydrogenase level (LDH), 262 $U \cdot l^{-1}$; creatine kinase level, 603 $U \cdot l^{-1}$; and creatine kinas MB isoenzyme level, 31 $U \cdot l^{-1}$. Plasma levels of myocardium-related enzymes were elevated. The maximum creatine kinase level was 1,862 $U \cdot l^{-1}$ (CK-MB, 39 $U \cdot l^{-1}$) on day 1 after surgery, which was not considered to be a significant increase. The plasma

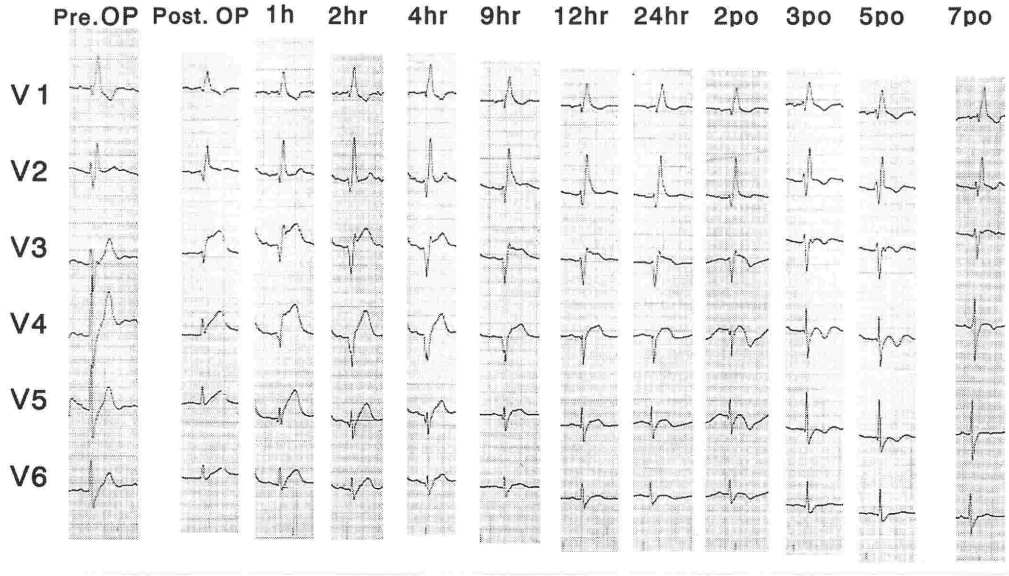
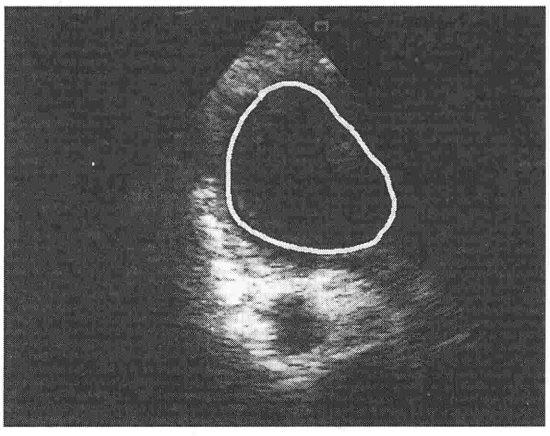



**Fig.1 Electrocardiogram before and after surgery.**



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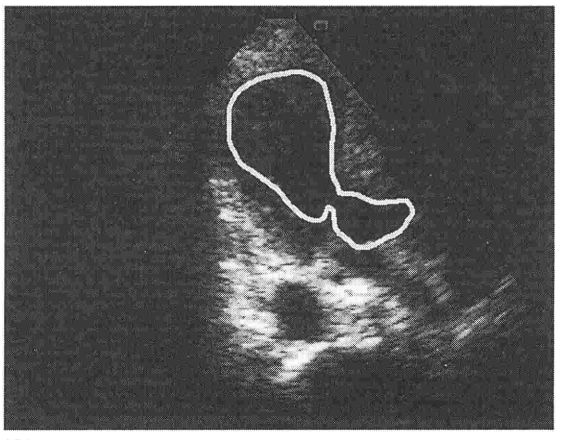

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**Fig.2 Transthoracic echocardiogram view at level of apex.**
(1)end-diastolie phase, (2)end-systolic phase.
The short-axis view at the levels of apex shows the finding of ampulla-like space of the left ventricle in the end-systolic period.

**Table Plasma hormonal and datas, hemodyanamics**

| | | 0POD | | | 1POD | | 2POD | 3POD | 4POD |
|---|---|---|---|---|---|---|---|---|---|
| | | 20:00 | 21:00 | 23:00 | 9:00 | 12:30 | 9:00 | 9:00 | 9:00 |
| Norepinephrine | ($ng \cdot ml^{-1}$) | 2.58 | 2.51 | 2.60 | 1.27 | 1.45 | 1.27 | 1.60 | 1.33 |
| Epinephrine | ($ng \cdot ml^{-1}$) | 2.73 | 1.30 | 1.09 | 0.34 | 0.32 | 0.25 | 0.37 | 0.10 |
| Dopamine | ($ng \cdot ml^{-1}$) | 14.10 | 2.40 | 2.30 | 0.74 | 0.25 | 0.22 | <0.10 | <0.10 |
| ABP (mmHg) | | 140/75 | 165/90 | 140/80 | 85/50 | 165/70 | 145/60 | 150/68 | 150/80 |
| HR (bpm) | | 80 | 95 | 120 | 100 | 90 | 95 | 85 | 95 |
| CI ($l \cdot min^{-1} \cdot BSA^{-1}$) | | | | 2.1 | 2.4 | 2.6 | 2.8 | 2.1 | |
| RAP (mmHg) | | | | 4 | 6 | 10 | 10 | 9 | 7 |
| PAP (mmHg) | | | | 20/8 | 19/7 | 35/17 | 27/16 | 26/14 | |
| LVOTPG (mmHg) | | | | 27.5 | 13.5 | 4.5 | | 1.9 | |
| Drugs | Dopamine | 5γ | | | | | | | |
| | Dobutamine | | | 5γ | 2.5γ | | | | |
| | ISDN | | | 1γ | 0.5γ | | | | |
| | Diltiazem | | | 2mg/hr | 2mg/hr | 2mg/hr | 2mg/hr | 2mg/hr | |

ABP; arterial blood pressure, HR; heart rate, CI; cardiac index,
RAP; right atrium pressure, LVOTPG; left ventricular outflow tract pressure gradient

catecholamine concentrations at entry to the ICU were abnormally high: norepinephrine, 2.58 $ng \cdot ml^{-1}$ (normal range, 0.07-0.31 $ng \cdot ml^{-1}$); epinephrine, 2.73 $ng \cdot ml^{-1}$ (<0.10 $ng \cdot ml^{-1}$); and dopamine, 14.1 $ng \cdot ml^{-1}$ (<0.10 $ng \cdot ml^{-1}$) (Table 1). The ECG on day 1 after surgery showed ST-T elevation, similar to the previous examination. On day 2 the ECG showed T-wave inversion in leads V3-6. Transthoracic echocardiography on day 1 after surgery revealed an ejection fraction of 55%, with no backflow. Left ventricular wall motion at the apex of the heart was decreased, but the left ventricular outflow tract pressure gradient was 13.5 mmHg. Therefore, dobutamine treatment was discontinued. The left ventricular outflow tract pressure gradient fell to 4.5 mmHg after 30 min, decreasing further to 1.9 mmHg on day 3 (Fig.2). The endotracheal tube was removed, and respiratory and hemodynamic variables stabilized. The patient was

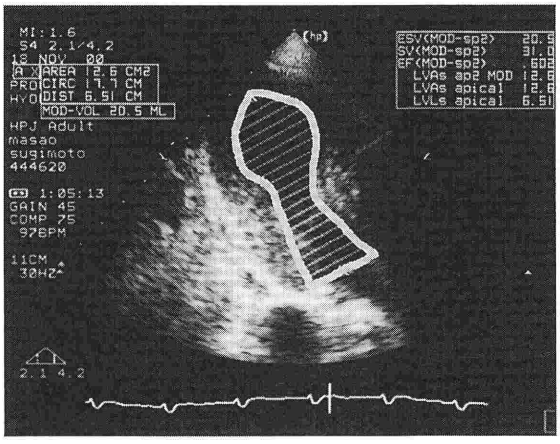
discharged from the ICU on day 4 after surgery. The ECG showed the ST-T elevation in leads II, III, aft, and V2-6 was getting normalized until the 7th postoperative day (Fig.1). Echocardiography on day 30 after surgery revealed an ejection fraction of 67%, with resolution of the pressure gradient in the left ventricular outflow tract. There was no systolic wall abnormality and cardiac function was normal.

## Discussion

'Takotsubo' cardiomyopathy has many similarities to acute myocardial infarction[1,2]. Both conditions are characterized by a sudden onset of chest pain, ST-T elevation, and elevated plasma creatine kinase levels[3~5]. During systole early after onset, there is decreased motion of the apex and increased motion of the base of the left ventricle. Similar to stunned myocardium, these systolic abnormalities resolve in 1 week. The systolic abnormalities associated with 'takotsubo' cardiomyopathy cannot be attributed to a control region at a single branch of the coronary arteries, and clinically significant stenosis is absent. Underlying diseases or factors include non-cardiac surgery in elderly patients[2], sudden, large dose loading of catecholamines[6], and severe psychologic trauma[7], subarachnoid hemorrhage[8,9], pheonochromocytoma[10] and Guillain-Barre syndrome[11]. Two potential causes are stunned myocardium due to multiple coronary onstrictions and direct cardiomyopathy due to catecholamine excess[6].

The present case of 'takotsubo' cardiomyopathy was diagnosed on the basis of echocardiographic findings and clinical course. Excessively high doses of catecholamine and prolonged highly invasive surgery in an elderly patient were considered potential causes. Although stunned myocardium due to multiple coronary contrictions might also have been involved, coronary angiography and acetylcholine loading tests were not performed. However, the involvement of stunned myocardium cannot be ruled out because wall motion markedly improved after the withdrawal of dopamine and dobutamine.

Our patient received a low dose of dopamine to maintain hemodyanamic stability and renal blood flow

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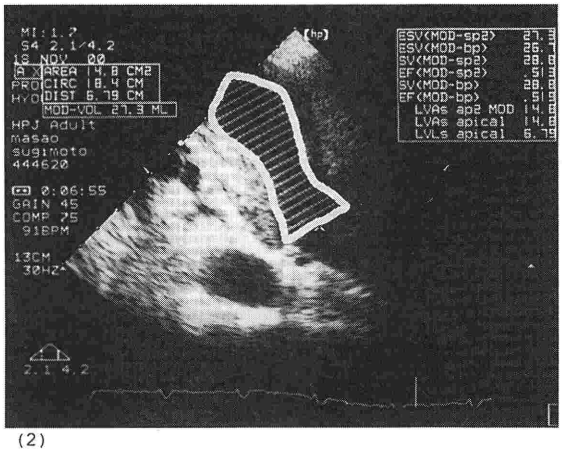


(2)

**Fig.3 Transthoracic echocardiogram view at level of apex. With and without dobutamine loading in the end-systolic phase.**

(1) 2.5 μg/Kg/min of dobutamine loadng

(2) 30 min after the discontinuation of dobutamine loading

The left ventricular outflow tract pressure gradient was 13.5 mmHg. Although, the gradient fell to 4.5 mmHg after 30 min after the discontinuation of dobutamine loading. The volume of the left ventricle was increased from 20.5 ml to 27.3 ml according to dobutamine unloding.

from the start of surgery. Infusions and transfusions were given to compensate for the decreased blood pressure caused by the considerrable loss of blood, but there was no increase in blood pressure. A high dose of dopamine was therefore given to maintain blood pressure. Because blood pressure remained unstable at

the time of entry to the ICU, an intravenous infusion of dobutamine was started. However, the postoperative ECG indicated 'takotsubo' cardiomyopathy. After the withdrawal of dobutamine, the left ventricular outflow tract pressure gradient improved markedly.

The plasma catecholamine concentrations were abnormally high on admission to the ICU. Thus, our case was apparently caused by stress due to mild level of anesthesia and surgical invasion as well as by direct cardiomyopathy due to an exogenous overdose of catecholamine[6]. In previously reported cases, plasma concentrations of catecholamines such as epinephrine and norepinephrine ranged from several times to several tens of times the upper limits of normal. In our case, the plasma catecholamine level was at least 20 times the upper limit of normal, and this increase was considered to have led to stenosis of the left ventricular outflow tract.

Transesophageal and/or transthoracic echocardiography is considered more useful than ECG for the intraoperative diagnosis and evaluation of myocardial ischemia. In patients who have intraoperative or postoperative ST-T changes or decreases in blood pressure, catecholamines should not be the primary treatment of choice; other treatments should be given after (for, to improve, to restore, to mainstain ) cardiac functions, for example, transesophageal or transthoracic echocardiography.

In conclusion, patients undergoing surgery with adverse effects on cardiac function should be intraoperatively monitored by transesophageal echocardiography to confirm the diagnosis. In patients with takotsubo-like wall systolic abnormalities catecholamine treatment should promptly be discontinued.

## References


1) Sassa H, Tsuboi H, Sane T, et al : Clinical significance of transitory myocardial infarction-like ECG pattern in postoperative patients. (In Japanese with English Abstract) Shinzou 15 : 669-678, 1983

2) Tokioka M, Miura H, Masaoka Y, et al : Transient appearance of asynergy on the echocardiogram and electrocardiographic changes simulating acute myocardial infarction following non-cardiac surgery. (In Japanese with English Abstract) J Cardiogr Suppl 15 : 639-653, 1985

3) Kawai S, Suzuki H, Yamaguchi H, et al : Ampulla cardiomyopathy (takotubo cardiomyopathy)-reversible left ventricular dysfunction with ST segment elevation- Jpn Circ J 64 : 156-159, 2000

4) Dote K, Mituda H, Ninomiya M, et al : Acute reversible cathecholamine cardiomyopathy. (In Japanese with English Abstract)In: Okada R, editor, Syndrome of Cardiovascular Diseases, Ⅲ. Tokyo : Nihon Rinsho 166-169, 1996

5) Ishihara M, Sato H, Tateishi H, et al : 'Takotsubo'-like cardiomyopathy. (In Japanese with English Abstract) Kokyuu to Jyunkan 45 : 879-885, 1997

6) Anzai H, Komiyama N, Kinoshita N, et al : Case of stunned myocardium caused by overdose of epinephrine. (In Japanese with English Abstract) Kokyu to Jyunkan 44 : 199-204, 1996

7) Tsujimoto G, Ohnishi K, Fujibayashi R, et al : A case of acute myocardial infarction with normal coronary artery induced by severe emotional stress. (In Japanese with English Abstract) Shinzou 23 : 768-772, 1991

8) Sakamoto H, Nishimura H, Imataka K, et al : Abnormal Q wave, ST-segment elevation, T-wave inversion, and widespread focal myocytolysis associated with subarachnoid hemorrhage. Jpn Circ J 60 : 254-257, 1996

9) Pollick C, Cujec B, Parker S,et al : Left ventricular wall motion abnormalities in subarachnoid hemorrage:An echocardiographic study. J Am Coll Cardiol 12 : 600-605, 1988

10) Yamanaka O, Yasumasa F, Nakamura T, et al : "Myocardial stunning"-like phenomenon during a crisis of pheochromocytoma. Jpn Circ J 58 : 737-742, 1994

11) Iga K, Himura Y, Izumi C, et al : Reversible left ventricular dysfunction associated with Guillain-Barre syndrome. An expression of catecholamine cardiotoxicity? Jpn Circ J 59 : 236-240, 1995


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