Takotsubo cardiomyopathy caused by acute respiratory stress from extubation
A case report
Kohei Taniguchi, MD, PhD\textsuperscript{a,b,}\textsuperscript{*}, Syogo Takashima, MD\textsuperscript{c}, Ryo Iida, MD\textsuperscript{a,b}, Koshi Ota, MD\textsuperscript{a}, Masahiko Nitta, MD, PhD\textsuperscript{a}, Kazushi Sakane, MD, PhD\textsuperscript{d}, Tomohiro Fujisaka, MD, PhD\textsuperscript{d}, Nobukazu Ishizaka, MD, PhD\textsuperscript{d}, Osamu Umegaki, MD, PhD\textsuperscript{e}, Kazuhsa Uchiyama, MD, PhD\textsuperscript{b}, Akira Takasu, MD, PhD\textsuperscript{a}

Abstract
Rational: Takotsubo cardiomyopathy (TCM) is a transient systolic dysfunction of the left ventricular apex without stenosis of coronary arteries and is induced by various psychological and physical factors. TCM sometimes causes lethal complications such as arrhythmia, thrombogenesis, and even cardiac rupture, and thus it should be diagnosed appropriately and managed carefully. Intensive care unit (ICU) patients are exposed to overstress during the treatment process and therefore can are at potential risk for TCM.

Patient concerns: The patient was diagnosed as having pneumonia because of influenza A virus mixed with bacteria and underwent intensive care with intubation and mechanical ventilation in the ICU. His respiratory condition soon improved, and so extubation was carried out; however, redeterioration with pulmonary edema occurred at half of a day following extubation.

Diagnosis: The chest x-ray revealed pulmonary edema. The electrocardiogram pattern significantly changed with time, and the echocardiogram showed weakness of wall motion around the left ventricular apex. Hence, to confirm the diagnosis, we performed cardiac catheterization immediately, with the results showing a Takotsubo-like form at the systolic phase without significant stenosis of the coronary arteries.

Intervention: The patient was reintubated with administration of catecholamine for decreasing blood pressure caused by left ventricular dysfunction. Also, diuretics for pulmonary edema and anticoagulants for prevention of thrombogenesis were administered.

Outcomes: As the respiratory condition improved with stabilization of cardiovascular hemodynamics, reextubation was done at ICU day 11 and was discharged from the ICU at ICU day 15. The patient was subsequently treated for pneumonia after leaving the ICU but suffered from repetitive aspiration pneumonia and was finally transferred to another hospital at hospital day 111.

Lessons: TCM should be considered especially under the situation of intensive care, and prompt diagnosis should be followed by appropriate management.

Abbreviations: ABG = arterial blood gas, ECG = electrocardiogram, ICU = intensive care unit, TCM = Takotsubo cardiomyopathy.

Keywords: apical ballooning syndrome, broken heart syndrome, extubation, stress cardiomyopathy, takotsubo cardiomyopathy

1. Introduction
Takotsubo cardiomyopathy (TCM) is known as psychological and physical stress-induced cardiomyopathy accompanied by transient systolic dysfunction of the left ventricular apex.\textsuperscript{[1]} Intensive care unit (ICU) patients are exposed to overstress during treatment and therefore are potentially at risk for TCM. Precise diagnosis and prompt treatment for it are thus required because
TCM sometimes results in lethal heart failure or cardiac shock, especially in ICU patients. Herein, we report a case of TCM induced by acute respiratory stress including extubation.

2. Case report

An 86-year-old man was hospitalized in emergency department with a diagnosis of pneumonia because of an influenza A virus/bacteria mixed infection and had been already treated with an anti-influenza agent in our department (Fig. 1A). He had an extensive medical history including hypertension, diabetes mellitus, pulmonary tuberculosis, and hydrocephalus, and a surgical history involving partial pulmonary resection for lung cancer. He was administered antibiotics immediately after admission, but his respiratory condition rapidly deteriorated. Oxygen was given at the rate of 12 L/min by face mask with a reservoir. His arterial blood gas (ABG) examination showed a PaO$_2$ of 58.0 Torr (normal, 80.0–100), a PaO$_2$/fraction of inspiratory oxygen ratio (P/F ratio) of 61.1, and a PaCO$_2$ of 28.5 Torr (normal, 35.0–45.0). Hence, he was intubated and managed strictly with broad-spectrum antibiotics and mechanical ventilation in the ICU. As his respiratory condition smoothly recovered, he was extubated on ICU day 4. ABG analysis showed a PaO$_2$ of 129.7 Torr, (P/F ratio of 324.3) and a PaCO$_2$ of 39.1 Torr under the rate of 4 L/min O$_2$ flow via face mask. However, his respiratory condition redeteriorated, with pink foamy sputum appearing about half a day after extubation. Also, his decreasing blood pressure required support by administration of catecholamine such as dopamine and noradrenaline. The chest x-ray revealed pulmonary edema (Fig. 1B and C). High O$_2$ flow was again given at the rate of 15 L/min, but his ABG analysis remained at a PaO$_2$ of 91.7 Torr (P/F ratio of 91.7) and a PaCO$_2$ of 37.2 Torr, and so he was reintubated. At the same time, the electrocardiogram (ECG) pattern clearly changed (Fig. 2A and B).

Figure 1. (A) Noncontrasting chest computed tomographic image when the patient entered our hospital. Bilateral infiltration of the lungs was detected. (B) Chest x-ray image at ICU day 4 (when extubation was done). His respiratory condition was improved. (C) Chest x-ray image at ICU day 5. Massive infiltration of the lung field and cardiac dilatation occurred, suggestive of pulmonary edema.

Figure 2. After extubation, electrocardiogram (ECG) findings clearly changed along with respiratory deterioration. (A) ECG image at intensive care unit (ICU) day 4 (before extubation). (B) ECG image at ICU day 5 (after extubation). Abnormal Q waves were detected from lead V3, along with flat T waves from leads V3 to V6. Enlarged views of boxed areas in “A” and “B” show lead V3. The red arrow indicates an abnormal Q wave, and the blue arrow, a flat T wave from lead V3.
B), with the echocardiograph revealing weakness of wall motion around the left ventricular apex. Hence, cardiac catheterization was immediately performed, which showed systolic-phase Takotsubo-like forms without significant stenosis of coronary arteries (Fig. 3A and B, Supplementary File 1, http://links.lww.com/MD/B987). Based on these findings, a diagnosis of TCM after extubation was made. Deep inverted T waves appeared widely from chest and limb leads on the ECG at 48 hours after cardiac catheterization (Fig. 4A). Nadirs of the inverted T waves steadily rose under treatment with catecholamine for left ventricular dysfunction, diuretics for pulmonary edema, and anticoagulants for prevention of thrombogenesis (Fig. 4). As the respiratory condition improved, reextubation was done at ICU day 11. Although slight T-wave inversions still remained 3 weeks later on the ECG (Fig. 4C), his cardiovascular hemodynamics was stable, without administration of catecholamine at ICU day 8. The patient was discharged from the ICU at ICU day 15. The patient was subsequently treated for pneumonia after leaving the ICU but suffered from repetitive aspiration pneumonia and was finally transferred to another hospital at hospital day 111.

3. Discussion

TCM was first reported in 1989 in a pheochromocytoma patient as impaired reversible LV motion.[3] Possible onset mechanisms of TCM include spastic coronary microcirculatory disturbance, catecholamine cardio-injuries, and neurogenic stunning myocardium[4–6]; however, controversy remains regarding them. TCM is
thought to be induced by psychological stresses such as depression, anxiety, alcohol and drug abuses, and even mental disorders caused by disasters such as earthquake. Physical stresses including subarachnoid hemorrhage, acute respiratory distress syndrome, and acute exacerbation of chronic obstructive pulmonary disease can be also indicated as risk factors for TCM. Namely, many ICU inpatients have potentially high risk for TCM. In our present case, acute respiratory stress owing to pneumonia and extubation probably induced TCM. Also, a relatively high PEEP (8-cmH2O) cancellation after extubation might have contributed to it.

TCM should be diagnosed promptly and managed carefully because it sometimes causes lethal conditions such as cardiogenic shock, left ventricular outflow tract obstruction, heart failure, arrhythmia, thrombogenesis or cardiac rupture. ECG is one of the most versatile and easiest tools in the clinical situation. ST-segment depression in lead aVR without ST-segment elevation in lead V1 is a typical ECG finding for the acute phase of TCM, but it is not often revealed. In the present case, an abnormal Q wave and flat T wave were detected (Fig. 2B). Hence, it is important to suspect TCM without overlooking the various ECG pattern changes and to perform promptly a subsequent echocardiogram and cardiac catheterization.

TCM therapy is still empirical. Fortunately, in the present case, the cardiovascular hemodynamics was relatively stable with administration of catecholamine, and the patient recovered from TCM without serious complications following administration of only diuretics and anticoagulants. Although generally TCM has a relatively good prognosis, clinicians should consider the possibility of TCM in intensive care patients not to delay management of this disorder.

4. Conclusion

TCM should be considered especially under the situation of intensive care, and prompt diagnosis should be followed by appropriate management because delay management of this disorder sometimes induces lethal complications.

Acknowledgements

The authors are grateful for the cooperation of the staff involved in the cardiac catheterization and intensive care. Also, the authors thank the Department of Respiratory Medicine, Osaka Medical College, for management of the patient after discharge from the ICU.

References

[1] Lyon AR, Rees PS, Prasad S, et al. Stress (Takotsubo) cardiomyopathy—a novel pathophysiological hypothesis to explain catecholamine-induced acute myocardial stunning. Nat Clin Pract Cardiovasc Med 2008;5:22–9.
[2] Donohue D, Movahed MR. Clinical characteristics, demographics and prognosis of transient left ventricular apical ballooning syndrome. Heart Fail Rev 2005;10:311–6.
[3] Iga K, Gen H, Tomonaga G, et al. Reversible left ventricular wall motion impairment caused by pheochromocytoma—a case report. Jpn J Circ J 1989;53:813–8.
[4] Ako J, Sudhir K, Farouque HM, et al. Transient left ventricular dysfunction under severe stress: brain-heart relationship revisited. Am J Med 2006;119:10–7.
[5] Kume T, Akasaka T, Kawamoto T, et al. Assessment of coronary microcirculation in patients with takotsubo-like left ventricular dysfunction. Circ J 2005;69:934–9.
[6] Wittstein I, Thiemann DR, Lima JA, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. N Engl J Med 2005;352:539–48.
[7] El-Sayed AM, Brinjikji W, Salka S. Demographic and co-morbid predictors of stress (takotsubo) cardiomyopathy. Am J Cardiol 2012;109:1368–72.
[8] Summers MR, Lennon RJ, Prasad A. Pre-morbid psychiatric and cardiovascular diseases in apical ballooning syndrome (takotsubo/ stress-induced cardiomyopathy): potential pre-disposing factors? J Am Coll Cardiol 2010;55:700–1.
[9] Watanabe H, Kodama M, Okura Y, et al. Impact of earthquakes on Takotsubo cardiomyopathy. JAMA 2003;290:305–7.
[10] Sharkey SW, Winstead DC, Lesser JR, et al. Natural history and expansive clinical profile of stress (takotsubo) cardiomyopathy. J Am Coll Cardiol 2010;55:333–41.
[11] Kosuge M, Ebina T, Hibi K, et al. Simple and accurate electrocardiographic criteria to differentiate takotsubo cardiomyopathy from anterior acute myocardial infarction. J Am Coll Cardiol 2010;55:2514–6.
[12] Pilgrim TM, Wyss TR. Takotsubo cardiomyopathy or transient left ventricular apical ballooning syndrome: a systematic review. Int J Cardiol 2008;124:283–92.