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Two phase imaging of ^{99m}Tc-SESTAMIBI and ^{123}I-BMIPP for patients with angina pectoris

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We saw three cases of angina pectoris in which ^{99m}Tc-SESTAMIBI delayed images at rest were useful in diagnosing ischemia risk areas.

These findings indicated that delayed ^{99m}Tc-SESTAMIBI images may be more sensitive to slight ischemia than ^{123}I-BMIPP images, and suggested that imaging with ^{99m}Tc-SESTAMIBI twice at rest may be more effective. The addition of ^{123}I-BMIPP SPECT was considered to be useful in making an evaluation of the severity of ischemia.

Key words: effort angina, vasospastic angina, unstable angina, ^{99m}Tc-SESTAMIBI, ^{123}I-BMIPP

INTRODUCTION

^{99m}Tc-SESTAMIBI (MIBI) and ^{99m}Tc-Tetrofosmin (TF) are ^{99m}Tc-myocardial perfusion agents, which are taken up into the myocardium and are retained in the myocardium by the mitochondrial membrane potential. After ^{99m}Tc-SESTAMIBI (MIBI) is taken up into the myocardium, more than about 90% of it combines with the mitochondria[1,2] and is retained in the myocardium for many hours with slow washout.[3,4]

It has been reported in recent years, however, that the increased washout reverse redistribution phenomenon[5,6] was commonly observed after reperfusion therapy in patients with acute myocardial infarction (AMI). On the other hand, there have been few reports about reverse redistribution in patients with angina pectoris.

^{123}I-BMIPP (BMIPP)[7] is considered to reflect fatty acid metabolism and is used for the diagnosis of angina pectoris.[8,9] But the diagnostic sensitivity is not necessarily high for the diagnosis of effort angina.[10] It has been reported to be rather useful in assessing the myocardial salvage effect and in predicting wall motion recovery after reperfusion therapy for AMI patients.[11] We found that early and delayed MIBI images at rest and BMIPP images performed on suspicion of effort angina, vasospastic angina and unstable angina, were useful for the diagnosis. In this report, we describe these cases with an overview of the relevant literature.

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CASE REPORTS

Case 1: Effort angina (Fig. 1)

Patient: A 69-year-old male patient.

Chief complaint: Feeling of strangulation in the chest.

Past medical history: Arrhythmia had been detected during medical examination eight years ago, but no other abnormal signs or subjective symptoms were detected.

Current disease history: The patient complained of slight chest discomfort and chest pain when he climbed slopes and stairs since the beginning of May 2001. These symptoms subsequently occurred twice weekly but disappeared in a couple of minutes while the patient was at rest. He had an attack of chest pain on 14th of May while walking. Although the pain disappeared while he was at rest, the patient immediately consulted a doctor in another hospital. ECG revealed U-wave abnormality, and the patient was admitted since exertional angina was suspected. The patient began to receive an anti-angina drug, and the symptoms did not recur. The patient was referred

to our hospital and admitted for a thorough medical examination on 28th.

Myocardial perfusion SPECT with MIBI during exercise was performed on day 2 after admission. Changes in ST appeared at 6 minutes after the start of exercise, and SPECT revealed reduced uptake in the inferior wall and slightly reduced uptake in the anterior wall. On the next day, myocardial perfusion SPECT at rest was performed, and normal myocardial uptake at 30 minutes after administration of MIBI was observed in the early images. The delayed images were obtained at 6 hours after administration of MIBI and revealed reduced uptake in the inferior wall. Although the delayed image, in comparison with perfusion SPECT during exercise, indicated that the area and depth of uptake were a little underestimated and that there was normal uptake in the anterior wall, these findings were thought to be similar to those of images of perfusion SPECT during exercise. CAG performed 4 days after admission revealed 90% stenosis in RCA, 90% stenosis in LCX, and 75% stenosis in LAD. Left ventriculography (LVG) showed 72% LVEF with no wall motion abnormality. Seven days after admission, BMIPP SPECT was performed. Myocardial uptake 15 minutes after administration of BMIPP was normal and no fatty acid metabolism disorder was observed.

Based on the clinical course and the results of CAG, the patient was diagnosed as having effort angina and was transferred to the Department of Cardiovascular Surgery because his condition indicated the need for a coronary artery bypass graft (CABG).

Case 2: Vasospastic angina (Fig. 2)

Patient: A 54-year-old woman.

Chief complaint: Anterior chest pain.

Past medical history: The patient had received outpatient treatment for diabetes mellitus at another hospital about five years ago. In July 2000, she had an oppressive feeling in her chest with palpitation. She underwent Holter monitoring but no abnormality was observed.

Current disease history: Since about June 2001, the palpitation, shortness of breath and oppressive feeling in the chest became severe, and the patient was referred to our hospital. On June 7, the patient underwent ECG and hematological tests at the outpatient clinic, but there were no abnormal findings. Holter monitoring revealed premature ventricular contraction (PVC) just 2 times/day with no ST-T change. Because her chest discomfort persisted, the patient was admitted for a thorough medical examination on June 12. On day 2 after admission, CAG revealed 75% stenosis in LAD, but normal coronary arterial blood flow was maintained. Despite administration of acetylcholine, no narrowing of the left coronary artery or ECG change was observed. Since the patient frequently complained of chest pain during hospitalization and her symptoms were judged to be due to coronary stenosis angina, treatment with a calcium antagonist began. On day 4 after admission, BMIPP SPECT was performed, and the myocardial uptake of BMIPP was normal and no fatty acid metabolism impairment was observed at 15 minutes after administration of BMIPP. On day 8 after admission, MIBI SPECT at rest was performed and myocardial uptake was normal at 30 minutes after administration of MIBI, but when the delayed images were obtained at 6 hours after administration, uptake reduction was clearly observed in an area extending from the apex to the anterior wall. Moreover, reduced uptake was also found in the apex, and these findings indicate the possibility of due to the coronary spasm. Echocardiography was performed on the same day and revealed just slight expansion of the left ventricle. In view of the patient's clinical course, CAG results and myocardial SPECT findings, the patient was diagnosed as having vasospastic angina with consequences of LAD stenosis. It was decided that the patient would be followed up at the outpatient clinic.

Case 3: Unstable angina (Fig. 3)

Patient: A 60-year-old man.

Chief complaint: Anterior chest pain.

Previous history: Renal tuberculosis at the age of 16 years.

Current disease history: Chest pain occurred once or twice daily from the beginning of February 2001, lasted for about a minute and then ceased. Since the frequency of the manifestations increased to three or four times daily from February 2 or 3, the patient went to another hospital for a check-up. Since ECG showed increased ST, the patient was diagnosed as having unstable angina and was referred to our hospital. On admission, reduced wall motion of the anterior wall and the apex was observed. MIBI myocardial scintigraphy at rest was performed, and myocardial uptake at minute 30 after administration of MIBI was normal. Extensive uptake reduction in the anterior wall was noted in the delayed images obtained at 6 hours after MIBI administration. BMIPP SPECT was performed on the following day and revealed uptake reduction in the anterior wall, but both the area and depth of uptake reduction were more marked on the delayed MIBI images.

Coronary angiography revealed 90% stenosis in LAD and delay of the contrast medium. After percutaneous transluminal coronary angioplasty (PTCA), the chest pain disappeared and the patient subsequently received outpatient follow-up treatment.

DISCUSSION

It has been reported that in patients with AMI in whom early reperfusion therapy was successful, reverse redistribution of ^{99m}Tc myocardial perfusion agent at rest frequently occurred in the salvaged area.[12–14] We previously reported that in patients after reperfusion therapy for AMI, early and delayed MIBI images were obtained at

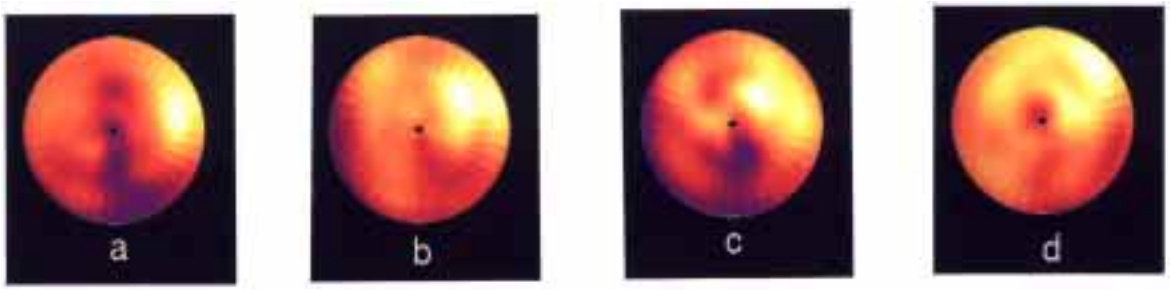

Fig. 1 Effort angina. a: ^{99m}Tc-SESTAMIBI stress image. b: ^{99m}Tc-SESTAMIBI early image. c: ^{99m}Tc-SESTAMIBI delayed image. d: ^{123}I-BMIPP image.

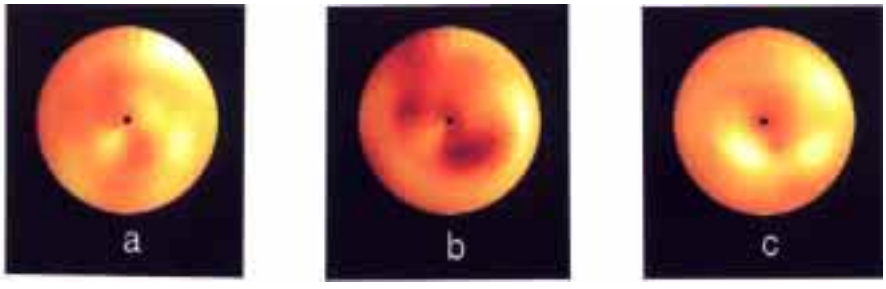

Fig. 2 Vasospastic angina. a: ^{99m}Tc-SESTAMIBI early image. b: ^{99m}Tc-SESTAMIBI delayed image. c: ^{123}I-BMIPP image.

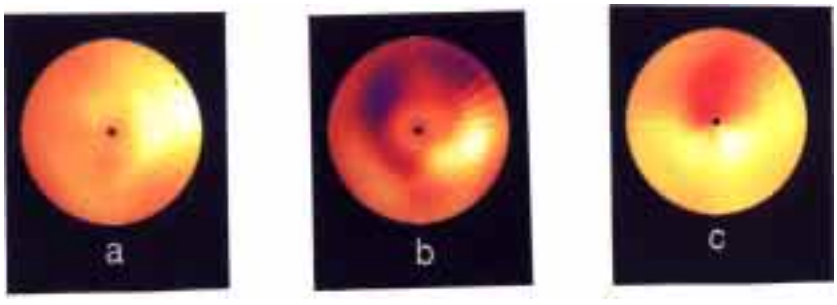

Fig. 3 Unstable angina. a: ^{99m}Tc-SESTAMIBI early image. b: ^{99m}Tc-SESTAMIBI delayed image. c: ^{123}I-BMIPP image.

rest within 5 to 25 days of the onset and that a reverse redistribution phenomenon was noted in 85% of the reperfusion area.[6] A similar phenomenon was also observed with TF, a ^{99m}Tc myocardial perfusion agent.[12] This reverse redistribution phenomenon was thought to vary with many factors including the time from the onset of AMI to reperfusion therapy, ischemic site, the width of the affected area, etc. In a few reports, MIBI retention was closely correlated to mitochondria membrane potential,[15,16] and myocardial cells in the increased washout area are presumed to be impaired due to ischemia, but no definite mechanisms of these have yet been reported.

The present study showed that MIBI washout increased in angina pectoris patients with no previous history of myocardial infarction as well. Furthermore, since BMIPP images of the same patient were normal or only slightly abnormal, the reduced MIBI retention capacity was considered to be more sensitive to ischemia than to abnormality of fatty acid metabolism. About 60 to 70% of the energy metabolism of the myocardium is undertaken by fatty acids, and fatty acid metabolism is thought to decline due to ischemia. The fatty acids synthesize ATP under β oxidation and protons are expelled from the mitochondrial matrix, which causes the membrane potential. ATP synthesis decreases due to reduced β oxidation of the fatty acids,[17] and this leads to a decline in the mitochondrial membrane potential. In other words, reduced fatty acid metabolism is closely correlated to a decline in mitochondria membrane potential.[18] Approximately 70% of BMIPP has been reported to accumulate in a triglyceride (TG) pool in normal myocardial cells.[7] Since in the case of slight ischemia, the effect on fatty acid metabolism is relatively small and the ability to synthesis ATP is not

impaired, detection of slight ischemia with BMIPP is thought to be limited. Early and delayed MIBI imaging and observation of increased washout due to the decline in mitochondria membrane potential is expected to increase sensitivity to ischemia.

The results of the present assessment suggested that it would be possible to obtain more information on myocardial impairment by using and comparing early and delayed images with ^{99m}Tc-myocardial perfusion agents, such as MIBI and BMIPP fatty acid metabolism scintigrams. These imaging data were considered clinically very useful if they made possible new nuclear cardiographic diagnosis in angina pectoris patients and allowed a more detailed diagnosis of ischemia.

Further investigation is considered necessary to clarify whether this method is useful in diagnosing ischemia, in evaluating the severity of the disease and in determining the therapeutic policy while focusing on the patient's prognosis.

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