Case Reports

Reversible Left Ventricular Systolic Dysfunction - Reversibility of Coronary Microvascular Abnormality

Junya AKO,¹ MD, Katsu TAKENAKA,² MD, Kansei UNO,² MD,
Fumitaka NAKAMURA,² MD, Tsuyoshi SHOJI,¹ MD, Katsuya IJIMA,¹ MD,
Yumiko OHIKE,¹ MD, Seungbum KIM,¹ MD, Tokumitsu WATANABE,¹ MD,
Masao YOSHIZUMI,¹ MD, and Yasuyoshi OUCHI,¹ MD

SUMMARY

Reversible left ventricular wall motion abnormalities mimicking myocardial infarction have been reported in patients with a noncardiac illness. Their coronary angiograms do not demonstrate organic stenosis or epicardial coronary vasospasm. In this article, two cases of reversible left ventricular contraction abnormality are presented. Electrocardiography showed deep inverted T waves in precordial leads, and the echocardiography revealed diffuse akinesis of the apical region in the acute phase. Coronary angiography showed no significant stenosis or occlusion in either patient. Thallium scintigraphy showed no defect, while the metaiodobenzylguanidine scintigraphy demonstrated significant defects in the apex. The relative coronary flow reserve ratio, measured with an intracoronary Doppler flow wire, was significantly reduced in both patients. Myocardial contrast echocardiography revealed a reversible perfusion defect in the apex in the acute phase in case 2. Transiently impaired coronary microcirculation was thought to be involved in the pathogenesis of the reversible left ventricular dysfunction observed in these patients. (Jpn Heart J 2001; 42: 355-363)

Key words: Ventricular function, Myocardial stunning, Stress, Coronary flow reserve, Microcirculation

SHARKEY, *et al* reported reversible myocardial contraction abnormalities in patients with an acute noncardiac illness.¹⁾ They reported the occurrence of prolonged but reversible contraction abnormalities complicating the hospital course of patients with a variety of acute noncardiac illnesses. The patients demonstrated characteristic abnormalities of the T wave and QT interval on ECG. Reversible left ventricular dysfunction is observed in patients under strong emotional stress or in patients with subarachnoid hemorrhage.¹⁻⁷⁾ The exact mechanism of this phenomenon, however, is still unknown.

From ¹ Department of Geriatric Medicine, ² Department of Cardiovascular Medicine, Graduate School of Medicine, University of Tokyo, Tokyo Japan.

Address for correspondence: Yasuyoshi Ouchi, MD, Department of Geriatric Medicine, Graduate School of Medicine, The University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113-8655, Japan.

Received for publication December 15, 2000.

Revised and accepted January 15, 2001.

We report two cases that showed acute reversible wall motion abnormalities without any corresponding coronary stenosis or structural heart disease. The relative coronary flow reserve (rCFR) was significantly decreased in both patients. Myocardial contrast echocardiography of the left ventricle revealed a reversible perfusion defect in case 2. Our findings suggest that reversible coronary microvascular impairment is involved in this transient left ventricular dysfunction.

CASE REPORTS

Case 1: An 83-year-old Japanese man with a history of hypertension and chronic renal failure was admitted to our hospital for the treatment of worsening dyspnea lasting for 7 hours. Initial laboratory data yielded the following: white blood cell count 10,000 / μ l, aspartate aminotransferase (GOT) 59 IU / l, lactate dehydrogenase (LDH) 454 / IU / l, and creatine kinase (CK) 843 IU / l (CK-MB; 21 IU / l). An ECG showed complete right bundle branch block, and ST elevation was observed in V_{3,4} (Figure 1A). Echocardiography revealed severe akinesis in the apical region. Acute myocardial infarction of the anterior wall was suspected. Emergent coronary angiography, however, revealed no significant stenosis or occlusion in the coronary arteries (Figure 2). Left ventriculography revealed diffuse hypokinesis of the left ventricle, especially in the apical region

Figure 1. (Case 1) Electrocardiograms on admission (A), day 7 (B), and day 30 (C). Complete right bundle branch block and first-degree atrioventricular block, and mild ST-segment elevation in V_{3,4} were observed on admission. (A) Deep inverted T waves were observed in precordial leads in follow up studies. (B, C)

Figure 2. (Case1) Coronary arteriogram of right coronary artery (A) and left coronary artery (B) on admission. Both coronary arteries were patent with no significant stenoses.

Figure 3. (Case 1) Left ventriculogram in right oblique view on admission (A, B) and at the follow-up (C, D). Diffuse akinesis in the apical region was observed on admission. (A; diastole, B; systole) The left ventricular dysfunction was reversible one month after admission. (C; diastole, D; systole)

(Figure 3A, B). A thallium scan showed no defect, whereas an Iodine-123 metaiodobenzylguanidine (MIBG) scan demonstrated markedly decreased uptake in the apical region with an increased washout ratio (Figure 4). The ECG showed marked inverted T waves in the precordial leads 1 week after admission (Figure 1B, C). Echocardiography revealed an improvement in left ventricular function three weeks after admission.

The catheterization was repeated four weeks after admission, when the left ventricular function had not yet fully recovered. The left ventriculography showed significant improvement in left ventricular function (Figure 3 C, D). The provocation test for coronary spasm with intracoronary acetylcholine induced significant stenosis only in the diagonal branch. The relative coronary flow reserve (rCFR) was measured at the mid portion of the left anterior descending artery using a 0.014-inch intracoronary Doppler flow wire (Flomap, Endosonic, CA, USA) with an intracoronary injection of 2.5 mg of isosorbide dinitrate and 50 μ g of adenosine triphosphate disodium (ATP). The coronary flow at baseline was 26 cm / sec, and the flow at maximal coronary vasodilation was 35 cm / sec, which gives an rCFR of 1.3. Endomyocardial biopsy revealed patchy interstitial fibrosis, swelling of the nucleus, and mild infiltration of polymorphonuclear leukocytes (Figure 5). The patient was clinically stable and was discharged after the initiation of chronic hemodialysis.

Case 2: A 75-year-old Japanese female had been admitted to our hospital for the treatment of a tumor in the lung. After fiberoptic bronchoscopy, she experienced

Figure 4. (Case 1) Bull's eye view of the thallium and MIBG scans. The thallium scan at rest showed no defect (A). The MIBG scan showed a marked defect in the anterior wall and apex. (B)

chest discomfort. Her blood pressure was 132 / 76 mmHg, and her pulse rate was 92 beats per minute. The white blood cell count was $10,300 / \mu\text{l}$, and the serum creatin kinase level was $216\text{IU} / \text{l}$ with a CK-MB of $14\text{IU} / \text{l}$. The ECG showed sinus tachycardia and inverted T waves in leads II, III, aV_F, and V₃₋₆ (Figure 6B). Echocardiography revealed severe hypokinesis in the apical region of the left ventricle. The myocardial contrast echocardiographic studies were performed by intravenously administering 4 ml of Levovist (Schering, Germany). Contrast echocardiography of the left ventricle revealed a perfusion defect in the apex (Figure 7A). Coronary arteriography showed no significant stenosis (Figure 8). The rCFR, measured with 50 μg of ATP as described above, was 1.8. Thallium scintigraphy revealed no defects, whereas MIBG scintigraphy demonstrated markedly decreased uptake in the apical region (Figure 9).

Follow-up echocardiography demonstrated a marked improvement in left ventricular systolic function four weeks after the onset of symptoms. The contrast echocardiography of the left ventricle using intravenously administered Levovist revealed a homogenous signal in the myocardium, suggesting that the coronary microcirculation abnormality was reversible (Figure 7B).

Figure 5. (Case 1) Endomyocardial biopsy specimen. Patchy interstitial fibrosis and swelling of the nucleus were observed.

Figure 6. (Case 2) Electrocardiograms before chest pain (A), onset of the symptoms (B), and day 7 (C). The ECG before the attack was within normal limits. (A) Deep inverted T waves were observed in II, III, aV_F and precordial leads. (B)

Figure 7. (Case 2) Myocardial contrast echocardiogram in apical long-axis view. Levovist was administered intravenously. The echocardiogram of the end systolic phase was obtained with 4:1 ECG-triggered powered Doppler mode. The apical half of the left ventricle was not perfused with contrast media in the acute phase. (A, Arrows; the defect.) The perfusion defect was not observed 4 weeks after admission. (B)

Figure 8. (Case 2) Coronary arteriogram of the right coronary artery (A) and left coronary artery (B). No significant stenosis or occlusion was observed.

Figure 9. (Case 2) Bull's eye view of the thallium and MIBG scans. The thallium scan showed no defect (A). The MIBG scan showed a marked defect in the apical region. (B)

DISCUSSION

A reversible contraction abnormality involving the apical region of the left ventricle can complicate the clinical course of critically ill patients in the absence of coronary artery disease.¹⁾ These patients have the following characteristics: the appearance of deep T-wave inversion in the precordial leads of the ECG, the presence of apical wall motion abnormality on an echocardiogram, and mild CK elevation.¹⁾ Apical left ventricular dysfunction without any lesions in the corre-

sponding coronary arteries is reported to occur in many clinical circumstances, especially after strong emotional stress or in subarachnoid hemorrhage.¹⁻⁷⁾ The pathogenesis of the apical left ventricular dysfunction is thought to be a result of epicardial vasospasm,⁸⁾ myocarditis,²⁾ catecholamine cardiotoxicity,⁹⁾ cardiomyopathy,⁵⁾ or microvascular dysfunction.⁷⁾ The exact mechanism of this transient left ventricular dysfunction remains uncertain.

Kawai, *et al* first described the pathological changes in patients with this transient left ventricular dysfunction in noncardiac illnesses, and called it ampulla cardiomyopathy.⁵⁾ They demonstrated pathological changes consisting of focal myocyte injury, myocardial depletion with cell infiltrates, including polymorphonuclear leukocytes, or focal fibrosis. Transient left ventricular dysfunction with similar pathological changes has been described in patients with acute cerebral injury.¹⁰⁻¹²⁾ Left ventricular dysfunction in patients with severe acute brain injury is also a reversible phenomenon, as reported in rats¹³⁾ and humans.¹⁴⁾ Reversible left ventricular dysfunction in patients with a noncardiac illness may have the same pathogenesis as the disorder seen in patients with acute brain injury. In a detailed histological analysis in experimental brain injury, increased intracranial pressure resulted in microvascular lesions in rat hearts.¹¹⁾ Myocardial damage in these experimental animals was believed to be the result of either microvascular abnormalities or a direct toxic effect of the marked catecholamine increase. Sadamatsu and coworkers first reported that patients with this form of reversible left ventricular dysfunction have an impaired coronary microcirculation.⁷⁾ They also reported that an MIBG scan showed a significant defect in the apical region. They concluded that microvascular dysfunction and sympathetic nervous abnormalities might be responsible for the reversible contractile impairment.

In the present two cases, coronary angiography revealed no occlusion in the coronary arteries, and the left ventricular dysfunction was reversible. Thallium scintigraphy showed no defect, and MIBG scintigraphy showed significantly decreased uptake in the apical region. The rCFR measured with a Doppler flow wire was significantly decreased in both cases, suggesting that the coronary microcirculation was impaired, as Sadamatsu, *et al*⁷⁾ have already stated. In case 1, an endomyocardial biopsy revealed the same pathological change as seen in Kawai's report.⁵⁾ The decreased rCFR might be a result of either impaired coronary microcirculation or myocardial damage. However, the decreased left ventricular perfusion measured with myocardial contrast echocardiography was reversible in case 2, suggesting that the coronary microcirculation abnormality was a reversible event. Reversible coronary microvascular impairment, rather than myocardial histological change, seems to be associated with the pathogenesis of the ventricular dysfunction seen in these patients.

This is the first report to demonstrate the reversibility of impaired coronary

microcirculation in patients with this disorder. The mechanism of this phenomenon remains unclear, however, transient coronary microvascular abnormalities are apparently involved. Further research will be needed to clarify the pathogenesis of this form of left ventricular systolic dysfunction.

REFERENCES

1. Sharkey SW, Shear W, Hodges M, Herzog CA. Reversible myocardial contraction abnormalities in patients with an acute noncardiac illness. *Chest* 1998; 114: 98-105.
2. Izawa A, Yazaki Y, Hayashi S, Imamura H, Kusama Y, Isobe M. Transient left ventricular aneurysm and hypertrophy accompanied by polymorphic ventricular tachycardia in a patient suspected of acute myocarditis. *Jpn Heart J* 2000; 41: 97-102.
3. Kono T, Morita H, Kuroiwa T, Onaka H, Takatsuka H, Fujiwara A. Left ventricular wall motion abnormalities in patients with subarachnoid hemorrhage: neurogenic stunned myocardium. *J Am Coll Cardiol* 1994; 24: 636-40.
4. Pavin D, Le Breton H, Daubert C. Human stress cardiomyopathy mimicking acute myocardial syndrome. *Heart* 1997; 78: 509-11.
5. Kawai S, Suzuki H, Yamaguchi H, *et al.* Ampulla cardiomyopathy ('Takotsubo' cardiomyopathy)—reversible left ventricular dysfunction: with ST segment elevation. *Jpn Circ J* 2000; 64: 156-9.
6. Sato K, Masuda T, Izumi T. Subarachnoid hemorrhage and myocardial damage: clinical and experimental studies. *Jpn Heart J* 1999; 40: 683-701.
7. Sadamatsu K, Tashiro H, Maehira N, Yamamoto K. Coronary microvascular abnormality in the reversible systolic dysfunction observed after noncardiac disease. *Jpn Circ J*. 2000; 64: 789-92.
8. Mathias P, Kerin NZ, Blevins RD, Cascade P, Rubenfire M. Coronary vasospasm as a cause of stunned myocardium. *Am Heart J* 1987; 113: 383-5.
9. Shaw TR, Rafferty P, Tait GW. Transient shock and myocardial impairment caused by pheochromocytoma crisis. *Br Heart J* 1987; 57: 194-8.
10. Greenhoot JH, Reichenbach DD. Cardiac injury and subarachnoid hemorrhage. A clinical, pathological, and physiological correlation. *J Neurosurg* 1969; 30: 521-31.
11. Shanlin RJ, Sole MJ, Rahimifar M, Tator CH, Factor SM. Increased intracranial pressure elicits hypertension, increased sympathetic activity, electrocardiographic abnormalities and myocardial damage in rats. *J Am Coll Cardiol* 1988; 12: 727-36.
12. Kolin A, Norris JW. Myocardial damage from acute cerebral lesions. *Stroke*. 1984; 15: 990-3.
13. Galinanes M, Hearse DJ. Brain death-induced impairment of cardiac contractile performance can be reversed by explantation and may not preclude the use of hearts for transplantation. *Circ Res* 1992; 71: 1213-9.
14. Seiler C, Laske A, Gallino A, Turina M, Jenni R. Echocardiographic evaluation of left ventricular wall motion before and after heart transplantation. *J Heart Lung Transplant* 1992; 11: 867-74.