Takotsubo-like Transient Biventricular Dysfunction with Pressure Gradients

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Abstract

A 78-year-old woman was admitted to our hospital due to chest oppressive sensation. Admission electrocardiography revealed ST-segment elevation in I, II, III, aVF and V2–6 leads. Left ventriculography showed apical akinesis and basal hyperkinesis with a pressure gradient of 60 mmHg between the left ventricular apex and the base. Right ventriculography also showed similar abnormal wall motion with a pressure gradient of 28 mmHg. Follow-up cardiac catheterization after 16 days showed normal wall motion with no pressure gradients. However, dobutamine stress (10 µg/kg/min) caused a pressure gradient of 60 mmHg between the left ventricular apex and the aorta.

Case Report

A 78-year-old woman with a history of bronchial asthma was admitted to a nearby hospital because of worsening cough and dyspnea 7 days after her grandchild's sudden death. Admission electrocardiogram (ECG) revealed sinus tachycardia but no ischemic changes. She was treated with intravenous theophylline and inhaled salbutamol. The following day, she experienced chest oppressive sensation at rest, and was referred to our hospital for cardiac examination.

On admission, the patient was fully conscious, her pulse rate was 130 beats/min, blood pressure was 130/70 mmHg, and temperature was 36.6°C. The peripheral pulses were normal and she did not have edema. A harsh 3/6 systolic murmur was noted over the apex and left parasternal border. Admission laboratory studies disclosed the following values: leukocyte count, 8.5×10^9/l; hemoglobin, 13.2 g/dl; platelet count, 221×10^9/l; aspartate aminotransferase, 71 U/l; creatine kinase, 227 U/l; creatine kinase-MB isozyme, 28 U/l; potassium, 5.1 mEq/l; C-reactive protein, 3.73 mg/dl. The plasma levels of circulating norepinephrine and epinephrine were 3,269 (normal, 100 to 450 pg/ml) and 1,514 (normal <100 pg/ml), respectively. Admission ECG revealed sinus tachycardia and ST-segment elevation in I, II, III, aVF and V2–6 leads (Fig. 1). Transthoracic echocardiography revealed akinesis of the left ventricle except in the basal region. Left ventricular diastolic diameter was 35 mm. Interventricular septal thickness and left ventricular posterior wall thickness were 13 mm and 10 mm, respectively. A pressure gradient through the left ventricular outflow tract, measured using continuous wave Doppler recording, was 92 mmHg. Mitral regurgitation and systolic anterior movement of the mitral valve anterior leaflet were observed, but apical thrombus was
not seen. Emergency cardiac catheterization was performed immediately after admission. Coronary angiography showed no significant coronary artery disease (Fig. 2). However, left ventriculography showed abnormal wall motion with apical akinesis and basal hyperkinesis. The left ventricular ejection fraction was 44%. A pressure gradient of 60 mmHg between the left ventricular apex and the base and moderate mitral regurgitation were observed. Coronary spasm provocation test was not performed. Subsequently, we measured the following pressures via the right jugular vein with pigtail catheter. Pulmonary artery pressure was 26/16 mmHg. Pressures in the right ventricular apex and in the base were 52/10 mmHg and 24/10 mmHg, respectively. Because a pressure gradient of 28 mmHg was observed between the right ventricular apex and the base, right ventriculography was performed. Right ventriculography also showed abnormal wall motion with apical akinesis and basal hyperkinesis (Fig. 3). On the basis of these characteristic findings, we diagnosed her with takotsubo-like biventricular dysfunction with pressure gradients.

Her symptoms disappeared about 6 hours after admission. After 24 hours, ST-segment elevation was normalized, and T wave was inverted. T wave deepened and reached the first peak of inversion after 2 days. T wave shallowed and subsequently deepened again. It reached the second peak of inversion after 3 weeks (Fig. 1). These findings were consistent with the time course of ECG findings of takotsubo syndrome that we have previously reported (4). Abdominal computed tomography revealed no evidence of pheochromocytoma.

Follow-up transthoracic echocardiography after 14 days revealed normal wall motion and disappearance of left ventricular outflow tract obstruction, mitral regurgitation or systolic anterior movement of the mitral valve anterior leaflet.

Follow-up cardiac catheterization was performed after 16 days. Coronary angiography showed no significant coronary artery disease, and left ventriculography and right ventriculography showed normal wall motion (Fig. 4). Pressures in the left ventricular apex and in the aorta were simultaneously measured. At rest, there was no significant pressure gradient. However, dobutamine stress (10 μg/kg/min) caused a pressure gradient of 60 mmHg (Fig. 5). She was discharged after 20 days with oral diltiazem (90 mg/day). No cardiac events occurred during the follow-up of 20 months.

**Discussion**

In this report, we demonstrated a case of takotsubo syndrome complicated by transient biventricular dysfunction.
Figure 2. Coronary angiography showed no significant coronary artery disease.

Figure 3. Left ventriculography showed apical akinesis and basal hyperkinesis with a pressure gradient of 60 mmHg between the left ventricular apex and the base. Right ventriculography also showed similar abnormal wall motion with a pressure gradient of 28 mmHg between the right ventricular apex and the base.
Several reports have described patients with transient left ventricular apical ballooning without significant coronary artery disease. In Japan, this asynergy has been widely called takotsubo-like left ventricular dysfunction (1–9), and this syndrome is gradually being established worldwide (10–17). Major clinical characteristics are that (1) most patients are elderly women; (2) the symptoms are similar to those of acute myocardial infarction; (3) takotsubo-like left ventricular dysfunction, which extends over more than one coronary artery region, is transient and dramatically resolves within several weeks. These findings are consistent with those of the current patient.

In this syndrome, emotional or physical stress is recognized as an important predisposing factor. In fact, she had had frequent cough and dyspnea due to bronchial asthma after her grandchild’s sudden death. These mental and physical stresses might be associated with the development of takotsubo syndrome in the current patient.

We, as well as other groups, have reported several possible mechanisms of takotsubo syndrome including epicardial coronary spasm, microvascular dysfunction (spasm), catecholamine cardiotoxicity (1–6), but the precise cause remains unclear. Excessive catecholamine production has been known to induce left ventricular dysfunction in patients with pheochromocytoma (18). The current patient had takotsubo-like left ventricular dysfunction and high levels of circulating norepinephrine and epinephrine. Whether increased catecholamine was the cause or the consequence of takotsubo syndrome with heart failure remained unclear. She was treated with inhaled salbutamol, which had a bronchodilator effect through beta-2 adrenoceptor stimulation, in a nearby hospital. It was a common treatment of bronchial asthma attack, and there has been no report demonstrating the

Figure 4. After 16 days, left ventriculography and right ventriculography showed normal wall motion with no pressure gradients.
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Development of left ventricular dysfunction as a definite adverse effect of inhaled beta-2 agonist (19). We thought that there was little possibility of a relation between the treatment and the development of takotsubo syndrome. The other possible mechanism was myocarditis localized in the apical region. Because myocardial biopsy was not performed in the current patient, this could not be excluded completely.

A pressure gradient through the left ventricular outflow tract was sometimes documented during the early phase of takotsubo syndrome. Tsuchihashi et al (5) reported that this finding was observed in 13 of 72 patients (18%) during the early phase, but not in 56 patients during the subacute phase. Until now, we also encountered 5 patients with pressure gradient, and all patients were discharged after the disappearance of this finding. This complication does not appear to influence the clinical outcome in takotsubo syndrome. Several mechanisms of this complication are postulated. In general, most patients with takotsubo syndrome are elderly women. The current patient was also a 78-year-old woman, and her left ventricular diastolic diameter of 35 mm was relatively small. Thus, one possible mechanism is that the small left ventricular outflow tract and reduced left ventricular volume may cause dynamic left ventricular outflow tract obstruction, which may manifest under intense adrenergic stimulation and hypovolemia. The current patient had mild cardiac hypertrophy on transthoracic echocardiography. On predischarge cardiac catheterization, there was no significant pressure gradient through the left ventricular outflow tract at rest. However, dobutamine stress (10 μg/kg/min) caused a pressure gradient of 60 mmHg. Thus, the other possible mechanism is that subclinical cardiac hypertrophy also may contribute to the development of dynamic left ventricular outflow tract obstruction. Because myocardial biopsy was not performed in the current patient, the precise etiology of cardiac hypertrophy remained unclear.

The current patient had high levels of catecholamines and spontaneous left ventricular outflow tract obstruction during the early phase, and dobutamine stress-induced left ventricular outflow tract obstruction at predischarge. From the viewpoint of these pathophysiological findings, beta-blocker was a promising treatment. In fact, Villareal et al (20) have previously reported that intravenous beta-blocker abolishes left ventricular outflow obstruction in 3 patients with anteropapical myocardial stunning which is probably the same as takotsubo-like left ventricular dysfunction. However, this complication was transient, and beta-blocker might make heart failure worse through a negative inotropic effect. In addition, the current patient had a history of bronchial asthma which was one of the side effects of beta-blocker, and coronary spasm could not be excluded as a cause of takotsubo syndrome. These were why we treated the patient not with beta-blocker, but with diltiazem which has been used for the treatment of hypertrophic cardiomyopathy or variant angina through negative inotropic, negative chronotropic and antianginal effects.

A few case reports have recently demonstrated that the right ventricle is involved in takotsubo syndrome (21). Because we have not performed right ventriculography routinely, it is unclear how often takotsubo-like right ventricular dysfunction occurs during the early phase of takotsubo syndrome. In addition, whether right ventricular dysfunction occurs actively or passively accompanied by left ventricular dysfunction remains unclear. Further studies are necessary to clarify the incidence or the mechanism of takotsubo-like right ventricular dysfunction.

Figure 5. Pressures in the left ventricular apex and in the aorta were simultaneously measured. At rest, there was no significant pressure gradient. However, dobutamine stress (10 μg/kg/min) caused a pressure gradient of 60 mmHg.

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<td>Left ventricular apex at rest</td>
<td>148/4 mmHg</td>
<td>Aorta at rest</td>
<td>142/64 mmHg</td>
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<td>Pressure gradient</td>
<td>6 mmHg</td>
<td>Pressure gradient</td>
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<td>Left ventricular apex during dobutamine stress</td>
<td>180/6 mmHg</td>
<td>Aorta during dobutamine stress</td>
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Internal Medicine Vol. 44, No. 7 (July 2005)
References


