Morphologically Unique Feature of Recurrent Ampulla (Takotsubo) Cardiomyopathy

Etsuko Ikeda, MD; Kenichi Hisamatsu, MD; Yasufumi Kijima, MD; Hiroki Mizoguchi, MD; Shigemi Urakawa, MD; Hideo Kimura, MD; Katsumasa Miyaji, MD; Mitsuru Munemasa, MD; Yoshihisa Fujimoto, MD; Hiromi Matsubara, MD; Hiroshi Mikouchi, MD

Two similar rare cases of recurrent ampulla (takotsubo) cardiomyopathy, which was induced by physical stress of recurrent rhabdomyolysis in case 1 and aggravation of respiratory disease in case 2, are presented. At the initial admission, both patients had typical ampulla cardiomyopathy, which was indicated by transient left ventricular (LV) apical ballooning, but at the second admission, they both had atypical ampulla cardiomyopathy, as diagnosed by transient basal midventricular ballooning. Electrocardiograms at each admission showed a specific T-wave inversion, which might indicate the region of LV asynergy, and prolongation of the QT interval. In both cases, the plasma level of endogenous catecholamines was high. It is possible that excessive sympathetic stimulation induced by physical stress was the cause of this cardiomyopathy, but the cause of the differences in wall motion abnormalities between the first and second admissions was not identified. Appropriate management and treatment of the underlying disease and determining the mechanisms of recurrent ampulla cardiomyopathy might prevent its recurrence. (Circ J 2009; 73: 371–375)

Key Words:  Catecholamines; Left ventricular ballooning; Recurrence; Takotsubo cardiomyopathy

Ampulla (takotsubo) cardiomyopathy is a novel heart syndrome characterized by transient left ventricular (LV) dysfunction, mimicking acute myocardial infarction.1 2 Guidelines for the diagnosis of ampulla cardiomyopathy were recently established in Japan.3

We report 2 rare cases of recurrent ampulla cardiomyopathy. Both patients experienced typical ampulla cardiomyopathy at the initial admission and atypical ampulla cardiomyopathy at the second admission. We diagnosed the transient LV apical ballooning as typical ampulla cardiomyopathy and the other types of transient LV ballooning as atypical ampulla cardiomyopathy in accordance with the guidelines.

Case Reports

Case 1

A 55-year-old woman with a history of rhabdomyolysis was admitted to the Department of Internal Medicine because of severe general fatigue, vomiting and weakness of the extremities related to recurrent rhabdomyolysis. She did not have chest oppression or dyspnea at the initial admission. At that time, her pulse rate was 127 beats/min, blood pressure 130/79 mmHg, and temperature 36.4°C. The leukocyte count was elevated at 11,800/μl. The serum levels of aspartate aminotransferase (AST) (208 IU/L), lactate dehydrogenase (LDH) (840 IU/L), creatine kinase (CK) (7,972 IU/L), CK-MB (68 IU/L) and C-reactive protein (CRP) (6.2 mg/dl) were also elevated. Electrocardiogram (ECG) revealed sinus rhythm and T-wave inversion in leads II, III, aVF and V1–6 with prolongation of the QT interval (QTc 0.52 ms) (Fig 1B). Transthoracic echocardiography on admission revealed akinesis of the left ventricle, except in the basal region (ejection fraction 41%) (Fig 2A). She recovered 4 weeks later and was discharged because her general condition had improved with treatment for rhabdomyolysis and repeat echocardiography showed normalization of LV wall motion. The T wave inversion and the QT interval also normalized before discharge.

One month later, she again experienced general fatigue, vomiting, weakness of the extremities again because of recurrent rhabdomyolysis, but she also had chest oppression and dyspnea. The leukocyte count was elevated (21,600/μl), as were the serum levels of AST (166 IU/L), LDH (709 IU/L), CK (2,713 IU/L), CK-MB (108 IU/L), CRP (5.9 mg/dl) and noradrenalin (NA) (1.492 pg/ml). ECG on admission revealed sinus rhythm and T-wave inversion in leads V1–3 with prolongation of the QT interval (QTc 0.50 ms) (Fig 1C). Transthoracic echocardiography on admission revealed a hypercontractile LV apex with an akinetic basal- to mid-LV (ejection fraction 43%) (Fig 2B). Urgent coronary angiography (CAG) did not reveal a significant stenotic lesion. Computed tomography of the abdomen and iodine-131-metaiodobenzylguanidine (MIBG) scintigraphy did not show pheochromocytoma. Her acute heart failure was medically treated, she recovered and was discharged.

Case 2

A 75-year-old man with a history of bronchial asthma was admitted to a nearby hospital because of worsening cough and dyspnea. He was treated with intravenous the-
ophylline and inhaled salbutamol. The following day, he experienced frequent chest oppression at rest and was referred for cardiac examination.

On admission, he was fully conscious, his pulse rate was 110 beats/min, blood pressure 113/75 mmHg, and temperature 36.2°C. The leukocyte count was elevated at 14,500/μl. The serum concentrations of AST (951 IU/L), LDH (2,187 IU/L) and CRP (5.2 mg/dl) were also elevated; however, the serum levels of CK (188 IU/L) and CK-MB (26 IU/L) were within normal limits. ECG revealed sinus rhythm and a negative T-wave in leads II, III, aVF and V3–6 with prolongation of the QT interval at initial admission (B) and in leads V1–3 with prolongation of the QT interval at the second admission (C).

Fig 1. Case 1. (A) Normal electrocardiogram (ECG) at medical checkup 1 year before the initial admission. ECG showing T-wave inversion in leads II, III, aVF and V3–6 with prolongation of the QT interval at initial admission (B) and in leads V1–3 with prolongation of the QT interval at the second admission (C).

Fig 2. Case 1. Echocardiograms of the left ventricle. Apical 2-chamber views of the left ventricle at end-diastole and end-systole at the initial admission (A) and second admission (B). The arrows indicate wall motion abnormalities.
Recurrent Ampulla Cardiomyopathy

Circulation Journal   Vol.73, February 2009

apical area of the LV (Fig 5A). We collected blood samples from the coronary sinus and measured the serum levels of brain natriuretic peptide (BNP: 4,400 pg/ml), adrenaline (AD: 202 pg/ml), NA (3,321 pg/ml) and dopamine (Dopa: 202 pg/ml). All these parameters were elevated above normal. Computed tomography of the abdomen did not show pheochromocytoma. His acute heart failure was medically treated. Transthoracic echocardiography performed 4 weeks later revealed marked improvement of the LV asynnergy and the ECG also showed normalization of T-wave

![Figure 3](image)

**Fig. 3.** Case 2. (A) Normal electrocardiogram (ECG) at medical checkup 6 months before the initial admission. ECG showing T-wave inversion in leads II, III, aVF and V5–6 at the initial admission with prolongation of the QT interval (B) and in leads V1–3 at second admission with atrial fibrillation (C).

![Figure 4](image)

**Fig. 4.** Case 2. Left ventriculograms (LVG) in the right anterior oblique view. (A, B) LVG at end-diastole and end-systole at initial admission (A) and at second admission (B). The arrows indicate wall motion abnormalities.
inversions and the QT interval. He had recovered from heart failure 1 month later and was discharged.

However, 3 months later, he was referred to a nearby hospital again because of infectious pneumonia and heart failure and was referred to us again. The leukocyte count was elevated (19,000/μl), as were the serum levels of AST (24 IU/L), LDH (213 IU/L) and CRP (3.2 mg/dl). However, the serum concentrations of CK (133 IU/L) and CK-MB (22 IU/L) were within normal limits. ECG on admission revealed atrial fibrillation and a negative T-wave in leads V1–3 (Fig 3C) with prolongation of the QT interval (QTc 0.52 ms). Transthoracic echocardiography and LVG on admission revealed a hypercontractile LV apex with an akinetic basal- to mid-LV (ejection fraction 32%) (Fig 4B).

The MIBG imaging showed improvement of uptake from the mid-portion to the apical area of the LV compared with the initial MIBG image (Fig 5B). The 201Tl imaging showed normalization of uptake. Serum levels of BNP (1,450 pg/ml), AD (1,125 pg/ml), NA (5,096 pg/ml) and Dopa (151 pg/ml) were evaluated using samples from the coronary sinus and all were elevated above normal. His acute heart failure was medically treated again, he recovered and was discharged.

Discussion

Ampulla cardiomyopathy has been reported as a novel acute cardiac disease, initially identified in the Japanese population and described as “takotsubo cardiomyopathy” (named for the similarities in the appearance of the LVG during systole to the “short-necked, round flask” appearance of the Japanese fishing pot used for trapping octopuses)4–6 Ampulla cardiomyopathy has subsequently been well described worldwide7–11 It involves transient regional systolic dysfunction in not only the LV but also the right ventricle12,13 and recently, a new variant of transient LV ballooning, defined as atypical ampulla cardiomyopathy, was reported. The LVG of this cardiomyopathy demonstrates midventricular dilatation and akinesis with a hypercontractile apex and base.14,15

Recurrent ampulla cardiomyopathy is infrequent, with one study reporting a recurrence rate of 11.4% over 4 years after initial presentation.16 Both emotional stress and physical stress cause recurrent ampulla cardiomyopathy and the time-to-recurrence ranges from 3 months to 13 years after initial presentation.2,8,17,18 In the present cases, typical ampulla cardiomyopathy was documented at the initial admission and atypical ampulla cardiomyopathy, indicated by transient basal midventricular ballooning, was documented at the second admission. We thought that these 2 cases were very rare because of the unique feature of the recurrence. Additionally, in each patient, physical stress triggered both the initial occurrence and the recurrence. We consider that appropriate management and treatment of the underlying disease are necessary in order to prevent the recurrence of the ampulla cardiomyopathy.

Electrocardiographic changes in patients with ampulla cardiomyopathy in comparison with the findings of acute myocardial infarction have been reported. Ogura et al found that the ratio of the ST-segment elevation in leads V4–6 to V1–3, the absence of reciprocal changes and the absence of abnormal Q-waves were useful for diagnosing ampulla cardiomyopathy.19 Kuris et al stated that the admission ECG usually showed ST-segment elevation or T-wave inversion in leads V1–6 and that the T-wave became inverted within 2 days and the T-wave inversion deepened progressively to its first negative peak, which occurred at approximately 3 days.20 In the present cases, the ECG on the initial admission showed T-wave inversion in leads V3–6 and on the second admission showed T-wave inversion in leads V1–3. These ECG changes might indicate the region of LV asynergy.

Multivessel epicardial spasm, coronary microvascular dysfunction or spasm, myocarditis, and catecholamine-mediated myocardial dysfunction have been proposed as potential mechanisms of ampulla cardiomyopathy1,8,21–26

Fig 5. Cardiac radionuclide single-photon emission computed tomography using iodine-123-metaiodobenzylguanidine (MIBG) and thallium-201 (201Tl) at the initial admission (A) and second admission (B).
Catecholamine-mediated myocardial dysfunction was considered to be the probable mechanism in these cases because each patient had physical stress shortly before the onset of symptoms and the plasma levels of catecholamine were high in both cases.

However, it is difficult to identify the cause of the differences in the wall motion abnormalities between the initial admission and the second admission. Hurst et al reported that the differences in the wall motion abnormalities of LV apical ballooning and midventricular ballooning reflect temporal variation in the resolution of apical ballooning by the time of angiographic diagnosis. A diffuse reduction in the uptake of MIBG indicates downregulation of \( \beta \)-adrenergic receptor density induced by high levels of circulating plasma catecholamines in patients with heart failure. So on that basis the present MIBG images indicate the possibility that the first excessive catecholamine stimulation led to downregulation of catecholamine receptors in the midportion to apical area of the LV. During the process of healing after severe damage to the LV, each patient was exposed to physical stress again. The reactivity or sensitivity difference to the second excessive catecholamine stimulation between the basal- to mid-portion and the apical area might have induced a hypercontractile LV apex with an akinetic basal- to mid-LV.

Further studies that elucidate the underlying mechanisms of typical and atypical ampulla cardiomyopathy are necessary to assist clinicians in preventing recurrence.

### References


