Reversible Ventricular Dysfunction Takotsubo (ampulla-shaped) Cardiomyopathy

Key words: takotsubo, cardiomyopathy apical ballooning, catecholamine, cytokine, heart failure

In recent years, several patients with a clinical presentation resembling acute myocardial infarction have been found to have normal coronary arteries and a left ventricle shaped like an octopus trap (takotsubo in Japanese) on ventriculography or echocardiography. This condition has come to be known as “takotsubo” cardiomyopathy (1–12). Literature to date has included fairly frequent reports from Japan (1–12) and three reports from other parts of the world (13–15). In most of the cases reported, the left ventricular (LV) dysfunction resolved within a few weeks. The combined data from previous reports and our own clinical experience suggest that takotsubo cardiomyopathy accounts for about 1 to 2% of all patients presented with apparent manifestation of acute myocardial infarction (6). However, the etiology and clinical features of this form of reversible LV dysfunction still remain unclear.

Sato et al (12) published what we believe to be the first report of a case of takotsubo cardiomyopathy associated with microscopic polyangiitis. Based on their experience with this very rare case, they concluded that microscopic polyangiitis might be a causative factor of this disease. Although they did not perform cardiac catheterization, they clearly demonstrated wall motion abnormalities using echocardiography. Moreover, in repeated electrocardiographic examination over the first 2 months after the onset of microscopic polyangiitis, the disease presented the same T-wave inversion characteristically seen in patients with takotsubo cardiomyopathy. The patient of Sato et al (12) manifested two possible etiologies for this syndrome: microscopic angiitis and inflammatory myocardial damage. In the case of the former, impairment of the coronary microcirculation due to the polyangiitis might have been the mechanism behind the reversal ventricular dysfunction. In the case of the latter, a skin biopsy proved that the small vessel was inflamed, though the cardiac muscle itself was never biopsied.

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When this disease was known as a systematic inflammatory disease, no one doubted that this inflammatory process would influence the cardiac tissue, i.e., the coronary vascular tissue or the muscle itself. As soon as focal inflammation occurred in the cardiac muscle, consensus was that reversal ventricular dysfunction might have been present. While the wall motion has completely recovered within a few weeks in most of the reported cases with takotsubo cardiomyopathy, the attending physicians have insisted on treatment with high-dosage methylprednisolone drip.

Treatment with an anti-inflammatory agent was remarkably effective for the systemic inflammation and focal cardiac damage in the case of Sato et al (12). We speculate that the treatment may have suppressed the excessive secretion of various cytokines. Again, their case manifested two apparent causations of the takotsubo cardiomyopathy. When considered together with all of the previous findings in sum, the report from Sato’s group will have a great influence on the further research of this disease.

Reversible LV dysfunction is usually attributed to myocardial stunning due to impaired coronary blood flow (13). Some authors have suggested that impaired coronary microcirculation might be the mechanism behind the reversible LV dysfunction in takotsubo cardiomyopathy, but myocardial perfusion scintigraphy shows few abnormal findings (3, 4). Myocardial stunning due to vasospastic angina has been proposed as another possible mechanism, but this has also been cast into doubt by a study on coronary vasospasms using ergonovine and/or acetylcholine in 10 patients with takotsubo cardiomyopathy. As it turned out, all 10 of the patients had normal coronary arteries (3). Furthermore, the ST segment changed in various leads on the ECG, which is not consistent with the obstruction of a specific coronary artery. Histological evidence of myocardial damage in the absence of coronary artery disease has been reported in patients with fatal subarachnoid hemorrhage (14).

I propose that takotsubo cardiomyopathy may represent a myocardial response to excessive circulating catecholamines or cytokines. The elevation of catecholamines may have been the primary cause of takotsubo cardiomyopathy, or a result of the condition (2). On the other hand, circulating plasma norepinephrine levels were reported to be close to normal in patients with takotsubo cardiomyopathy (5–8). While this suggests that the overactivation of the cardiac catecholamine receptors may have taken place secondarily to the heart failure, it may also have been the cause of the cardiomyopathy. In experiments by Ueyama et al (9) in rats, the cardiac change induced by emotional stress occurred primarily via the activation of alpha- and beta-adrenoceptors.
They also reported an upregulation of natriuretic peptide genes in the myocardium. Sato et al (12) performed the methylprednisolone pulse therapy in their patient with *takotsubo* cardiomyopathy. The high-dosage steroid infusion might reduce the secretion of norepinephrine, as well as suppress the production of cytokines.

*Takotsubo* cardiomyopathy is also a new entity of acute heart failure. This cardiomyopathy should be noted as a possible cause of sudden cardiac death in individuals without obvious heart disease. Fortunately, the prognosis is good among patients who survive the initial severe heart failure without complications. Catecholamine overload, adrenoceptor hypersensitivity, or abnormal catecholamine dynamics due to stress may be the primary cause of this condition. For this reason, adrenoceptor blockade has the potential to prevent this syndrome. Systemic anti-inflammatory agents may also be effective in preventing deterioration of the heart failure. Worldwide research is necessary to clarify the etiology and clinical features of *takotsubo* cardiomyopathy.

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References


