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Transient Left Ventricular Apical Ballooning Without Coronary Artery Stenosis: A Novel Heart Syndrome Mimicking Acute Myocardial Infarction

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OBJECTIVES To determine the clinical features of a novel heart syndrome with transient left ventricular (LV) apical ballooning, but without coronary artery stenosis, that mimics acute myocardial infarction, we performed a multicenter retrospective enrollment study.

BACKGROUND Only several case presentations have been reported with regard to this syndrome.

METHODS We analyzed 88 patients (12 men and 76 women), aged 67 ± 13 years, who fulfilled the following criteria: 1) transient LV apical ballooning, 2) no significant angiographic stenosis, and 3) no known cardiomyopathies.

RESULTS Thirty-eight (43%) patients had preceding aggravation of underlying disorders (cerebrovascular accident [n = 3], epilepsy [n = 3], exacerbated bronchial asthma [n = 3], acute abdomen [n = 7]) and noncardiac surgery or medical procedure (n = 11) at the onset. Twenty-four (27%) patients had emotional and physical problems (sudden accident [n = 2], death/funeral of a family member [n = 7], inexperience with exercise [n = 6], quarreling or excessive alcohol consumption [n = 5] and vigorous excitation [n = 4]). Chest symptoms (67%), electrocardiographic changes (ST elevation [90%], Q-wave formation [27%] and T-wave inversion [97%]) and elevated creatine kinase (56%) were found. After treatment of pulmonary edema (22%), cardiogenic shock (15%) and ventricular tachycardia/fibrillation (9%), 85 patients had class I New York Heart Association function on discharge. The LV ejection fraction improved from 41 ± 11% to 64 ± 10%. Transient intraventricular pressure gradient and provocative vasospasm were documented in 13/72 (18%) and 10/48 (21%) of the patients, respectively. During follow-up for 13 ± 14 months, two patients showed recurrence, and one died suddenly.

CONCLUSIONS A novel cardiomyopathy with transient apical ballooning was reported. Emotional or physical stress might play a key role in this cardiomyopathy, but the precise etiologic basis still remains unclear. (J Am Coll Cardiol 2001;38:11–8) © 2001 by the American College of Cardiology

A heart syndrome exhibiting acute onset, transient (reversible) left ventricular (LV) apical wall motion abnormalities with chest symptoms, electrocardiographic (ECG) changes (ST elevation or depression, abnormal Q-wave) and minimal myocardial enzymatic release mimicking acute myocardial infarction (AMI) in patients without angiographic stenosis on coronary angiogram (CAG) has been reported. It was first described by Satoh et al. (1) and Dote et al. (2) and was named "Takotsubo"-shaped cardiomyopathy due to its unique "short neck round-flask"-like LV apical ballooning resembling the *tako-tsubo* (Japanese for octopus pot or trap) of Japan. Several cases have been reported in Japan (3–6). A similar type of apical wall motion abnormality has also been reported in myocardial injury in several systemic disorders, including multivessel vasospasm, cerebrovascular accidents, gastrointestinal bleeding and pheochromocytoma (7–13). However, previous case reports from single centers have only presented some of the clinical characteristics, and no clinical studies using the same diagnostic criteria have been performed. Therefore, the precise clinical features and the etiologic basis of this syndrome remain unclear.

To determine the clinical characteristics of transient apical ballooning, the members of Angina Pectoris-Myocardial Infarction (AP-MI) investigations in Japan have retrospectively registered and analyzed patients.

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Abbreviation and Acronyms

AMI = acute myocardial infarction
AP-MI = Angina Pectoris-Myocardial Infarction investigations
CAG = coronary angiogram or coronary angiographic
CK = creatine kinase
ECG = electrocardiogram or electrocardiographic
LV = left ventricle or left ventricular
LVG = left ventriculography or left ventriculographic

SUBJECTS AND METHODS

Registration criteria. From December 1991 to June 2000, a total of 125 patients with transient LV apical wall motion abnormalities without stenosis on CAG were retrospectively enrolled from cardiovascular institutes of AP-MI investigations in Japan (see Appendix). In this study, data from 88 patients were selected for analysis based on the following criteria: 1) patients with suspected AMI based on chest symptoms or ECG changes (ST-T changes, abnormal Q-wave formation); 2) transient LV ballooning confirmed by left ventriculography (LVG) or echocardiography; and 3) CAG-confirmed normal epicardial artery (luminal narrowing of <50% in all three coronary arteries) within 48 h of the onset.

In these selected patients, LV apical ballooning was confirmed by LVG in 77 patients (88%) in the acute phase (8 ± 9 h after onset; range, 1 to 48 h) and by echocardiography in all the subjects immediately after the onset. Patients with idiopathic cardiomyopathy, febrile disorders, pheochromocytoma or prior history of myocardial infarction and those receiving coronary revascularization therapy were excluded from this study. Thirty-seven of the 125 patients were excluded from this study due to a lack of coronary angiographic evaluation in the acute period (n = 35) or due to an underlying disorder (pheochromocytoma, n = 2). For analyses of 12-lead ECG findings and quantitative LV wall motion, patients with atrial fibrillation, intraventricular conduction abnormalities and frequent premature ventricular contractions were also excluded.

Methods. Clinical characteristics (age, gender, onset, coronary risk factors) and the condition that preceded onset as a possible triggering factor were analyzed. Major coronary risk factors were determined by the Sixth Report of the Joint National Committee (1997) in hypertension and by the American Diabetes Association (1998) in diabetes. Hyperlipidemia was defined as hypercholesterolemia of ≥220 mg/dl or hypertriglycemia of ≥150 mg/dl. Cardiac enzyme release (creatine kinase [CK] release measured every 3 or 4 h [n = 88] and troponin T release measured once a day [n = 43]) for determining peak values and 12-lead ECG findings (ST shifts, T-wave changes and Q-wave formation in all leads) were examined in each registered center.

In the acute period, LV end-diastolic pressure and intraventricular pressure gradient, in which >30 mm Hg is defined as significant, were measured in 72 patients. Left ventricular wall motion was analyzed using contrast LVG. In the subacute period (24 ± 11 days; range: 13 to 53 days), vasospasm was assessed in 48 (55%) of the patients by a previously validated method using intracoronary acetylcholine administration (14). The functional change in LV wall motion was studied by LVG in 56 (64%) of the patients, and intraventricular pressure gradient was also examined.

Complications (arrhythmias, pulmonary edema and cardiogenic shock) and the use of intravenous catecholamine and assist devices (intra-aortic balloon pumping, percutaneous cardiopulmonary support system) were examined by review of medical records. In-hospital death and late follow-up of recurrences were also investigated by direct interviews with patients and by reviewing medical records.

Statistical analysis. All of the data are expressed as mean ± 1 SD. The differences between cardiac functions on LVG in the acute and subacute periods were compared using paired Student *t* tests. The differences between incidences in two groups were analyzed by the chi-square test. A p value < 0.05 was considered to be statistically significant.

RESULTS

Representative patients. CASE 1. A 72-year-old woman was admitted to Sapporo Medical University (Sapporo, Japan) on September 17, 1997 due to exacerbation of bronchial asthma and was transferred from another hospital. Ten days later, she felt chest pain at rest. A 12-lead ECG showed ST elevation in I, aVL and V_1 to V_5 (max +4.5 mm in V_3), reciprocating ST depression II, III, aVF and V_6 and abnormal Q-wave in leads V_1 to V_4 (Fig. 1). One hour later, LVG revealed LV apical ballooning (Fig. 1), but no significant stenosis on CAG was confirmed. Intracardiac pressure recording (Fig. 2) showed intraventricular pressure gradient estimated at 75 mm Hg. Maximally released CK was 242 IU/l. After 14 days, the ECG had no ST elevation or abnormal Q-wave but showed a typical coronary T-wave in leads aVL and V_1 to V_4. The LVG demonstrated remarkable functional recovery with an ejection fraction of 72% (Fig. 1), and the intraventricular pressure gradient disappeared (Fig. 2).

CASE 2. A 75-year-old woman was admitted to National Cardiovascular Center (Suita, Osaka, Japan) after sudden onset of chest pain. The ECG showed ST elevation in leads II, III, aVF and V_3 to V_6 (max +2.2 mm in V_5). Initial LVG revealed typical apical ballooning (Fig. 3). The CAG did not show any significant luminal narrowing. At 28 days after admission, the ECG improved and only exhibited a negative T-wave. Follow-up CAG was performed, and it was found that apical ballooning had completely disappeared. Maximal CK release was 206 IU/l. Intracoronary acetylcholine did not reveal any vasospasm. Nuclear cardiographic evaluations showed marked perfusion-metabolic mismatches, mainly at the LV apex (Fig. 4). After five months, all of the nuclear images became normal, and positron emission computed tomogram by N-13 ammonia

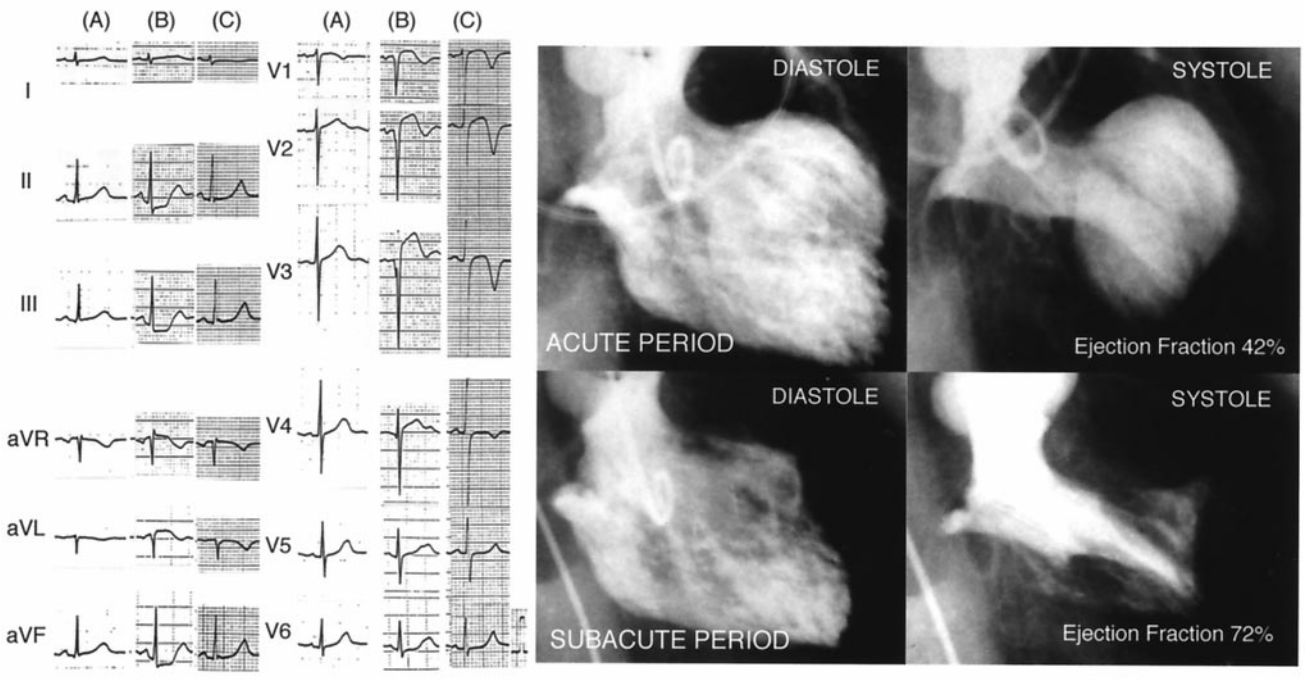

Figure 1. Representative electrocardiographic changes and left ventriculogram of transient left ventricular (LV) apical ballooning (Case 1). **(Left)** 12-lead electrocardiogram during chest pain **(B)** demonstrated ST elevation in leads I, aVL, V_1 to V_5 and reciprocating ST depression in leads II, III and aVF compared with control **(A)**. Fourteen days after onset **(C)**, a coronary T-wave was confirmed. **(Right)** Left ventriculogram demonstrated LV apical ballooning. After 15 days, almost all of the contracted LV configuration recovered to normal.

showed depressed flow-reserve. However, five months later the positron emission computed tomogram was normal.

Possible triggering factors at the onset of transient LV apical ballooning. Various psychological and physical conditions have been documented. Eighteen patients had emotional problems at the onset: sudden accidents (n = 2: a house fire in which the husband suffered severe burns, witnessing a grandson's traffic accident) and death/funeral (n = 7: sudden death of a husband, attending the funeral of a relative, anxiety over a congenital disorder in a family member), quarreling or excessive alcohol consumption (n = 5) and vigorous excitation (n = 4: while watching TV or

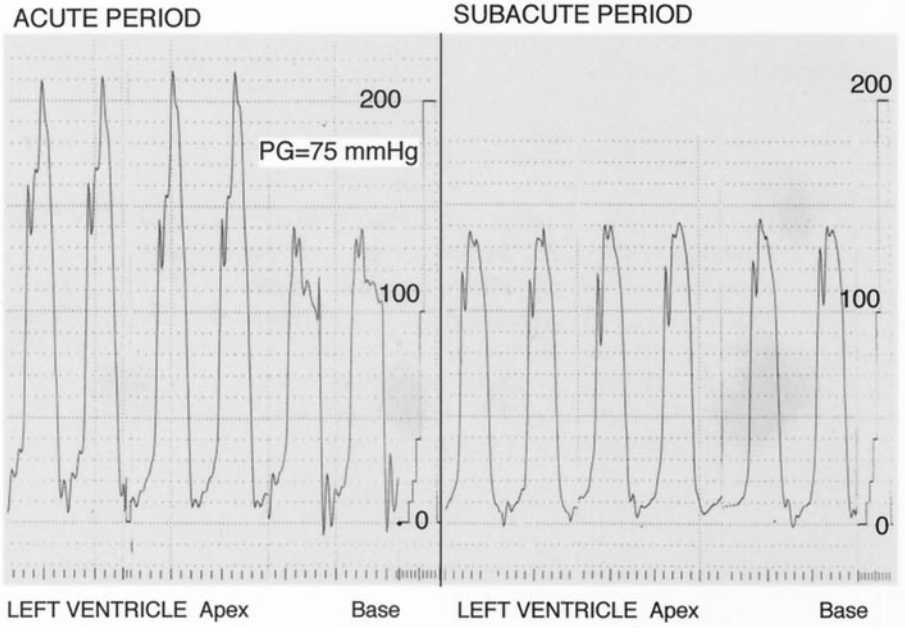

Figure 2. Changes in intracardiac pressure recording (Case 1). Intraventricular pressure recording immediately after onset revealed a significant intraventricular pressure gradient (PG), estimated to be 75 mm Hg, with a systolic ejection murmur (Levine III/VI). In the subacute period, no significant pressure gradient was recorded.

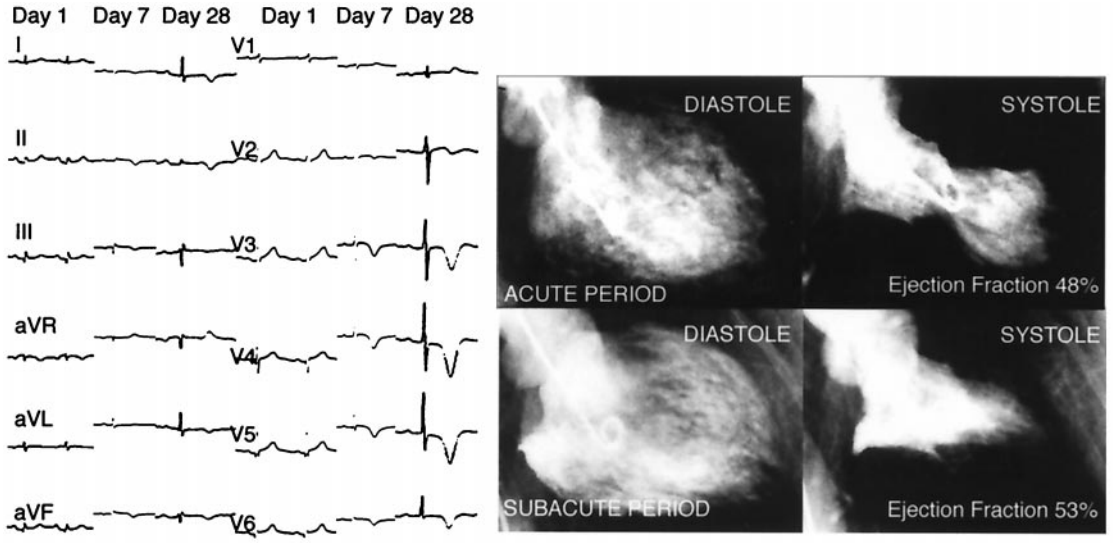

Figure 3. Electrocardiography and left ventriculographic findings of a representative case (Case 2). **(Left)** 12-lead electrocardiogram showed ST elevation in leads II, III, aVF and V_3 to V_6. In the subacute period, the electrocardiogram exhibited a negative T-wave. **(Right)** Initial left ventriculogram revealed apical ballooning only in the acute period.

during sexual intercourse). Inexperienced exercise (dancing, bowling, gateball; lifting work during house moving) was also documented in six patients.

As shown in Table 1, 38 patients had a wide spectrum of onset and aggravation of systemic disease including acute-phase cerebrovascular accidents (n = 3), attacks of epilepsy (n = 3), exacerbation of bronchial asthma (n = 3), commencement of dialysis therapy (n = 4) and acute abdomen with pain (n = 7). Moreover, 11 patients exhibited this syndrome during noncardiac surgery or during a procedure (intubation, tracheotomy, transbronchial lung biopsy, delivery, general anesthesia for orthopedic surgery, cholecystectomy, subtotal gastrectomy and colonectomy). The remaining 23 patients had no such specific conditions.

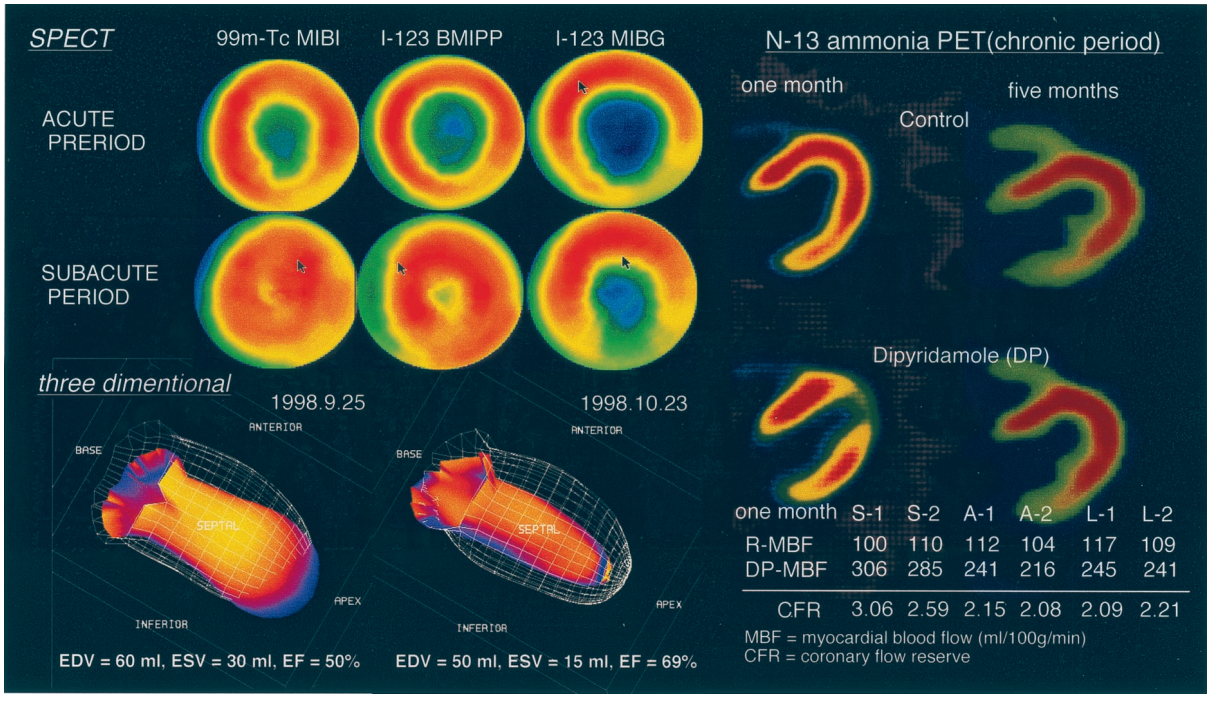

Figure 4. Scintigraphic and positron emission computed tomographic (PET) findings (Case 2). Nuclear cardiographic evaluations showed marked perfusion (Tc-99m sestamibi [MIBI]) metabolic (I-123 beta-methyl-p-iodophenyl pentadecanoic acid [BMIPP] or I-123 metaiodobenzyl-guanitidine [MIBG]) mismatches mainly at the left ventricular apex. However, in the subacute period, this perfusion metabolic mismatch decreased after the functional recovery (three-dimensional left ventriculography by Tc-99m MIBI). After five months, PET by N-13 ammonia showed improvement in the coronary flow reserve (CFR) assessed by dipyridamole administration. EDV = end-diastolic volume; EF = ejection fraction; ESV = end-systolic volume; MBF = myocardial blood flow; SPECT = single photon emission computed tomography.

Table 1. Possible Triggering Conditions at the Onset of Transient Left Ventricular Apical Ballooning

	Number of Patients (%)
Total	88 (100%)
Psychological backgrounds:	18 (20%)
Accidents in family members	2†
Relation's death or funeral	7
Quarrel or alcohol intake	5†
Vigorous excitation	4
Unusual exercise	6 (7%)
Exacerbated systemic disorders:	
Cardiovascular disease:	3 (3%)
Ventricular tachycardia attack	1
Acute chordal rupture	1
Leg pain due to embolism	1
Noncardiovascular disease:	
Neurogenic:	6 (7%)
CVA episode	3*
Epileptic attack	3*
Pulmonary:	7 (8%)
Aggravated pneumonia	2
Exacerbated bronchial asthma	3
Embolism	1
Metabolic and endocrine:	2 (2%)
Diabetic nonketotic coma	1
Hypoglycemia episode	1
Renal disease and urinary tract:	5 (6%)
Uremia/dialysis	4
Bladder pain due to obstruction	1
Gastrointestinal:	6 (7%)
Bleeding	2
Gall bladder stone	2*
Acute pancreatitis	2
Noncardiac surgery and procedure:	11 (13%)
Intubation	1
TBLB	1
Delivery	1
Subtotal gastrectomy	1
Cholecystectomy	1
Tracheotomy	1
Orthopedic surgery	4
Colonectomy	1

*†Cases combined or recurrent cases.
CVA = cerebrovascular accident; TBLB = transbronchial lung biopsy.

Table 2. Patients' Backgrounds and Characteristics of Left Ventricular Apical Ballooning (n = 88)

Age (yr)	67 ± 13 (10–88)
Gender (male/female)	12/76
Coronary risk factors (%):	
Hypertension	42 (48%)
Diabetes	10 (12%)
Hyperlipidemia	21 (24%)
Familial history	2 (2%)
Onset:	
Chest pain/discomfort	59 (67%)
Dyspnea	6 (7%)
Shock	4 (5%)
Electrocardiographic abnormalities	18 (20%)
Enzyme elevation:	
Creatine kinase	49 (56%)
Electrocardiogram (%):	
ST elevation	79 (90%)
Abnormal Q-wave	24 (27%)
T-wave inversion	39 (44%)
Complications:	
Arrhythmias:	
Sinus bradycardia	9 (10%)
Atrioventricular block	4 (5%)
Atrial fibrillation	6 (7%)
Ventricular tachycardia fibrillation	8 (9%)
Pulmonary edema	19 (22%)
Cardiogenic shock	13 (15%)
Therapy:	
Balloon pumping	7 (8%)
Dopamine/dobutamine	17 (19%)
Outcome:	
In-hospital death	1 (1%)
Heart failure at discharge	1 (1%)
Recurrences	2 (2%)
Sudden death	1 (1%)

Clinical backgrounds, symptoms and ECG findings. The mean age of the selected patients was 67 ± 13 years (range: 10 to 88 years). The number of women (n = 76) was about 6.3-fold higher than the number of men (n = 12). The percentage of women patients without psychological problems, exacerbated systemic disorders or surgical procedures was higher than the percentage of those with such conditions (94% vs. 74%, p = 0.033). Age distribution in patients with and without the above mentioned conditions was similar. The incidences of major coronary risk factors (hypertension, diabetes and hyperlipidemia) are shown in Table 2.

Chest pain/discomfort occurred in 45 (90%) of the patients without any preceding conditions and in 14 (37%) with exacerbated underlying disorder and procedure (p = 0.0001). Elevated CK release ranging from 209 to 1,625 IU/l was documented in 26 (52%) patients without and in 23 (61%) patients with possible triggering factors. Only seven patients exhibited a peak CK value of more than 1,000 IU/l. Elevated troponin T (≥0.25 ng/ml) was confirmed in 31 of the 43 patients (72%). In the acute period (6 ± 9 h; range, 1 to 48 h), ST elevation was observed in 79 (90%) of the patients, including four patients with solitary ST elevation of limb-lead and 13 patients without right precordial (V_1, V_2) ST elevation. ST depression was found in 33 patients, 32 of which had reciprocating ST depression and one without ST elevation. The remaining eight patients exhibited T-wave inversion without ST shifts. In the subacute period (21 ± 11 days; range: 14 to 46 days), only nine (10%) patients exhibited persistent Q-waves on ECG. No differences in ECG findings were observed between patients with or without preceding conditions at the onset. Electrocardiogram findings are summarized in Table 3. The V_3 and V_4 leads most frequently showed both ST elevation and Q-wave formation (Table 3).

Thus, 34 (39%) of the patients fulfilled all of the three MONICA criteria (15), and 38 (43%) of the patients were considered as probable cases for AMI. The remaining 16 patients exhibited only ECG changes.

Table 3. Electrocardiographic Findings of Left Ventricular Apical Ballooning

	ST Elevation		Abnormal Q-Wave		T-Wave Inversion	
	Acute Period	Subacute Period	Acute Period	Subacute Period	Acute Period	Subacute Period
I	37 (42%)	4 (5%)*	4 (5%)	3 (3%)	11 (15%)	44 (51%)*
II	29 (33%)	1 (1%)*	5 (6%)	1 (1%)	21 (24%)	45 (52%)*
III	22 (25%)	2 (2%)*	7 (8%)	2 (2%)	21 (24%)	41 (47%)*
aVL	24 (27%)	3 (3%)*	4 (5%)	3 (3%)	11 (15%)	30 (35%)*
aVF	26 (30%)	1 (1%)*	3 (3%)	2 (2%)	19 (26%)	40 (49%)*
V_1	19 (22%)	1 (1%)*	2 (2%)	0 (0%)	7 (8%)	20 (24%)*
V_2	58 (66%)	5 (6%)*	9 (10%)	2 (2%)	13 (15%)	59 (68%)*
V_3	68 (77%)	3 (3%)*	16 (18%)	3 (4%)*	23 (26%)	70 (81%)*
V_4	67 (76%)	2 (2%)*	12 (14%)	1 (1%)*	26 (30%)	68 (78%)*
V_5	55 (63%)	1 (1%)*	6 (7%)	1 (1%)	26 (30%)	68 (78%)*
V_6	48 (55%)	1 (1%)*	2 (2%)	0 (0%)	24 (27%)	61 (70%)*

*Statistical significance between electrocardiograms in acute and in subacute period.

Hemodynamics and LV function. The results of LVG in the acute and in subacute periods are summarized in Table 4. All of the patients exhibited characteristic apical ballooning with mean ejection fraction of 41 ± 11% (range: 10% to 62%). However, in the subacute period, the mean ejection fraction significantly increased to 64 ± 10% (ranging from 44% to 88%, $p < 0.0001$). In the acute period, 12 of 72 (18%) patients had a significant intraventricular pressure gradient >30 mm Hg. However, no patients exhibited residual pressure gradient in the subacute period. In an acetylcholine provocative test, coronary spasm was provoked in 10 of the 48 (21%) patients.

Complications and clinical outcome. Twenty-four patients exhibited arrhythmias (atrioventricular block [n = 4], sinus bradycardia [n = 9], paroxysmal atrial fibrillation [n = 6], ventricular tachycardia [n = 8], including two with ventricular fibrillation). Lung congestion and cardiogenic shock were observed in 19 (22%) and in 13 (15%) of the patients, respectively. Eighteen patients (20%) required intravenous dopamine or dobutamine infusion and mechanical supports, including a percutaneous cardiopulmonary support system used in seven (8%) of the patients in the acute period. In-hospital death due to multiorgan failure after pulmonary thromboembolism was documented in only one patient (1%).

Prescribed medications were calcium channel antagonist in 47% of the patients, beta- blockers in 18%, angiotensin-converting enzyme inhibitor in 15%, long-acting nitrate in 47% and diuretics in 19%. Exercise capacities on discharge were New York Heart Association class I in 85 (97%) of the patients, but the remaining two patients had a functional limitation due to advanced age. During a follow-up period of 13 ± 14 months, two of the 72 patients (2.7%) exhibited recurrence due to other emotional stress, and one patient, in whom multivessel spasms had been provoked by an intracoronary acetylcholine test, died suddenly.

Table 4. Catheterization Data

Left ventricular pressure:	
End-diastolic	17 ± 6
Intraventricular pressure gradient:	
Acute	13/72 (18%)
Subacute	0/56 (0%)
Left ventriculography:	
Acute:	(n = 76)
EDVI (ml/sqm)	80 ± 18
ESVI (ml/sqm)	47 ± 14
EF (%)	41 ± 11
Subacute:	(n = 56)
EDVI (ml/sqm)	69 ± 21*
ESVI (ml/sqm)	26 ± 12*
EF (%)	64 ± 10*
Provocation of vasospasm (%):	10/48 (21%)
RCA	2
LCA	3
RCA + LCA	5

*Statistical significance compared with acute period.
EDVI = end-diastolic volume index; EF = ejection fraction; ESVI = end-systolic volume index; LCA = left coronary artery; RCA = right coronary artery.

DISCUSSION

Several case studies on transient LV apical ballooning without stenosis on CAG have been reported in Japan (1–6), but this is the first report of a multicenter study on a novel heart syndrome. A total of 88 patients with transient LV apical ballooning were retrospectively analyzed. The main results of this study were: 1) acute onset and aggravation of various systemic disorders (cerebrovascular accidents, epileptic attacks, exacerbation of bronchial asthma, acute abdomen), noncardiac surgery/procedure and emotional/physical problems (sudden accidents, death/funeral of a family member, inexperienced exercise, quarreling or excessive alcohol consumption, vigorous excitation) were found to be possible triggering factors; 2) there were no differences between clinical characteristics of patients with and without the above mentioned factors except for gender likelihood and chest pain/discomfort as an initial symptom; and 3) transient intraventricular pressure gradient and provocative coronary vasospasm were observed in some cases.

Pathophysiologic basis of transient LV apical ballooning. The precise etiologic basis of transient LV apical wall motion abnormalities could not be determined from the results of this study. Stunned myocardium is generally defined as a prolonged postischemic LV dysfunction after

brief myocardial ischemia (16). The results of CAG performed immediately after onset showed no definite evidence of myocardial ischemia originating from epicardial obstruction in any of the subjects. Therefore, we could not confirm reversible wall motion abnormality as in apical stunned myocardium and, instead, named this clinical syndrome "transient LV apical ballooning."

Transient wall motion abnormality after multiple vasospastic angina has also been postulated to be a cause of stunned myocardium (2,7–12,17–19). In our series of cases, provocative vasospasm was confirmed only in limited cases (10/48, 21%). Therefore, multiple vasospasm is not thought to be a main cause. Another possible mechanism is myocardial ischemia due to microvascular spasm. Recently, Mohri et al. (17) indicated that microvascular spasm is one type of myocardial ischemia without significant stenosis in an epicardial artery. Of course, we cannot exclude the possibility of microvascular spasm and the watershed infarction, such that occurs in a cerebrovascular accident, because we could not examine microvascular function.

Several possible triggering conditions that preceded onset were documented in this study. Exposure to internal (emotional) and external stresses (physical, exacerbated disorder, procedural and perioperative) was confirmed. As has been shown in the neurogenic stunned myocardium (7–9) during acute cerebrovascular accidents and catecholamine cardiomyopathy during the endocrine crisis of pheochromocytoma (11,12), enhanced sympathetic activities might be a cause of similar types of myocardial damages. In our retrospective registered cases, we did not measure neurohumoral factors such as the endogenous norepinephrine level, which would have been helpful in confirming this possibility. Triggering factors such as emotional exposure, physical stress and preceding disorders are more important clinical information as the pathophysiologic basis of this heart syndrome. The histologic finding in the syndrome by Kawai et al. (6) in this heart syndrome revealed similar myocardial damage in catecholamine-induced cardiomyopathy. This novel heart syndrome might be one of the clinical models of stress-related sudden death (20–22). However, we found various heterogeneous disorders and procedures as possible triggering factors. All of these conditions might be stressors for patients, but we cannot rule out the possibility of coincident conditions.

Regional apical ballooning and intraventricular pressure gradient. It was also not evident why the LV apex is selectively vulnerable and subsequently forms balloons. Several anatomic and physiologic factors might contribute to LV apical wall motion abnormalities: 1) the fact that the LV apex does not have a three-layered myocardial structure; 2) the easy loss of elasticity of LV apex after excessive expansion; 3) the fact that the LV apex is the border zone (locus minoris) of the perfusion area of major coronary arteries; and 4) the delay of functional recovery from global dysfunction.

Intraventricular pressure gradients were documented in several cases in this study. It is unlikely that acute exacerbation of midventricular obstruction in hypertrophic cardiomyopathy is a main cause because no case exhibited ECG or echocardiographic myocardial hypertrophy. However, a similar mechanism in apical aneurysm formation in midventricular obstruction of hypertrophic cardiomyopathy might contribute to apical ballooning. Compensatory transient basal hypercontraction may produce midventricular obstruction and plays an important role in causing apical ballooning, which might contribute to secondary ischemia due to increased wall tension.

Clinical implications. This novel clinical syndrome with chest symptoms and ECG changes mimicking AMI is of clinical importance even though its etiologic basis is not clear. First, we had difficulty in differentiating from stenotic AMI when considering intravenous thrombolysis therapy. Indeed, chest symptoms and ECG findings are similar to those in typical cases of AMI. Second, in many patients, this syndrome occurred in the clinical course of various systemic diseases in the absence of predisposing angina, making it difficult to predict the occurrence of attacks. In patients with a preceding disorder, there might be a diagnostic difficulty because of the absence of typical chest pain/discomfort and the higher incidence of pulmonary congestion. Therefore, careful ECG monitoring will be required. In-hospital prognosis is generally good after appropriate treatment of acute phase complications such as hypotension, pulmonary congestion and ventricular tachyarrhythmias.

Study limitations. Our study was a retrospective investigation, and there are several limitations. First, the incidence of this syndrome is not clear, nor is it clear why there was a large percentage of women with this heart syndrome. The incidence in women is very high (approximately 6.3-fold higher than that in men), which is clearly different from the established male dominance in coronary artery diseases, including vasospastic angina. However, we could not obtain specific evidence of female dominance. Third, most previous case studies of this syndrome have been conducted in Japan (1–6). Only two case studies outside Japan have been reported (23,24). Therefore, further cases should be investigated to determine regional and racial differences. Fourth, CK was serially examined in these patients, but a more specific method, such as measurement of troponin T levels, would be helpful for precise determination of myocardial injury.

Conclusions. Precise clinical features of a novel heart syndrome with transient LV ballooning mimicking AMI occurred and were related to various exacerbated systemic disorders; noncardiac surgical procedure and various types of psychotic exposure were shown, but the etiologic basis should be examined in future prospective studies.

APPENDIX

Cardiovascular Institutes of AP-MI Investigations

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