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Increasing myocardial ^{123}I-BMIPP uptake in non-ischemic area in a patient with acute myocardial ischemia

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The subject was a 65-year-old woman with chest pain. An electrocardiogram revealed T-wave-inversion in leads III, aV_F, V_1–V_5. ^{99m}Tc-tetrofosmin myocardial SPECT showed mildly reduced uptake in the anteroseptal wall and the apex. These findings suggested acute myocardial ischemia. Coronary angiography did not show any stenotic lesions, but diffuse coronary ectasia was noted in three vessels. Coronary flow velocity was remarkably reduced on coronary angiography. Epicardial coronary spasm was not provoked by ergonovine loading test. Left ventriculography showed diffuse hypokinesis. ^{123}I-BMIPP myocardial SPECT showed mildly reduced uptake in the anteroseptal wall and the apex on the early images. But 4-hour delayed images showed an increase of 8% in myocardial ^{123}I-BMIPP uptake. We treated this patient with ticlopidine and nicorandil. After drug therapy her symptoms and left ventriculography improved. ^{123}I-BMIPP myocardial SPECT findings on the early images improved, whereas delayed images showed a decrease of 28% in myocardial ^{123}I-BMIPP uptake after two weeks and 36% after four weeks. These dynamic changes in ^{123}I-BMIPP findings might be a reflection of myocardial fatty acid metabolism in patients with acute myocardial ischemia. Delayed ^{123}I-BMIPP myocardial SPECT images are useful for the assessment of fatty acid metabolism.

Key words: acute myocardial ischemia, ^{123}I-BMIPP, fatty acid metabolism

INTRODUCTION

^{123}I-15-(*p*-iodophenyl)-3-*R*,*S*-methylpentadecanoic acid (^{123}I-BMIPP) myocardial single photon emission computed tomography (SPECT), which evaluates fatty acid metabolism, is used for the diagnosis of ischemic heart diseases and assessment of pathology. Several recent reports have indicated that the decreased uptake of ^{123}I-BMIPP in patients with ischemic heart disease represents a memory image of past ischemic myocardial damage. The present case report describes a rare case of acute myocardial ischemia with increasing myocardial ^{123}I-BMIPP uptake.

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CASE REPORT

The subject was a 65-year-old woman with chest pain. She had a history of laparoendoscopic cholecystectomy because of cholelithiasis 6 days previously. She had no coronary risk factors. Physical examination revealed the following: blood pressure was 136 over 76 mmHg; An S_3 sound and moist rale were heard. Blood examination was normal. A chest x-ray showed cardiomegaly and congestion of the lungs, and the cardiothoracic rate was 64%. An electrocardiogram showed T-wave inversion in leads III, aV_F and V_1 through V_5 without abnormal Q waves (Fig. 1). Echocardiography showed moderately diffuse hypokinesis of the left ventricle. ^{99m}Tc-tetrofosmin myocardial SPECT showed mildly reduced uptake from the

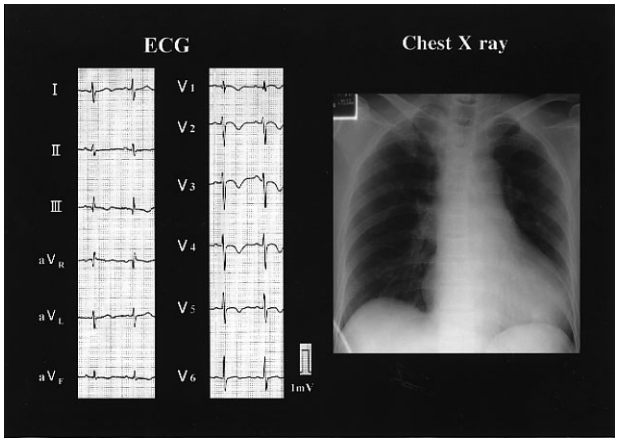

Fig. 1 ECG and chest x-ray. ECG showed T-wave inversion in leads III, aV_F, V_1 through V_5 without abnormal Q waves. Chest x-ray showed cardiomegaly and congestion of the lung, and cardiothoracic rate was 64%.

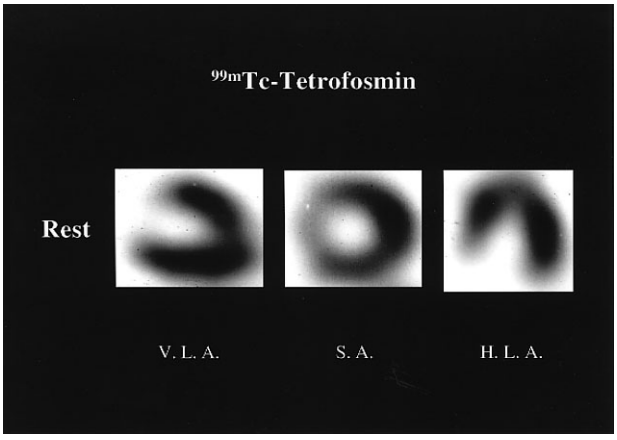

Fig. 2 ^{99m}Tc-tetrofosmin myocardial SPECT. ^{99m}Tc-tetrofosmin myocardial SPECT showed mildly reduced uptake from the anteroseptal region to the apex on the rest images.

anteroseptal region to the apex on the rest images (Fig. 2). Coronary angiography did not show any stenotic lesions, but diffuse coronary ectasia was noted in three vessels and coronary flow velocity was remarkably reduced on coronary angiography (Fig. 3). Epicardial coronary spasm was not provoked by ergonovine loading test. Left ventriculography showed diffuse hypokinesis, the end diastolic volume (EDV) was 139 cm^3, the end systolic volume (ESV) was 72 cm^3 and the ejection fraction (EF) was 48% (Fig. 4). Furthermore, the coronary flow reserve (the ratio of peak hyperemic to resting coronary flow velocity) was measured by placing a Doppler blood flow guide wire in the left anterior descending artery and administering intracoronary adenosine triphosphate disodium. The average peak velocity was 7.7 cm per second, but it improved to 32 cm per second after administration of aden-

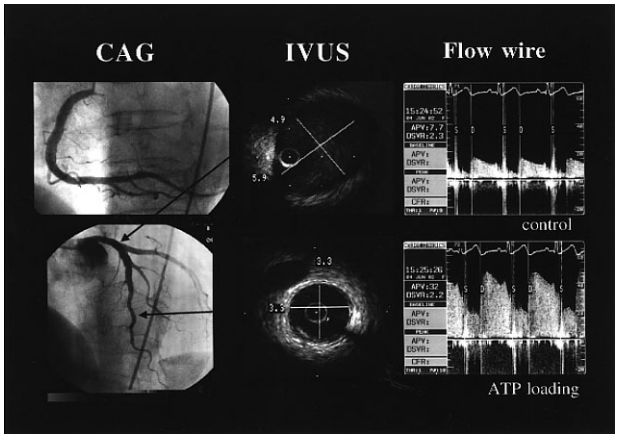

Fig. 3 Coronary angiography, Intravascular ultrasound and Doppler blood flow wire. Coronary angiography did not show any stenotic lesions, but diffuse coronary ectasia was noted in three vessels. The maximal diameter of the left anterior descending artery measured by intravascular ultrasound was 5.9 mm. The average peak velocity measured by Doppler blood flow guide wire was 7.7 cm per second, but it improved to 32 cm per second after administration of adenosine triphosphate disodium.

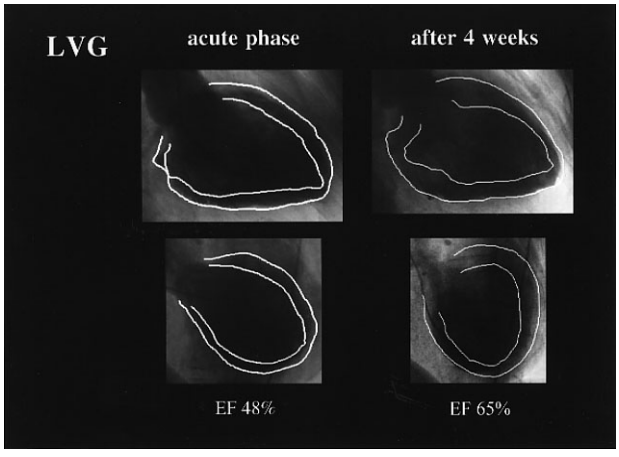

Fig. 4 Left ventriculography. On the acute phase it showed diffuse hypokinesis, and the ejection fraction was 48%. After 4 weeks the ejection fraction improved to 65%.

osine triphosphate disodium (Fig. 3). The next day, ^{123}I-BMIPP myocardial SPECT was performed. While fasting at rest, 111 MBq of ^{123}I-BMIPP (Nihon Medi-Physics Co., Nishinomiya, Japan) was intravenously injected, then early and delayed images were obtained by SPECT starting 15 minutes and 4 hours after injection, respectively, with a digital gamma camera 901A (Toshiba Co., Tokyo, Japan) to which a collimator exclusively for ^{123}I was attached. Data were collected from a 64 × 64 matrix in 32 directions, namely ever 6° between a left posterior oblique angle of 45° and a right anterior oblique angle of 45°, and for 30 seconds per direction. Data were

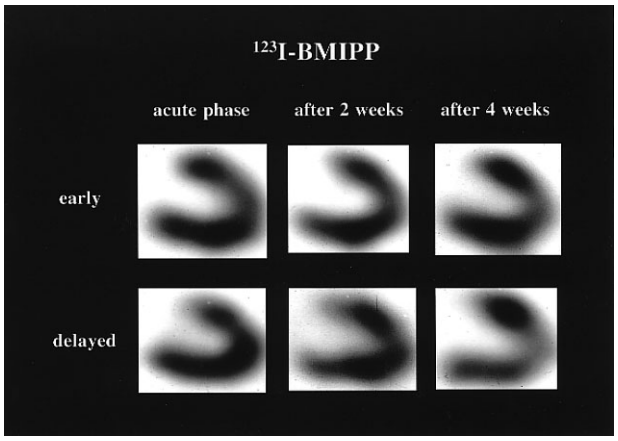

Fig. 5 Serial change of ^{123}I-BMIPP myocardial SPECT. ^{123}I-BMIPP myocardial SPECT showed mildly reduced uptake in the anteroseptal wall and the apex on the early images, but on the delayed images these findings were improved on the acute phase. After medication ^{123}I-BMIPP myocardial SPECT findings improved, but the washout of ^{123}I-BMIPP from myocardium accelerated.

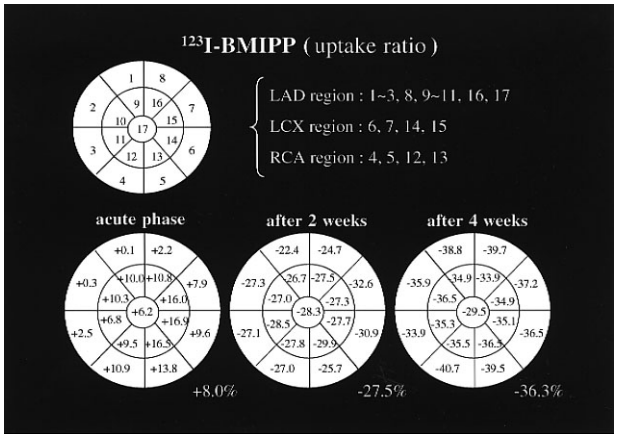

Fig. 6 Serial change of ^{123}I-BMIPP uptake ratio. The increased uptake of ^{123}I-BMIPP was lower in the LAD than in other regions on the acute phase. But after medication the washout of ^{123}I-BMIPP from myocardium accelerated in all regions.

entered into an on line nuclear medicine data processor, GMS550U (Toshiba Co., Tokyo, Japan). The original image was reconstituted by smoothing at 5 points. Tomographic images along the vertical long, horizontal long and short axis were created with a Shepp & Logan filter. The threshold level was 20% and absorption was not corrected. ^{123}I-BMIPP myocardial SPECT showed mildly reduced uptake in the anteroseptal wall and the apex on the early images. But on the 4-hour delayed images these findings improved (Fig. 5). The left ventricle on an ^{123}I-BMIPP myocardial bull's-eye plot was divided into 17 segments as follows: the basal and middle regions of the short axis were divided into 8 segments each, and the apical region made up the 17th segment. These segments were divided into the regions of the left anterior descending artery (LAD), the left circumflex branch of the left coronary artery (LCX) and the right coronary artery (RCA). With a bull's-eye plot of the early and delayed images, the uptake ratio (%) between 15 minutes and 4 hours after the intravenous injection of ^{123}I-BMIPP in the LAD, LCX and RCA regions was calculated with the following equation: (count at 15 minutes − count at 4 hours)/(count at 15 minutes) × 100. These uptake ratios were calculated without correction with the half life of ^{123}I. The overall uptake rate was +8.0% after 4 hours. The uptake ratio was +5.46% in the LAD, +12.7% in the LCX and +12.6% in the RCA. These uptake rate findings corresponded to the myocardial SPECT findings (Fig. 6).

We treated this patient with an antiplatelet agent (ticropidine 100 mg/day and aspirin 81 mg/day), K channel opener (nicorandil 15 mg/day), angiotensin-converting enzyme inhibitation (perindopril erbumine 4 mg/day), diuretic (furosemide 40 mg/day and spironolactone 25 mg/day). After drug therapy her symptoms and ^{99m}Tc-tetrofosmin myocardial SPECT findings improved. Left ventriculography showed improved wall motion, after 4 weeks the EDV was reduced to 128 cm^3, the ESV was reduced to 45 cm^3 and the EF was improved to 65% (Fig. 4). ^{123}I-BMIPP myocardial SPECT findings on the early images improved (Fig. 5), and on the delayed images, after 2 weeks the uptake ratio was −26.5% in the LAD, −29.6% in the LCX and −27.6% in the RCA. After 4 weeks the uptake ratio was −34.2% in the LAD, −35.9% in the LCX and −38.1% in the RCA (Fig. 6). These uptake ratio findings suggested that the difference between ischemic and non-ischemic regions was small.

DISCUSSION

Her symptoms, electrocardiogram, chest x-ray and ^{99m}Tc-tetrofosmin findings suggested that acute myocardial ischemia caused congestive heart failure. Coronary angiography findings suggested that a microcirculation disturbance, such as microvascular thrombi and spasm, caused acute myocardial ischemia. Mental or physical stress after operation might have predisposed to myocardial ischemia. ^{123}I-BMIPP myocardial SPECT was expected to show severely reduced uptake, but it showed only mildly reduced uptake. Furthermore, the 4-hour delayed images showed increasing myocardial ^{123}I-BMIPP uptake. Under aerobic conditions and at rest while fasting, 60% to 90% of the energy requirement is supplied by fatty acid metabolism. Cardiac muscle cells efficiently oxidize fatty acids to produce high levels of energy. Free fatty acids incorporated from the blood, which are straight fatty acids (arachidonic acid, stearic acid and palmitic acid etc.), are acylated with ATP as an energy source and β-oxidized in mitochondria. Under hypoxic or ischemic conditions, fatty acid metabolism, which needs a large amount of

oxygen, is easily suppressed. ^{123}I-BMIPP, which is a branched fatty acid analogue, is not β-oxidized in mitochondria after incorporation. It is mainly accumulated in the lipid pool (about 70%). Some ^{123}I-BMIPP is β-oxidized in mitochondria after being α-oxidized.

An electrocardiogram mainly showed abnormality in the chest leads. ^{99m}Tc-tetrofosmin myocardial SPECT and ^{123}I-BMIPP myocardial SPECT showed reduced uptake in the anteroseptal wall and the apex. These findings suggested that myocardial ischemia occurred in the LAD. The delayed ^{123}I-BMIPP images were expected to show decreasing myocardial ^{123}I-BMIPP uptake,[1] but revealed increasing myocardial ^{123}I-BMIPP uptake. Increasing myocardial ^{123}I-BMIPP uptake was marked in the lateral wall and the inferior wall. These findings suggested that increasing myocardial ^{123}I-BMIPP uptake was marked in the non-ischemic region. It has been reported that the uptake ratio of normal human cardiac muscle cells is +18 ± 3.0% after 4 hours. And it has also been reported that it decreases during the acute phase of ischemia and conversely increases during the chronic phase of ischemia.[2,3] β-oxidation in mitochondria is suppressed during the acute phase. When cardiac muscle cells become acutely ischemic, the blood catecholamine concentration increases, the degradation of fat tissue is accelerated throughout the body, and the blood free fatty acid concentration increases. Excess free fatty acids produced as a result may exert adverse effects on cardiac muscle cells, including the induction of fatal arrhythmias,[4,5] decreased cardiac contractility[6,7] and membranous dysfunction.[8,9] To prevent these events, the lipid pool in cardiac muscle cells expands and incorporates excess free fatty acids. Moreover, free fatty acids incorporated into the expanded lipid pool are retained in this pool without being metabolized or being washed out into the blood stream.[1,10–13] These functions are remarkable in the non-ischemic regions. In our patient, expansion of the lipid pool in response to ischemia was expected to cause a decreasing washout rate, but the delayed images showed increasing myocardial ^{123}I-BMIPP uptake. These findings suggested that the lipid pool expanded, washout from the lipid pool into the blood was suppressed, and ^{123}I-BMIPP in the blood and production of ^{123}I-BMIPP metabolized in the liver and striated muscle was increasingly accumulated in cardiac muscle cells. On the delayed images in both the ischemic and the non-ischemic regions, the decreased uptake of ^{123}I-BMIPP was accelerated after medication. This finding suggested that a decrease in the catecholamine concentration caused a decrease in free fatty acids, the lipid pool was reduced and washout from the lipid pool into the blood was accelerated.[2,3] After 4 weeks the washout of ^{123}I-BMIPP from the myocardium was accelerated further, so it would take much time to improve the uptake.

These unusual dynamic changes in ^{123}I-BMIPP myocardial SPECT imaging may reflect a change in fatty acid metabolism in the acute ischemic and recovery states.

REFERENCES

1. Lopaschuk GD, Belke DD, Gamble J, Itoi T, Schonekess BO. Regulation of fatty acid oxidation in the mammalian heart in health and disease. *Biochemica et Biophysica Acta* 1994; 1213: 263–276.
2. Ito K, Sugihara H, Kawasaki T, Kato S, Azuma A, Nakagawa M. Dynamic changes in cardiac fatty acid metabolism in the stunned human myocardium. *Ann Nucl Med* 2001; 15: 343–350.
3. Zen K, Ito K, Hikosaka T, Adachi Y, Yoneyama S, Kato S, et al. Unusual Changes Detected by Iodine-123 15-(*p*-Iodophenyl)-3-*R*,*S*-Methylpentadecanoic Acid Myocardial Single Photon Emission Computed Tomography in the Process of Acute Myocardial Infarction. *J Cardiol* 2001; 37: 215–222.
4. Oliver MF, Kurien VA, Greenwood TW. Relation between serum-free fatty acid and arrhythmias and death after acute myocardial infarction. *Lancet* 1968; I: 710–714.
5. Corr PB, Gross RW, Sobel BE. Amphipathic metabolites and membrane dysfunction in ischemic myocardium. *Circ Res* 1984; 55: 135–154.
6. Katz AM, Messineo FC. Lipid-membrane interactions and the pathogenesis of ischemic damage in the myocardium. *Circ Res* 1981; 48: 1–16.
7. Liedtke AJ. Alteractions of carbohydrate and lipid metabolism in the acutely ischemic heart. *Prog Cardiovasc Dis* 1981; 23: 321–336.
8. Mjos OD. Effect of free fatty acids on myocardial function and oxygen consumption in intact dogs. *J Clin Invest* 1978; 50: 1386–1389.
9. Liedtke AJ, Nellis SH, Neely JR. Effects of excess free fatty acids on mechanical and metabolic function in normal and ischemic myocardium in swine. *Circ Res* 1978; 43: 652–661.
10. Schwaiger M, Schelbert HR, Ellison D, Hansen H, Yeatman L, Vinten-Johansen J, et al. Retention and clearance of ^{11}C-palmitate in ischemic and reperfused canine myocardium. *J Am Coll Cardiol* 1985; 6: 336–347.
11. Rosamund TL, Abendschein DR, Sobel BE, Bergmann SR, Fox KA. Metabolic fate of radiolabeled palmitate in ischemic canine myocardium: implications for positron emission tomography. *J Nucl Med* 1987; 28: 1322–1329.
12. Staeter-Knowlen IM, Evanochko WT, Hollander JA, Wolkowicz PE, Balschi JA, Caulfield JB, et al. ^{1}H NMR spectroscopic imaging of myocardial triglycerides in excised dog heart subjected to 24 hours of coronary occlusion. *Circulation* 1996; 93: 1464–1470.
13. Milled DD, Gill JB, Livin E, Elmaleh DR, Aretz T, Boucher CA, et al. Fatty acid analogue accumulation: a maker of myocyte viability in ischemic-repurfused myocardium. *Circ Res* 1988; 63: 681–692.