Effect of Intravenous Propranolol on Left Ventricular Apical Ballooning Without Coronary Artery Stenosis (Ampulla Cardiomyopathy)

— Three Cases —

Michifumi Kyuma, MD; Kazufumi Tsuchihashi, MD; Yasuyuki Shinshi, MD; Mamoru Hase, MD; Tomoaki Nakata, MD; Hitoshi Ooiwa, MD*; Masayoshi Abiru, MD*; Nobuichi Hikita, MD*; Tateo Adachi, MD*; Tetsuro Shoji, MD*; Yukiyasu Fujise, MD*; Kazuaki Shimamoto, MD

The precise etiological basis of transient left ventricular apical ballooning without coronary artery stenosis (ampulla or so-called ‘takotsubo’ cardiomyopathy) remains unknown, so the present study examined the acute effects of intravenous propranolol (2–4 mg) in 3 female patients (age range, 61–76 years) with the condition. Although one patient who did not have any intraventricular pressure gradients showed no improvement in the electrocardiographic and left ventricular wall motion abnormalities, the other 2 patients, who had significant intraventricular pressure gradients, did show improvement. Dynamic intraventricular obstruction might play a role in maintaining apical ballooning, at least, in patients exhibiting an intraventricular pressure gradient.

Key Words: Ampulla cardiomyopathy; Propranolol; Regional apical ballooning; Takotsubo cardiomyopathy

Case Reports

Case 1

A 61-year-old woman was first admitted to Sapporo Medical University Hospital on December 3, 1999 with the symptoms of frequent episodes of rest and effort chest pain. Treadmill exercise and a Holter electrocardiogram showed ST elevation (CM5 or II, III, aVF) with and without chest pain. Coronary angiography did not reveal any significant stenosis in the epicardial coronary artery. After administration of long-acting diltiazem (200 mg/day), her attacks and asymptomatic ST elevation were well-controlled. While taking a bath at 00.00 h on February 2, 2001, she experienced nitroglycerine-resistant chest pain without any somatic and/or psychological stress, and she was re-admitted 4 h after onset. ST elevation and Q wave formation in leads aVL, V2 and V3 and minimal cardiac enzyme release (peak creatine kinase, 173 L; troponin T, 0.79 ng/ml) were confirmed. There was no pulmonary congestion, but her blood pressure on admission was 88/58 mmHg. Cardiac catheterization revealed left ventricular apical ballooning (ejection fraction (EF), 36%) and the intraventricular pressure gradient was 45 mmHg. Eight h after onset, intravenous propranolol (4 mg) was administered for 5 min under electrocardiographic monitoring. The electrocardiographic changes (ST elevation and Q wave, Fig 1) and echocardiographic wall motion abnormalities (basal hypercontraction and apical ballooning) improved, and the intraventricular pressure gradient decreased to 24 mmHg immediately after injection. Oral carvedilol (10 mg/day for 3 days) was instituted and the electrocardiographic and wall motion abnormalities disappeared within 1 week. Left ventriculography performed 26 days after readmission showed normal wall motion with an EF of 68%.
Case 2
A 76-year-old woman with Shy-Drager syndrome was admitted to the intensive care unit of Oji General Hospital on August 28, 2000 because of hemoptysis and bronchopneumonia. Intubation and mechanical ventilation were begun, but the next day she suddenly developed persistent hypotension (60/40 mmHg) with ST elevation and Q wave formation in leads II, III, aVr, and V2-6 (Fig 2) and a peak creatine kinase of 178 L and troponin T of 1.08 ng/ml. A harsh 2/6 systolic murmur was heard in the apex and left parasternal border. A left ventriculogram and coronary angiogram revealed apical ballooning without coronary stenosis (Fig 2). After cautious intravenous administration of propranolol (2 mg) under echocardiographic monitoring, her depressed blood pressure recovered to 160/80 mmHg with minimal apical asynergy, ECG changes and systolic
Effect of IV Propranolol on Ampulla Cardiomyopathy

Circulation Journal Vol.66, December 2002

Ejection murmur, and an estimated reduction in the intraventricular pressure gradient from 140 to 40 mmHg (Fig 3). However, 1 h after the acute challenge, she once again developed hypotension with systolic murmur, which required continuous intravenous administration of propranolol (0.03 μg·kg⁻¹·min⁻¹) plus oral metoprolol (20 mg/day) for 10 days. Two months later, her ECG and echocardiogram were normal, but she subsequently died from uncontrolled recurrent pulmonary infection.

Case 3
A 76-year-old woman with paroxysmal atrial fibrillation, sick sinus syndrome and hypertension was admitted to Muroran General Hospital on May 26, 2001 because of persistent chest pain without any somatic and/or psychological stress. Her blood pressure on admission was 134/70 mmHg and there was no audible heart murmur. An ECG showed ST elevation in leads I, II, III, aVL, aVF and V2–6, and Q wave formation in leads I, aVL and V2–6 (Fig 4). Her creatine kinase level was elevated to 649 L. Emergency coronary angiography showed no systolic wall motion disturbance, and left ventriculography confirmed the presence of severe anterolateral dyskinesis with basal hypercontraction (Fig 5). However, the left ventricle to aorta pull back pressure tracing revealed no significant intraventricular pressure gradient. Intravenous administration of propranolol (4 mg) resulted in no significant improvement in the left ventriculography findings, hemodynamic state or ECG changes (Fig 4). Eighteen days later, coronary angiography, left ventriculography and acetylcholine challenge were performed. Left ventriculography showed mild anterior hypokinesis and improvement in LV function, and coronary spasm was achieved after a challenge with 100 μg of acetylcholine to the left coronary artery (left anterior descending artery) (Fig 5). Serial ECGs demonstrated resolution of the aforementioned abnormalities. At 1-month follow-up, the patient showed excellent functional recovery.

Discussion
Case studies of transient left ventricular apical ballooning without coronary artery stenosis (ampulla or so-called takotsubo cardiomyopathy) have been concentrated mainly in Japan.1–8 This novel heart syndrome is characterized by (1) various systemic disorders (eg, cerebrovascular accidents, epileptic attacks, exacerbation of bronchial asthma, acute abdomen, noncardiac surgery) and an emotional/physical background (sudden accidents, death/funeral of a family member, unusual exercise, quarreling and/or excessive alcoholic consumption, vigorous excitement) as triggering factors; (2) no differences between the clinical characteristics of patients with and those without underlying disorders except for gender likelihood and chest pain/discomfort as an initial symptom; and (3) transient intraventricular pressure gradient and provocative coronary vasospasm in some cases.1–15 However, the precise pathophysiological bases, such as the mechanism of onset and female dominancy, and of the localized apical asynergy, are still not clear.

Regional Apical Ballooning and Intraventricular Pressure Gradient
It is not clear why the ventricular apex is selectively vulnerable and subsequently balloons, but several anatomical and physiological factors might contribute to the left ventricular apical wall motion abnormalities; for example, the left ventricular apex does not have a 3-layered myocardial structure16 and the adrenoreceptor density varies throughout the heart, with its greater density in the apex of the LV.17 Another possible explanation of apical ballooning is
Dynamic midventricular obstruction.

Our previous multicenter retrospective study revealed that only 12 of 72 (18%) patients with this condition had a significant intraventricular pressure gradient of more than 30 mmHg in the acute period (<48 h after onset), so dynamic midventricular obstruction is not the main cause. Although the configuration of left ventricular asynergy is different from that of midventricular obstruction, apical aneurysm formation in midventricular obstruction of hypertrophic cardiomyopathy has been reported. Additionally, the improvement in apical asynergy in specific cases following acute propranolol injection suggests that dynamic intraventricular obstruction does play a role in the persistent hemodynamic, electrocardiographic, and echocardiographic wall motion abnormalities when there is a definite intraventricular pressure gradient. Secondary ischemia caused by the increased wall tension and dynamic midventricular obstruction, as in sigmoid septum and obstructive cardiomyopathy, might also be important contributory factors. In the present study, the activation of sympathetic nerves in the cases that showed significant intraventricular pressure gradient may be stronger than when there is no an intraventricular pressure gradient and β-blockers might be very effective in such cases. The case that did not show any effects of the β-blocker did not have an intraventricular pressure gradient and the presence of this pressure gradient may differentiate between β-blocker effective and non-effective cases. However, we need to investigate further cases and gather more information to confirm this.

Clinical Implications

Cruickshank et al. showed that there was a correlation between catecholamine concentration and ECG changes and that oral propranolol depressed ST segment elevations observed in leads V5,6. Pharmacologic sympathetic blockade with propranolol and phenolamine also prevents myocardial necrosis after subarachnoid hemorrhage. Our case presentations highlight the possibility of using short-acting β-blocker for this syndrome. The frequent complications of hypotension and pulmonary edema in this syndrome might not be effectively controlled by inotropic agents or intra-aortic balloon pumping, although Villareal et al. have recently shown that intravenous administration of metoprolol resulted in resolution of the intraventricular pressure gradient and clinical improvement. Intravenous administration of propranolol must be performed with careful monitoring, because there are many contraindications of β-blocker use, such as asthma, respiratory failure, diabetic coma, uncontrolled pheochromocytoma, vasospasm and brady-arrhythmias, all of which are frequently seen in transient left ventricular ballooning. An ultra-short-acting β-blocker is more appropriate in such cases. Adjunctive administration of an oral β-blocker might be needed to overcome short-term remission such as was observed in case 2; however, considering the risk of exacerbating the vasospasm by β-blocker use, further case-controlled studies must be undertaken to confirm the usefulness of this therapy in transient apical ballooning.

Conclusions

The effect of intravenous propranolol on the hemodynamic, electrocardiographic and wall motion abnormalities in 3 patients with transient left ventricular apical ballooning has been described. The results in 2 cases suggest that functional intraventricular obstruction plays a deleterious role in the apical asynergy, at least when there is an intraventricular pressure gradient.

References