Coronary Microvascular Abnormality in the Reversible Systolic Dysfunction Observed After Noncardiac Disease

Kenji Sadamatsu, MD; Hideki Tashiro, MD; Naoya Maehira, MD; Kunihiko Yamamoto, MD

Acute reversible left ventricular wall motion abnormalities mimicking myocardial stunning have been reported with noncardiac disease and their coronary angiograms did not demonstrate organic stenosis or vasospasm in the epicardial coronary arteries. Thus, this mechanism has not yet been fully clarified. Two patients are reported as demonstrating acute reversible wall motion abnormalities after noncardiac disease. The electrocardiographic and echocardiographic findings mimicked myocardial stunning and confirmed the previous reports. The coronary angiograms did not show any corresponding coronary stenosis or vasospasm, but did show a reduced coronary flow reserve. Cardiac metaiodobenzylguanidine scintigraphy demonstrated regional defects involving the apex, a decreased heart/mediastinum ratio and an enhanced washout rate, which partially returned to normal after 3 months. Microvascular dysfunction and sympathetic nervous abnormalities might be responsible for the reversible contractile impairment. (Jpn Circ J 2000; 64: 789–792)

Key Words: Coronary flow reserve; Iodine-123 metaiodobenzylguanidine scintigraphy; Microvascular disease; Myocardial stunning

A

acute reversible left ventricular wall motion abnormalities mimicking myocardial stunning have mainly been reported with subarachnoid hemorrhage and many investigators have implicated the catecholamine-mediated neural pathways and elevated circulating catecholamine levels as the possible mechanism. A similar reversible left ventricular dysfunction has also been described in patients with other types of noncardiac disease and their electrocardiogram (ECG) findings resembled those of myocardial ischemia, although a coronary angiogram did not demonstrate organic stenosis or vasospasm in the epicardial coronary arteries. There have been few experimental or clinical studies on wall motion abnormalities with these other noncardiac diseases, therefore the mechanism has not yet been clarified.

We report on 2 patients who developed acute reversible wall motion abnormalities and ST–T segment changes without any corresponding coronary stenosis or structural heart disease and in whom cardiac imaging with iodine-123 (¹²³I) metaiodobenzylguanidine (MIBG) scintigraphy demonstrated regional defects, in addition, the coronary flow reserve was reduced.

Case Reports

The 2 patients had been admitted to other divisions of St. Mary's Hospital with almost normal ECG findings (Figs 1A, 4A), but after admission they were referred to the Division of Cardiology for evaluation of abnormal ECG changes. We obtained informed consent from all patients to measure the coronary flow reserve.

(Received March 6, 2000; revised manuscript received June 12, 2000; accepted July 4, 2000)

Division of Cardiology, St. Mary's Hospital, Kurume, Japan
Mailing address: Kenji Sadamatsu, MD, Division of Internal Medicine, Sasebo Kyoui Hospital, 10-17 Shimanjicho, Sasebo 857-8575, Japan. E-mail: kenjisdm@wave.plia.or.jp

Japanese Circulation Journal Vol. 64, October 2000

Patient 1

A 72-year-old previously healthy man was admitted with a syndrome of inappropriate antidiuretic hormone secretion and hypogonadotropism. On the fifth day, his ECG had giant negative T waves in leads I, II, III, aV₁, aV₅ and V₂–6, and a prominent QT interval prolongation (QTc=740 ms) (Fig 1B). An echocardiogram revealed apical dyskinesis, but no cardiovascular symptoms were seen and no remarkable changes were observed in his vital or physical signs. Creatine kinase and troponin T levels were normal. The ECG abnormalities gradually resolved, except for the inverted T waves. The systolic dysfunction normalized 2 weeks later. An elective coronary angiogram did not demonstrate coronary stenosis or vasospasm with ergonovine. The coronary blood flow velocity was measured with a 0.014-inch Doppler guide wire (FloWire, Cardiometrics, CA, USA) at the proximal site of the left anterior descending artery. Next, a bolus of nicorandil 2.0 mg, whose vasodilatory effects were equivalent to those induced by intracoronary papaverine, was injected into the left anterior descending coronary artery, which slightly increased the average peak velocity and the coronary flow reserve was calculated as 2.1. The pressure values were: pulmonary artery 28/14 mmHg; mean pulmonary artery wedge 12; left ventricle at end-diastole 19 mmHg. The cardiac index was 2.7 L·min⁻¹·m⁻². The ventriculogram findings were normal (Fig 2). The MIBG image showed a regional defect in the apex (Fig 3), and the heart/mediastinum count ratio on an early scan was 1.9, whereas on a delayed scan it was 1.6. In addition, the washout rate was 57%. Thallium-201 imaging revealed a smaller perfusion defect in the apex. Three months later, the inverted T waves of the ECG had significantly recovered (Fig 1C), and the MIBG imaging defect had also improved (Fig 3) but the heart/mediastinum count ratio on an early scan was 2.2, and 1.9 on a delayed scan. In addition, the washout rate was 49%.
Patient 1

End diastole

End systole

Patient 2

A 65-year-old previously healthy man had a brain infarction, and was admitted to hospital. An ECG on the third day revealed slight ST-segment elevation in leads II, III, and V4-6 (Fig 1B), and an echocardiogram showed apical akinesis; apart from that, the patient was asymptomatic. The creatine kinase level was high (1,362 IU/L) but the MB fraction was not significantly elevated. On the 4th day, an ECG showed negative T waves in leads I, II, III, aVL, aVF, and V3-6, and the QTc was 667 ms (Fig 1C). The ECG abnormalities gradually resolved, except for the inverted T waves, which persisted (Fig 1D). The contraction dysfunction normalized 4 weeks later. An elective coronary angiogram disclosed 75% stenosis in the posterior descending artery of right coronary artery (Fig 1E) and 99% stenosis in the diagonal branch of left anterior descending artery (Fig 1F), but the territory of the coronary stenosis did not correspond to the regional wall motion abnormality. The coronary flow reserve, which was measured by a bolus injection of nicorandil, was 2.0. The pressure values were: pulmonary artery 31/12 mmHg; mean pulmonary artery wedge 8; left ventricle at end-diastole 13 mmHg. The cardiac index was 3.3 L/min/m². The left ventriculogram did not demonstrate local asynergy (Fig 2). The MIBG image showed a decrease in the apex and inferior region (Fig 3), and the heart/mediastinum count ratio on an early scan was 1.9, and 1.8 on a delayed scan. In addition, the washout rate was 37%. Three months later, the inverted T waves of ECG still remained. The defect on MIBG imaging had improved (Fig 3), but the heart/mediastinum count ratio on an early scan was 2.0 and 2.2 on a delayed scan. The washout rate was 22%. One year later, the ECG changes had all disappeared.

Discussion

The ECG and echocardiographic findings, and their serial changes, in the present patients closely confirmed previous reports of wall motion abnormalities after subarachnoid hemorrhage and noncardiac disease.

"Japanese Circulation Journal" Vol. 64, October 2000
However, syndrome X and microvascular spasm have been reported to cause ST-segment elevation with angiographically normal coronary arteries\textsuperscript{18,19} and, moreover, previous reports have shown a limited coronary flow reserve in patients of syndrome X and concluded that coronary microcirculation dysfunction could result in myocardial ischemia\textsuperscript{20,21} These observations led us to hypothesize that microvascular dysfunction may cause the reversible contractile impairment, and the coronary flow reserve in the present patients did decrease according to the normal value proposed by Baumgarten et al\textsuperscript{22} despite an improvement in the wall motion. We could not measure the coronary flow reserve during systolic dysfunction, so it remains unclear as to whether or not the coronary flow reserve was lower. However, the reduced coronary flow reserve suggests a microvascular abnormality, which might have caused the ECG changes and wall motion abnormalities.

We also observed abnormal cardiac MIBG images, which partially returned to normal after 3 months. The decreased MIBG uptake indicates sympathetic denervation and/or noradrenaline depletion\textsuperscript{23,24} whereas the hastened washout rate reflects sympathetic activation\textsuperscript{25} These findings support the speculation that sympathetic activation played an important role in the ECG changes and wall motion abnormalities. Experimental studies have demonstrated that a sympathetic nervous abnormality can affect the ECG and

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{example.png}
\caption{123I-metaiodobenzylguanidine scintigraphy images in patient 1 (Left) and patient 2 (Right) show regional defects involving the apex one month after being referred (1M) and improvements in the defects 3 months later (3M).}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{example.png}
\caption{Electrocardiograms recorded in patient 2 at admission (A), the third day (B), fourth day (C), and before discharge (C). (A) Normal ECG. (B) ST-segment elevation is evident in the inferior and lateral leads. (C) ECG shows negative T waves with QT interval prolongation. (D) Inverted T waves remain. Coronary angiograms demonstrate significant stenosis in the posterior descending branch of the right coronary artery (E) and in the diagonal branch of left anterior descending artery (F), but the territory does not correspond to the regional wall motion abnormality.}
\end{figure}
reflects damaged myocardium. Other reports have also shown regional defects on MIBG images in patients with reversible left ventricular dysfunction after noncardiac disease, while the MIBG images in patients with syndrome X show a low heart/mediastinum count ratio and global or regional defects with QTC prolongation also reported. Therefore, the wall motion abnormalities in the present patients and those in patients with syndrome X are similar with regard to the abnormal sympathetic nervous system and the reduced coronary flow reserve. Too little is known to elucidate the correlation among abnormalities of wall motion, the sympathetic nervous system and the coronary microcirculation. However, reversible wall motion abnormalities and syndrome X may have a similar microvascular dysfunction in their causation. The partial reversibility of the abnormal distribution in the MIBG images suggests that some factors may have led to a worsening of the microvascular abnormalities, and such factors might include microvascular spasms due to sympathetic nerve activation.

Two unresolved questions remain. First, we did not investigate any metabolic changes by measuring lactate concentration or by positron-emission tomography or 123I-β-methyl-iodophenyl pentadecanoic acid images, thus our findings are not sufficient evidence to prove myocardial ischemia. Second, a regional discrepancy was observed in the ECGs, echocardiograms and MIBG images. The giant negative T waves in the precordial leads corresponded to apical asynergy, but the ECG abnormalities also occurred in the inferior leads, although the changes were smaller than those in the precordial leads, and this phenomenon may either correspond to apical dysfunction or the myocardial damage in the inferior region might not have been sufficient to cause a wall motion abnormality. In patient 1, the regional defect on the MIBG images corresponded to the wall motion abnormality, but the defects in patient 2 were observed in the apical and inferior regions. The uptake of MIBG tends to decrease in the inferior region even in healthy people, and thus the inferior defect in patient 2 might have been insignificant or too small to induce local asynergy.

In conclusion, we have described 2 patients who developed acute reversible wall motion abnormalities after noncardiac disease and in whom the findings and serial changes of ECGs and echocardiograms were similar to those previously reported. Cardiac catheterization showed a reduced coronary flow reserve, but no corresponding coronary stenosis. Cardiac sympathetic images disclosed regional defects, a decreased heart/mediastinum count ratio and an enhanced washout rate. These findings suggest that abnormalities in both the sympathetic nervous system and coronary microcirculation play an important role in wall motion dysfunction that mimics myocardial stunning.

Acknowledgments

We are grateful to Dr Makoto Katsuragi for his interpretations of the myocardial scintigrams.

References


Japanese Circulation Journal Vol. 64, October 2000