akotsubo cardiomyopathy has become well known to Japanese adult cardiologists since the report by Sato et al in 1990.1 It is characterized by transient left ventricular (LV) apical ballooning and specific electrocardiographic changes without coronary artery disease.1–8 We present a case of a 2-year-old Japanese girl with findings suggestive of takotsubo cardiomyopathy, and we believe this is the first report of the phenomenon in a young child. (Circ J 2006; 70: 509–511)

Key Words: Buprenorphine; Children; Takotsubo cardiomyopathy

A 2-year-old Japanese girl had transient left ventricular apical ballooning on echocardiography and ST-segment elevation and T-wave inversion on electrocardiogram after withdrawal of buprenorphine and midazolam. The findings improved within 2 weeks. There are many case reports of adults with takotsubo cardiomyopathy but none in children. Takotsubo cardiomyopathy is not well known by pediatric cardiologists, so pediatric cases may have been overlooked. Awareness of a phenomenon similar to takotsubo cardiomyopathy, even in young children, may be important. (Circ J 2006; 70: 509–511)

Case Report

A 16-day-old girl was referred to Kagoshima University Hospital because of tachycardia and tachypnea. She was diagnosed with ventricular septal defect, patent ductus arteriosus (PDA), and pulmonary hypertension. Normal coronary arteries were observed on left ventriculography. Because of the high pulmonary artery resistance (10 Wood units), when she was 2 months old she underwent division of the PDA and then pulmonary artery banding. She was referred to another hospital to be managed until the second operation. When she was 9 months old, she was referred back to us because of influenza encephalopathy and multiorgan failure.

After 3 months of intensive care, she recovered but with severe brain damage. During her rehabilitation, she had repeated episodes of respiratory failure because of infection and sometimes required mechanical ventilation.

When she was 32 months old, mechanical ventilation with administration of buprenorphine and midazolam was started because of respiratory failure caused by aspiration pneumonia. Vecuronium bromide was also used as the muscular relaxant. The infection was controlled and her general condition improved. Her Echocardiography showed normal LV wall motion, right ventricular and LV pressures were almost same, but the peak velocity of pulmonary flow was 3.9 m/s, and the estimated pulmonary arterial pressure was 30 mmHg. Therefore, administration of buprenorphine and midazolam was ceased on day 34 of mechanical ventilation after a 4-day staged withdrawal. On the evening of the 34th day, she began perspire heavily and developed tachycardia (170 beats/min). The next morning, hypotension (63/48 mmHg) and body weight loss (from 7,100 to 6,935 g) were obvious (Fig 1). A 12-lead electrocardiogram (ECG) revealed ST segment elevation and negative T-waves in leads 1, II, and V4–6 (Fig 2). Echocardiography showed akinesis with dilatation and systolic ballooning of the LV apical segment (Fig 3). Blood examination showed slightly elevated values for transaminases (aspartate aminotransferase: 59 IU/L, alanine aminotransferase: 45 IU/L) and normal values of creatine kinase (51 IU/L), troponin T (low), and myoglobin (<30 ng/ml). After buprenorphine
and midazolam administration was resumed, together with dopamine and dobutamine, the tachycardia and heavy perspiration disappeared. Lidocaine administration was also started after direct current defibrillation for the ventricular tachycardia. Two days later, there was recovery of LV wall motion on echocardiography and the ECG showed negative T-waves in V4–6 and prolonged QT intervals (Fig 2). The ECG findings improved within 2 weeks.

After this episode, administration of buprenorphine and midazolam were withdrawn slowly, and finally she was weaned from the mechanical ventilation support.

**Discussion**

Takotsubo cardiomyopathy is a cardiac syndrome comprising transient LV dysfunction with chest symptoms and ECG changes that mimic those of acute myocardial infarction. The clinical features of takotsubo cardiomyopathy are as follows: (1) transient LV apical ballooning on echocardiography or ventriculography that normalizes rapidly within a few weeks; (2) ST elevation on ECG at onset and then T-wave inversion in many leads, which increases a few days after the onset, and the QT-interval is prolonged; (3) mild peaks of creatine kinase, troponin etc. (4) rapid improvement within a few weeks in most cases, and recovery is satisfactory.

The present case had typical clinical features and the diagnosis was established retrospectively after her recovery from the acute symptoms. However, it is unknown whether takotsubo cardiomyopathy occurs in young children, because the mechanism of this cardiac abnormality has not yet been completely clarified. Therefore, the appropriate diagnosis of the present case is suspected takotsubo cardiomyopathy.

The incidence of takotsubo cardiomyopathy is approximately one in 150–200 adult cases of acute coronary syndrome. The majority of patients are older: the mean age is 66 years in men and 69 years in women. Cases of takotsubo cardiomyopathy are rarely reported in younger adults, therefore pediatric cardiologist would not be aware of it and cases in children may have been overlooked.

Various psychological and physical conditions are reported as possible triggering factors, including sudden accidents, aggravation of systemic disease, or surgery. The present patient developed heavy perspiration and tachycardia after withdrawal of buprenorphine and midazolam. Buprenorphine is an opioid partial agonist that is used for the treatment of acute and chronic pain. Mixed agonist–antagonists analgesics are commercially available for anal-

![Fig 2. Time course of electrocardiogram changes.](image)

![Fig 3. Echocardiographic findings. (A) Akinesis with dilatation and systolic ballooning of the left ventricular apical segment (arrow). (B) Two weeks later there is improved LV apical segment wall motion. LV, left ventricle; LA, left atrium; *ventricular septal defect.](image)
gesia, but prolonged use of buprenorphine can result in physical dependence.\textsuperscript{15} Symptoms of withdrawal include central nervous irritability, gastrointestinal dysfunction, and autonomic dysfunction\textsuperscript{16} such as the perspiration and central nervous irritability, gastrointestinal dysfunction, but prolonged use of buprenorphine can result in physical dependence.\textsuperscript{15} Symptoms of withdrawal include central nervous irritability, gastrointestinal dysfunction, and autonomic dysfunction\textsuperscript{16} such as the perspiration and tachycardia observed in our patient. A relationship between enhanced sympathetic activity and takotsubo cardiomyopathy has been postulated.\textsuperscript{2} Therefore, stress and/or enhanced sympathetic activity caused by the withdrawal of buprenorphine are the most likely factors triggering takotsubo cardiomyopathy in the present case. More careful withdrawal of buprenorphine and midazolam may be necessary to prevent the occurrence of takotsubo cardiomyopathy in young children.

The specific therapy for takotsubo cardiomyopathy has not been established; however, management of pump failure and arrhythmia is important,\textsuperscript{2} as is eliminating triggering factor(s). The present patient improved after re-starting buprenorphine and midazolam with administration of catecholamines and lidocaine.

In summary, a young child developed suspected takotsubo cardiomyopathy in addition to symptoms of withdrawal from buprenorphine. Awareness of the occurrence of a phenomenon similar to takotsubo cardiomyopathy, even in young children, may be important for pediatric cardiologists.

References


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