

Clinical Investigations

Left Ventricular Apical Ballooning: Not an Uncommon Variant of Acute Myocardial Infarction in Women

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Summary

Background: Left ventricular apical ballooning, a new syndrome recently described in Japan, is characterized by chest pain, electrocardiographic changes mimicking acute myocardial infarction, and transient apical dyskinesia with normal coronary arteries. Although several studies have defined the clinical characteristics, the prevalence of this syndrome remains unclear.

Hypothesis: This study sought to determine the prevalence of left ventricular apical ballooning syndrome.

Methods: From January 2002 to September 2004, clinical, echocardiographic, and angiographic data of hospitalization and follow-up were collected from 638 consecutive patients referred to our Heart Institute for primary percutaneous intervention.

Results: Thirteen patients (2%) were diagnosed with transient left ventricular apical ballooning. All but one patient were women, representing a 6% incidence for the female patients with acute myocardial infarction. A triggering factor was identified in eight. One patient died of cardiogenic shock. Left ventricular systolic function recovered completely within 4–5 weeks in the remaining 12 survivors.

Conclusion: This syndrome is not uncommon and should be considered particularly in female patients presenting with acute myocardial infarction.

Key words: coronary angiography, stress cardiomyopathy, apical ballooning, Takotsubo

Introduction

Recent reports, initially from Japan, have described a syndrome characterized by chest pain, electrocardiographic (ECG) changes, transient left ventricular (LV) apical wall motion abnormality, without any significant coronary artery disease. Patients were usually women aged > 50 years in whom a triggering event, mostly emotional distress, was identified. This condition has also been termed “Takotsubo-like LV dysfunction” because of the peculiar shape seen on left ventriculogram, which resembles a “tako-tsubo” pot (with a round bottom and narrow neck) used for trapping octopuses in Japan.^{1–3}

In this report we describe 13 patients with this entity treated at our Heart Institute over a 32-month period.

Methods

After the index case identified in January 2002, patients with LV apical ballooning were entered into a prospective register. From January 2002 to September 2004, 13 consecutive patients (12 women and 1 man) met the following criteria: sudden onset of chest pain with ST elevation in several ECG leads, reversible balloon-like LV wall motion abnormality at the apex with hypercontraction of the basal segment at left ventriculography, enzyme changes mimicking acute myocardial infarction (AMI), and absence of any significant coronary stenosis at coronary angiography. Transthoracic echocardiography was performed in each patient at Day 1 or 2 of hospitalization.

Results

During the study period, 13 patients with LV apical ballooning were identified among 638 consecutive patients with acute MI (435 men and 150 women) referred for primary percutaneous intervention (PCI). All but one patient were women with a mean age of 68 years, representing a 2% incidence for all patients and 6% for women.

Risk factors are summarized in Table I. Four patients reported a strong emotion preceding onset of pain, four had physical stress (asthma attack, tracheostomy, and bleeding). All patients had chest pain and all but one had ST-segment el-

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TABLE I Clinical features in 13 patients with left ventricular apical ballooning

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7	Pt 8	Pt 9	Pt 10	Pt 11	Pt 12	Pt 13
Gender	F	F	F	F	M	F	F	F	F	F	F	F	F
Age	72	60	80	82	46	62	50	79	71	61	69	68	79
Hypertension	No	No	No	Yes	No	No	No	No	No	No	Yes	No	No
Diabetes	No	Yes	No	No	No	No	No	No	No	No	No	No	No
Smoking	No	No	No	No	Yes	No	No	No	Yes	No	No	No	No
Hypercholesterolemia	Yes	No	Yes	No	Yes	No	No	No	No	Yes	No	No	No
Precipitating factor	No	PS	PS	No	ES	No	ES	ES	PS	No	ES	PS	No
Presenting symptoms	CP	PEd	CP	P	CP	CP	CP	CP	CP CS	CP	CP	PEd	CP
ST elevation	II aVL, aVF V ₃₋₆	V ₂₋₃	↓ST V ₃₋₆	II, III, aVF V ₁₋₆	V ₁₋₄	—	II, III, aVF V ₃₋₆	II aVF V ₂₋₆	I V ₁₋₆	V ₄₋₆	I aVL V ₁₋₆	I aVL V ₁₋₆	V ₂₋₄
Q-wave admission	III aVF ₂₋₄	III V ₁₋₄	—	—	—	—	—	—	V ₂₋₆	—	—	—	V ₂
Q-wave discharge	—	—	—	—	—	—	—	—	V ₁₋₄	—	—	—	—
Peak CK	330	489	123	300	—	90	408	188	—	166	330	1491	100
Peak troponin	3.2	—	2.3	—	—	0.1	7.6	10.4	—	2.6	—	—	2.9
IABP	Yes	No	No	No	Yes	No	No	No	Yes	No	No	Yes	No
Admission LVEF (%)	23	30	45–50	45	30	25	35	25	20	35	25	22	25
Cardiogenic shock	No	No	No	No	Yes	No	No	No	Yes	No	No	Yes	No
Death	No	No	No	No	No	No	No	No	Yes	No	No	No	No
NYHA—follow-up (%)	I	I	I	I	I	I	I	I	—	I	I	I	I
LVEF—follow-up (%)	60	60	60	60	45	50	65	60	—	60	60	55	60

Abbreviations: Pt = patient, F = female, M = male, ES = emotional stress, PS = physical stress, CP = chest pain, PEd = pulmonary edema, P = palpitations, IABP = intra-aorta balloon pulsation, CK = creatine kinase, LVEF = left ventricular ejection fraction, NYHA = New York Heart Association.

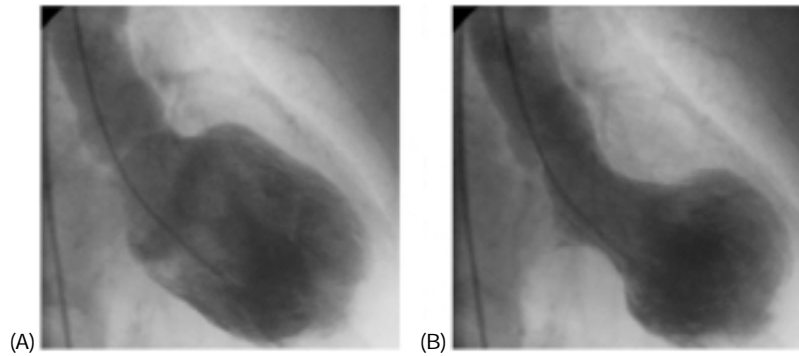


FIG. 1 Representative left ventriculogram in the acute phase in diastole (A) and systole (B) showing akinesia of the apical and mid portions of the left ventricle and hypercontractile basal segment.

evaluation on anterior chest leads. Extension of ST elevation in leads II, III, and aVF was found in four patients. Negative T waves in the precordial leads developed over the subsequent days. Q waves were seen on admission in five patients but only in one at discharge. Median time from onset of symptoms to admission to emergency room (ER) and from ER to the catheterization laboratory was 3.4 and 1.2 h, respectively, in patients with apical ballooning and 2.5 and 1.5 h, respectively, in all patients with AMI. At coronary angiography, the coronary arteries were normal in 12 patients. Noncritical coronary disease was found in one patient. Left ventricular ventriculography showed characteristic apical ballooning, that is, the base of the left ventricle was hypercontractile while the apex was dyskinesic (Fig. 1). Apical dysfunction involved the anterolateral, septal, apical, and mid-inferior and inferior-apical segments, that is, the distribution territory of more than one coronary artery. An intraventricular pressure gradient up to 30 mmHg was found in two patients. The mean admission LV ejection fraction (LVEF) was 32%. The mean creatine kinase and troponin I levels were 275 units (range 90–489) and 5.9 $\mu\text{g/l}$ (range 2.3–10.4), respectively.

In all patients, admission echocardiography exhibited dyskinesia of the apical and mid portions of the left ventricle. Mean LVEF was 32%. A sigmoid septum was found in all but one of the patients. Mean LVEF at discharge was 48%. In-hospital outcome was benign in the majority of cases, although four patients presented with cardiogenic shock. In these patients an intra-aortic balloon pump (IABP) was inserted after catheterization. One patient died of cardiogenic shock during hospitalization.

Follow-up was 36 months (mean 16 months). All patients were in New York Heart Association functional class I. Left ventricular function recovered completely in all patients but one, in whom LVEF increased from 30 to 45%. Mean echocardiographic LVEF for the entire group was 60%.

Discussion

Throughout 1990 and 1991, a syndrome characterized by transient LV apical dysfunction was described in Japan,^{1–3} but

recent reports have also been documented in the western world.^{4–6} Previous reports of dynamic LV outflow tract obstruction in the setting of acute anterior MI^{7,8} may be also related to this syndrome.

The incidence of this new syndrome in patients presenting with AMI was estimated between 1.5 and 2.2%.^{4,10} However, if one focuses on the female population, which represents the overwhelming majority of patients (12/13 in our series), the incidence of this syndrome seems much higher. In our series this syndrome occurred in 2% of 638 consecutive patients with AMI and referred for primary PCI. However, among the female patients the incidence was 6%, indicating that this condition is not uncommon in women.

The clinical features of our patients are consistent with those in previous studies: reversible balloon-like LV dysfunction mostly occurring after severe stress in elderly females with normal coronary arteries. Data on recurrence of this syndrome are scarce.⁵ One of our patients (No. 1) was diagnosed 10 years previously with an anterior MI with normal coronary arteries. Left ventriculography was not performed, but LV function recovered completely, suggesting that this may be a case of recurrent apical ballooning.

Several mechanisms have been hypothesized to explain the severe reversible myocardial dyskinesia with limited release of cardiac enzymes or troponin.^{11–13} In the majority of cases, triggering conditions that precede onset were described, consisting of exposure to internal (emotional) and external stress (trauma, surgical procedure, exacerbation of a preexisting condition). It has been reported that emotional stress precipitated severe LV dysfunction in 19 patients without coronary artery disease and elevated plasma catecholamine levels.¹⁴ This suggests that enhanced sympathetic activity may play a major role in the origin of this syndrome. Experimental data also support this hypothesis.^{15,16}

Sigmoid interventricular septum has been associated with transient dynamic LV obstruction in the setting of acute anterior MI.⁸ It may be argued that distorted LV geometry (present in 12/13 of our patients) together with neurogenic stress, cause an excessive burden on the apical segments of the LV to the point that contraction becomes impaired and dilatation starts.

Following dilatation, the increased wall stress enhances myocardial metabolic demand, worsening the stunning at the LV apex and causing the unique morphologic change of apical ballooning. The clinical features in our patients, characterized by the presence of sigmoid septum and of a stressful event preceding the onset of MI, are consistent with this hypothesis.

Conclusions

This novel clinical syndrome is not uncommon, especially among middle-aged women presenting with AMI.

Timely diagnosis of LV apical ballooning may avoid the risk of unnecessary treatment such as thrombolysis. The combination of a stressful event in an elderly female presenting with chest pain and ST elevation in the anterior leads, especially with inferior involvement, should raise the suspicion of LV apical ballooning.

Echocardiography at admission showing sigmoid septum and apical dyskinesia may further strengthen the suspicion and may prompt immediate cardiac catheterization.

Beta blockers may be recommended in patients with dynamic LV outflow obstruction.¹⁷ Intra-aortic balloon pump has been used in patients presenting with cardiogenic shock in several cases¹⁸ as well as in four of our patients.

References

- Dote K, Sato H, Tateishi H, Uchida T, Ishiara M: Myocardial stunning due to simultaneous multi-vessel coronary spasms: A review of 5 cases. *J Cardiol* 1991;21:203–214
- Tsuchihashi K, Ueshima K, Uchida T: Transient left ventricular apical ballooning without coronary artery stenosis: A novel heart syndrome mimicking acute myocardial infarction. *Angina Pectoris-Myocardial Infarction Investigations in Japan. J Am Coll Cardiol* 2001;38(1):11–18
- Sato H, Tateishi H, Uchida T: Tako-tsubo type cardiomyopathy due to multivessel spasm. In *Clinical Aspect of Myocardial Injury: From Ischemia to Heart Failure* (in Japanese), (Eds. Kodama K, Haze K, Hon, M), pp. 56–64. Tokyo: Kagakuyouronsya Co. 1990
- Bybee KA, Prasad A, Barenness GW, Lerman A, Jaffe AS, Murphy JG: Clinical characteristics and thrombolysis in myocardial infarction frame counts in women with transient left ventricular apical ballooning. *Am J Cardiol* 2004;94:343–346
- Desmet WJ, Adriaenssens BF, Dens JA: Apical ballooning of the left ventricle: First series in white patients. *Heart* 2003;89:1027–1031
- Ibanez B, Navaro F, Farre J, Marcos-Alberca P, Orejas M, Rabago R: Takotsubo syndrome associated with a long course of the anterior descending coronary artery along the apical diaphragmatic surface of the left ventricle. *Rev Esp Cardiol* 2004;59:209–216
- Hrovatin E, Piazza R, Pavan D, Mimo R, Macor F, Dall'Aglio V, Burelli C, Cassin M, Canterin FA, Brieda M, Vitrella G, Gilberto C, Nicolosi GL: Dynamic left ventricular outflow tract obstruction in the setting of acute anterior myocardial infarction: A serious and potentially fatal complication? *Echocardiography* 2002;19(6):449–455
- Di Chiara A, Werren M, Badano LP, Fioretti PM: Dynamic left ventricular outflow tract obstruction: An unusual mechanism mimicking anterior myocardial infarction with cardiogenic shock. *Ital Heart J* 2001;2(1):60–67
- Akashi J, Nakazawa K, Sakakibara M, Miyake F, Koikei H, Sasaka K: The clinical features of Takotsubo cardiomyopathy. *Q J Med* 2003;96:563–573
- Sharkey SW, Lesser JR, Zenovich AG, Maron MS, Lindberg J, Longe TF, Maron BJ: Acute and reversible cardiomyopathy provoked by stress in women from the United States. *Circulation* 2005;111:472–479
- Ito K, Sugihara H, Kawasaki T, Yuba T, Doube T, Tanabe T: Assessment of ampulla (Takotsubo) cardiomyopathy with coronary angiography, two-dimensional echocardiography and 99mTc-tetro fosmin myocardial single-photon emission computed tomography. *Ann Nucl Med* 2001;15:351–355
- Owa M, Aizawa K, Urasawa N, Ichinose H, Yamamoto K, Karasawav K, Kagoshima M, Koyama J, Ikeda S: Emotional stress-induced “ampulla cardiomyopathy:” Discrepancy between the metabolic and sympathetic innervation imaging performed during the recovery course. *Jpn Circ J* 2001;65:349–352
- Akashi YL, Nakazawa K, Sakakibara M, Miyake F, Koikei H, Sasaka K: 123I-MIBG myocardial scintigraphy in patients with “Takotsubo” cardiomyopathy. *J Nucl Med* 2004;45:1121–1127
- Wittstein IS, Thieman DR, Lima JAC, Baughman KL, Schulman SP, Gerstenblith G, Wu KC, Rade JJ, Bivalacqua TJ, Champion HC: Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med* 2005;352:539–548
- Moriya M, Mori H, Suzuki N, Hazaña M, Yano K: Six-month follow-up of tako-tsubo cardiomyopathy with I-123-beta-methyl-iodophenyl pentadecanoic acid and I-123-meta-iodobenzyl-guanidine myocardial scintigraphy. *Intern Med* 2002;41(10):829–833
- Ueyama T, Kasamatsu K, Hano T, Yamamoto K, Tsuruo Y, Nishio I: Emotional stress induces transient left ventricular hypocontraction in the rat via activation of cardiac adrenoceptors: A possible animal model of “Takotsubo” cardiomyopathy. *Circulation* 2002;66(7):712–713
- Maron BJ, Bonow RO, Canon RO: Hypertrophic cardiomyopathy: Interrelations of clinical manifestations, pathophysiology and therapy. *N Engl J Med* 1987;316:780, 844
- Barron HV, Every NR, Parsons LS, Angeja B, Goldberg RJ, Gore JM, Chou TM: The use of intra-aortic balloon counter-pulsation in patients with cardiogenic shock complicating acute myocardial infarction: Data from the National Registry of Myocardial Infarction 2. *Am Heart J* 2001;141(6):933–939