Ampulla Cardiomyopathy ('Takotusbo' Cardiomyopathy) — Reversible Left Ventricular Dysfunction With ST Segment Elevation —

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The clinicopathologic findings of reversible ampulla-like ventriculogram of the left ventricle were studied in 8 elderly women and one middle-aged man. Their coronary arteriograms were normal, even in the 7 patients who had ST elevation on electrocardiogram. Coronary spasm was positive in only 2 of the 7 patients who received provocation tests. Biopsy specimens revealed focal myocyte injury. Normal coronary arteriograms during ST elevation and the presence of pathologic myocardial lesions were not consistent with a concept of stunned myocardium. The presence of myocardial lesions suggested that focal and disseminated myocardial damage had occurred. (*Jpn Circ J* 2000; 64: 156–159)

Key Words: Endomyocardial biopsy; ST elevation; Stunned myocardium

In Japan, there have been a number of reports of patients with symptoms that mimic acute myocardial infarction with reversible asynergy. These cases display a balloon-like asynergy of the apical region with hypercontraction of the basal segment of the ventricle, ST elevation, and minimal elevation of cardiac enzymes. These patients are usually misdiagnosed as having acute myocardial infarction and undergo coronary angiography and left ventriculography, but no significant luminal narrowing of the coronary arteries is found, even during the acute phase with ST elevation. Furthermore, ventricular function returns to normal within several weeks. This peculiarly shaped ventriculogram was originally named by Dr Sato and his colleagues as 'Takotsubo' cardiomyopathy¹, after the fishing pot with a round bottom and narrow neck that is used for trapping octopuses in Japan.

Prolonged, postischemic ventricular dysfunction is known as myocardial stunning², which is observed in many clinical settings, such as exercise testing in patients with multi-vessel coronary artery disease, transient ischemia during percutaneous transluminal angioplasty, or in patients with unstable angina or coronary vasospasm³. It is difficult to determine whether or not this reversible left ventricular asynergy is the result of a postischemic event. If it is a

subtype of stunned myocardium, there should be confirmation of transient myocardial ischemia and absence of microscopic injuries to the myocytes⁴. To clarify the clinicopathology of this clinical setting, we investigated 9 patients who exhibited ampulla-like asynergy and underwent endomyocardial biopsies of the left ventricular apical area.

All patients had ampulla-shaped asynergy of the left ventricle confirmed by either left ventriculogram or echocardiogram, or both. Coronary cineangiography was performed during the period from the 1st to the 12th day after onset of the initial symptom. Subsequent left ventriculograms or echocardiograms were performed during the period from the 2nd to the 35th day after onset of the initial symptoms. Normalization of the wall motion was considered to have occurred when the moderately hypokinetic area disappeared and the left ventricular ejection fraction improved to more than 0.6.

Clinical data, including underlying disorders, trigger events, locations of the leads with ST-segment elevation on the electrocardiograms, the day on which the initial coronary angiography was performed, the clinical interval between the initial symptoms and normalization of the left ventricular contraction, peak titers of serum creatine kinase, results of provocation tests for coronary spasm, and pathologic findings of endomyocardial specimens, are listed in Table 1.

Hypertension was the underlying disorder in 4 patients, and emotional stress was the trigger event in 5 patients. Biventricular involvement with pressure gradients in the outflow tract of the ventricles was observed in 2 patients (cases 1 and 2). Coronary arteriography revealed no significant stenosis, even in the 7 cases with ST-segment elevation (cases 1–3 and 6–9). The degree of wall motion reduction did not correlate with the height of the ST-segment elevation. Deep negative T waves were characteristically seen during the course of recovery. Coronary spasms were positive in only 2 of the 7 patients who received a provoca-

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Table 1 Clinical and Pathologic Data

Case no.	Gender/ age	Underlying disorder	Trigger event	Symptoms	ST elevation	Day of first coronary angiography	Normalization of left ventricular contraction	Level of creatine kinase	Provocation of coronary spasm	Day of biopsy	Biopsy pathology
1	F/71	Premature ventricular contraction, hypertension	Status after sigmoid colon surgery, dehydration, cessation of beta blocking agent	Chest pain	II, III, aVL, V ₂₋₆	1*	24 days later (UCG, EF 86%)	132	Not performed	1	Focal fibrosis, myocardial depletion, cell infiltration
2	F/82	Neurosis	None	Anorexia, throat discomfort	II, III, aVL, V ₂₋₆	1*	35 days later (UCG, EF 65%)	1400	Not performed (spastic)	1	Slight increase of loose connective tissue, small round cell infiltration (including polymorphonuclear leukocytes), myocyte injury
3	F/64	Pulmonary fibrosis	Attempted suicide, near drowning	Dyspnea	I, II, aVL, V ₂₋₆	4*	30 days later (LVG, EF 81%)	271	Negative (acetylcholine, ergonovine)	4	Small round cell infiltration
4	F/63	Angina pectoris	Emotional stress	Palpitation, dyspnea, chest and back pain	I, aVL, V ₁₋₂	8	8 days later (LVG, EF 61%)	174	Positive, diffuse (ergonovine)	8	Myocardial fibrosis, myocardial depletion, fibrocellular proliferation
5	F/68	Paroxysmal atrial fibrillation, hypertension, angina pectoris, aortic regurgitation	None	Syncope, cough	aVL, V ₁₋₃	12	13 days later (UCG, EF 84%)	129	Negative (acetylcholine)	12	Old myocardial fibrosis, cell infiltration
6	F/60	Hypertension	None	Cough, dyspnea	I, II, aVL, V ₂₋₆	1*	15 days later (UCG, EF 79%)	84	Negative (acetylcholine)	15	Cell infiltration
7	F/59	Hypertension, hyperlipidemia	Memorial service for her grandmother	Chest pain	I, aVL, V ₂₋₆	1*	17 days later (LVG, EF 74%)	162	Positive (acetylcholine)	17	Focal myocardial depletion, increase of connective tissue with cell infiltration
8	F/76	Diabetes mellitus	None	Dyspnea	I, aVL, V ₂₋₄	1*	13 days later (UCG, EF 78%)	438	Negative (acetylcholine)	22	Focal myocardial depletion, focal fibrosis with increased cellularity
9	M/53	Heavy drinker, acute renal failure	Hypotension, hemofiltration, dopamine	Dyspnea	I, aVL, V ₂₋₆	1*	26 days later (LVG, EF 76%)	528	Negative (acetylcholine)	26	Patchy fibrosis, myocardial depletion, cell infiltration

LVG, left ventriculogram; UCG, ultrasonic echocardiogram; EF, ejection fraction. *indicates that coronary arteriography was performed during the ST elevation phase.

Fig1. Case 1. (A) Coronary angiogram. Right coronary artery in left anterior oblique position. There is mild irregularity in segment 2. (B) Coronary angiogram. Left coronary artery in left anterior oblique projection. The left anterior descending branch and circumflex branch show moderate tortuosity without stenosis. Note the monitor record of the electrocardiogram in the left upper corner, which indicates ST segment elevation. (C) Left ventriculogram (end-systolic phase) in right anterior oblique projection. The extensive area around the apex shows akinesis and the basal segments display hypercontraction. (D) Left ventriculogram (end-diastolic phase) in right anterior oblique projection. (E) Endomyocardial biopsy specimen reveals focal myocardial injury. (H&E, $\times 400$)

tion test. Peak levels of creatine kinase were less than 528 IU/L in 8 patients, but was 1400 IU/L in case 2, who had received hemofiltration for acute renal failure and intravenous infusion of dopamine for cardiogenic shock. The left ventricular wall motion normalized in all cases between 8 and 35 days after the onset.

Biopsy pathology revealed focal myocyte injury, myocardial depletion with cell infiltrates, including polymorphonuclear leukocytes, or focal fibrosis. Although fibrotic lesions were usually seen in cases biopsied more than 8 days after onset, they were also observed in the 2 cases biopsied on the 1st day (cases 1 and 2).

Case 1

A 71-year-old woman underwent emergency coronary angiography because of chest pain and ST elevation on electrocardiogram. The patient was hospitalized for surgical treatment of carcinoma of the colon. Preoperative echocardiography did not reveal left ventricular hypertrophy or asynergy. After surgery, she became dehydrated and developed sudden chest pain. A coronary cineangiogram demonstrated no significant stenosis (Fig 1A,B). The left ventriculogram revealed a large akinetic area around the apex and hypercontraction of the basal segments (Fig 1C,D). The pressure gradients were recorded in the left and right ventricular outflow tracts (74 and 22 mmHg, respectively).

Microscopic examination revealed focal myocardial fibrosis and focal myocyte depletion with cellular infiltrates (Fig 1E). The left ventricular wall motion returned normal on the 24th day after onset.

Discussion

This reversible left ventricular asynergy with ST-segment elevation has been thought to be stunned myocardium induced by multi-vessel coronary spasm.^{3,4} Although several case reports demonstrated a positive provocation test for coronary spasm with hypokinesis of the extensive left ventricular segment including the apex,^{5,6} spontaneous occurrence of diffuse multi-vessel spasm is a rare event⁷ and is inevitably unaccompanied by electrocardiographic changes.

The patency of the coronary artery during the acute phase with ST elevation, plus the discrepancy between the hypokinetic area and coronary artery perfusion, were not consistent with the concept of myocardial stunning. Coronary spasm was only seen in 2 of the 7 patients who received the provocation test. These 2 patients did not show any ventricular asynergy. However, the possibility of

microvascular injury could not be ruled out. Furthermore, this phenomenon was accompanied by focal myocardial injury. The presence of old lesions indicated latent and focal occurrence of myocardial injuries.

Transient ventricular asynergy resembles the left ventricular asynergy induced by subarachnoid hemorrhage⁸ or catecholamine crisis.⁹ However, this reversible ampulla-like asynergy of the left ventricle is not usually seen in either of these conditions. In an experimental study of catecholamine myocardial injury,¹⁰ myocardial fibrosis was observed 3 days after the infusion of sympathomimetic amine.

Although the exact mechanisms of apical akinesis and basal hyperkinesis are unclear, there is a possibility of a common factor that have both cardiotoxicity and a positive inotropic effect. Detailed examination of autopsy materials is needed to clarify the mechanisms for apical akinesis and basal hyperkinesis, the etiology of reversible asynergy of the wall motion and the presence of microvascular injury.

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