Annals of Nuclear Medicine Vol. 17, No. 8, 699–702, 2003

Case Report: Unstable angina with flow-fatty acid metabolism mismatch and reverse flow-glucose metabolism mismatch patterns

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A 79-year-old man with unstable angina underwent an emergency coronary angiography, and percutaneous balloon angioplasty was performed for LCX. Left ventriculography showed hypokinesis in the posterior wall, inferior and apical wall immediately after the PCI therapy. The defects on ^{123}I-BMIPP SPECT seen in the inferior, posterior and lateral wall were more extensive than those observed on ^{99m}Tc-MIBI SPECT, and a flow-fatty acid metabolism mismatch pattern was observed. The ^{18}F-FDG PET showed reduced uptake in the lateral segment, although ^{13}N-NH_3 PET showed normal perfusion, and a reverse flow-glucose metabolism mismatch pattern was observed. Left ventriculography showed significant improve to normal contraction on the 3-month follow up, and there was not significantly reduced uptake in ^{99m}Tc-MIBI SPECT, ^{123}I-BMIPP SPECT, ^{13}N-NH_3 PET or ^{18}F-FDG PET.

Key words: ^{18}F-FDG, ^{13}N-NH_3, ^{123}I-BMIPP, ^{99m}Tc-MIBI, repetitive myocardial stunning

INTRODUCTION

METABOLIC IMAGING with positron emission tomography (PET) using ^{18}F-fluorodeoxyglucose (^{18}F-FDG) permits the assessment of myocardial viability in patients with coronary artery disease and left ventricular dysfunction.[1–10] A hypoperfused myocardium with preserved uptake of ^{18}F-FDG under glucose loading is usually considered to be ischemic but viable myocardium.[7–10]

We present a patient with unstable angina who had demonstrated a reduced glucose uptake and normal myocardial blood flow on ^{13}N-NH_3 and ^{18}F-FDG PET imaging (reverse flow-metabolism mismatch pattern), which improved significantly three months later.

Received July 16, 2003, revision accepted September 19, 2003.

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CASE REPORT

The patient was a 79-year-old man who had been treated for hypertension in a neighborhood clinic for 16 years. One day, he developed his first episode of chest pain, which lasted for 15 minutes. Thereafter, the chest pain occurred almost every day and got worse. The patient visited our hospital and was admitted with a diagnosis of unstable angina. On admission, his vital signs were stable and there were no remarkable findings on physical examination. No abnormal laboratory data were obtained on admission, and WBC, AST, LDH and CPK followed every 6 hours did not increase. Electrocardiogram showed significant ST segment depression in leads $V_{4–6}$. An emergency coronary angiography revealed a 99% stenosis with delay in the proximal region of the left circumflex artery (LCX), as demonstrated in Figure 1A. Percutaneous coronary intervention (PCI) was performed for the LCX, and coronary blood flow recovered completely, as demonstrated in Figure 1B. Left ventriculography showed severe hypokinetic movement in the posterior wall and moderate hypokinesis in the apex and inferior wall immediately after the PCI, as demonstrated in Figure 2A. There were also significant stenoses in both the left anterior

descending artery (LAD) and right coronary artery (RCA), as shown in Figure 1C, and PCI for the LAD and RCA was performed the following day. After the PCI therapy for LCX, the patient had no chest pain and no significant ECG changes on exercise. He showed neither diabetes mellitus nor impaired glucose tolerance in oral glucose tolerance test.

After treatment for LCX, the patient underwent MIBI SPECT at rest on the third day of hospitalization and he underwent BMIPP SPECT on the 14th day. SPECT imaging was acquired with a triple-head camera (Prism 3000XP, Picker) and full-width at half-maximum (FWHM) of this camera was about 15 mm. On the 19th day, he also underwent ^{13}N-NH$_3$ PET and ^{18}F-FDG PET at rest. The PET imaging was performed using a full ring PET scanner (Advance, General Electric Medical System) with a resolution of 3.8 mm FWHM, and the ^{18}F-FDG PET was performed following oral administration of 50 g glucose. We judged the uptakes of both SPECT and PET images visually. The MIBI myocardial SPECT showed decreased perfusion in the posterior wall (Fig. 3A), and the BMIPP myocardial SPECT showed reduced uptake in the inferior, posterior and lateral walls (Fig. 3B). These defects were found to be more extensive on the BMIPP imaging as compared with the MIBI imaging, and a flow-fatty acid metabolism mismatch pattern was observed (Fig. 3A, B). The ^{13}N-NH$_3$ PET imaging showed no perfusion abnormality, but the ^{18}F-FDG PET imaging showed reduced glucose uptake in the lateral segment, and a reverse flow-glucose metabolism mismatch pattern was observed (Fig. 4A, B). The patient was discharged from hospital after PCI therapy for LAD and RCA.

Three months later, he was hospitalized again and underwent cardiac catheter examination. There was no restenosis observed in any coronary arteries, and left ventriculography demonstrated that contraction had improved significantly to normal, as demonstrated in Figure 2 right. Neither MIBI nor BMIPP SPECT imaging showed significant reductions in uptake (Fig. 3C, D), and both ^{13}N-NH$_3$ and ^{18}F-FDG PET imaging showed normal uptake (Fig. 4C, D).

DISCUSSION

There are few reports that have studied reduced glucose metabolism with normal blood flow in ^{13}N-NH$_3$ and ^{18}F-FDG PET imaging, the so-called reverse flow-metabolism mismatch pattern.[11–16] Some clinical studies have reported that the reverse flow-metabolism mismatch pattern is observed in ischemic but viable myocardium.[11–13,16]

Perrone-Filardi et al. first reported on the reduced FDG uptake in regions with normal blood flow in patients with chronic coronary artery disease using ^{18}F-FDG PET and ^{201}Tl SPECT.[11] They suggested that such regions represent an admixture of fibrotic and reversibly ischemic myocardium. Yamagishi et al. studied ^{13}N-NH$_3$/^{18}F-FDG PET use in 35 patients with acute myocardial infarction, and found a reverse flow-metabolism mismatch pattern.[12] They considered that the reverse mismatch pattern was closely related to multivessel disease. The present case also showed a multivessel disease, but after PCI therapy for LCX no ischemic signs were demonstrated on exercise. In another report,[13] Yamagishi et al. studied ^{13}N-NH$_3$/^{18}F-FDG PET in 54 patients with myocardial infarction and examined contraction thickening as represented by a count increase on ECG-gated ^{18}F-FDG PET during low-dose dobutamine stress. The percent count increase during dobutamine stress was more significant in the segments with a reverse flow-metabolism mismatch pattern, as compare to the segments with match or mismatch patterns. They considered that the reverse flow-metabolism would be a new marker of the viability of myocardium with a greater contractility during dobutamine stress than myocardium with a flow-metabolism mismatch pattern.

Mesotten et al. studied ^{13}N-NH$_3$/^{18}F-FDG PET in patients with acute myocardial infarction and found a reverse mismatch pattern in 19 of 68 patients 5 days after thrombolytic therapy.[16] In the patients with a reverse mismatch pattern, recoveries of ^{13}N-NH$_3$ and ^{18}F-FDG uptake were found, but no functional recovery was observed at the 3-month follow-up. Although the present case presented with unstable angina, not myocardial infarction, functional recovery was observed after 3 months, in contrast to Mesotten et al.

Di Carli et al. developed a dog model of myocardial stunning with repeated ischemia-reperfusion of the coronary artery, and ^{13}N-NH$_3$/^{18}F-FDG PET, ^{11}C-acetate PET and two-dimensional echocardiography were done to examine the serial recovery of regional blood flow, metabolism and wall motion.[14] In this model, regional wall motion was severely decreased after repeated brief ischemia, remained impaired for 24 hours after reperfusion, and was normalized 1 week later, although regional blood flow had already returned to near-normal 4 hours after reperfusion. Both oxygen metabolism and glucose use were reduced after reperfusion, remained impaired for 24 hours, and recovered to normal level in one week. The time course of the changes in myocardial metabolism paralleled that of the post-ischemic contractile dysfunction. Thus, the authors suggested that a unique metabolic adaptation occurring in repetitive myocardial stunning is different from the one typically seen with myocardial hibernation.

The present case showed repeated episodes of reversible ischemia prior to PCI therapy, and after recovery of myocardial blood flow, the degradation of fatty acid metabolism and glucose metabolism remained, likely through the same course as in the stunning model of Di Carli et al. After 3 months, these metabolic disorders improved along with improvement of left ventricular

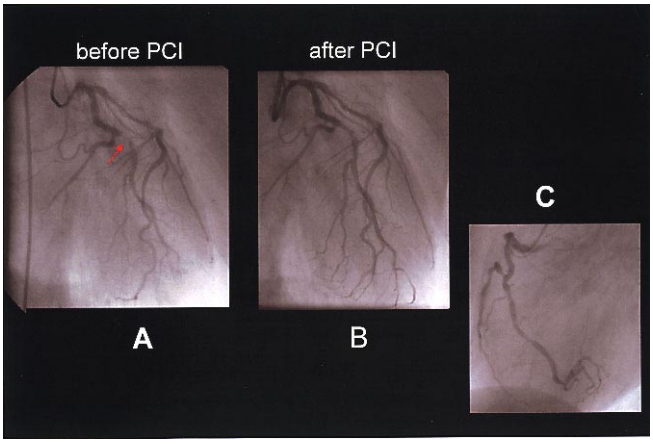

Fig. 1 Emergency coronary angiography revealed a 99% stenosis with delay in the proximal region of the LCX, as shown by the arrow (A). A percutaneous coronary intervention (PCI) for the LCX was performed and the stenosis in the LCX was completely improved (B). There were also significant stenoses in both the LAD (*left and middle panels*) and RCA (C).

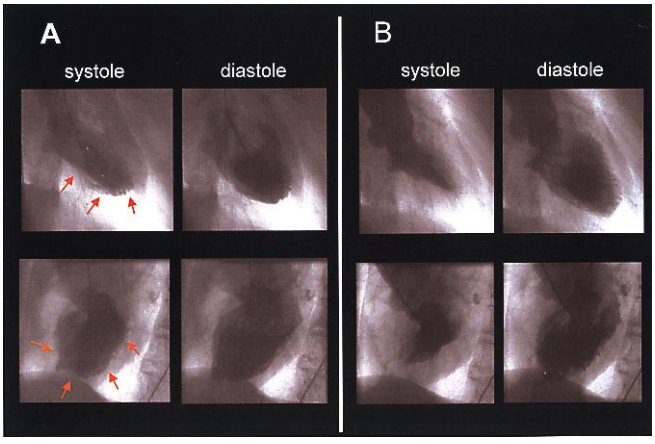

Fig. 2 Left ventriculography showed severe hypokinesis in the posterior wall and moderate hypokinesis in the apical and inferior wall (*shown by the arrows*) immediately after PCI therapy (A), and showed significantly improved to normal contraction on the 3-month follow up (B).

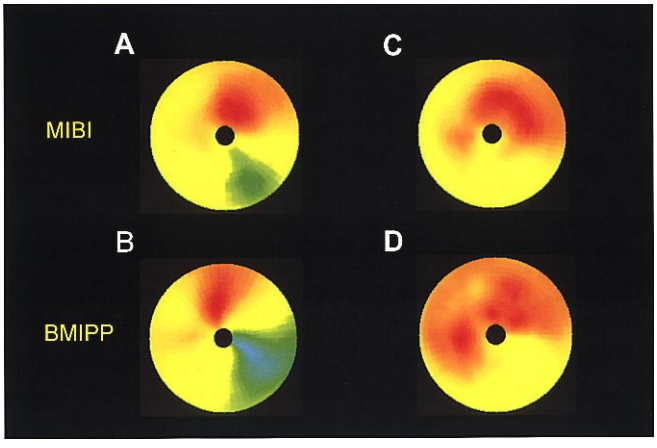

Fig. 3 The MIBI SPECT imaging showed decreased perfusion in the posterior wall (A), and the BMIPP SPECT imaging showed reduced uptake in the inferior, posterior, lateral and apical segments (B) in the subacute phase. Both the MIBI and BMIPP SPECT imaging showed almost normal findings on 3-month follow up (C, D).

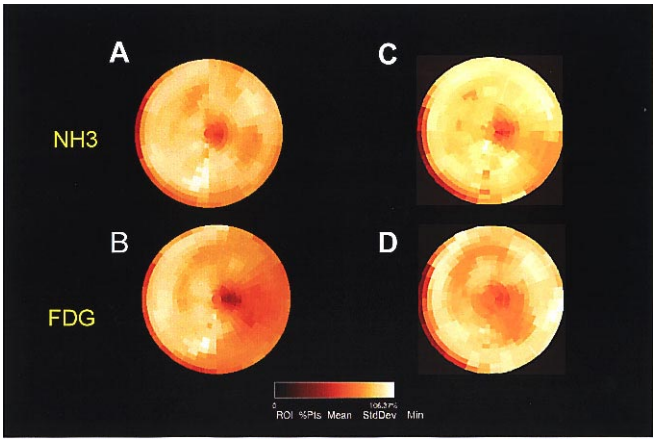

Fig. 4 The ^{13}N-NH_3 PET imaging showed no perfusion abnormality (A), but the ^{18}F-FDG PET imaging showed reduced glucose uptake in the lateral wall (B) in the subacute phase. Both the NH_3 and ^{18}F-FDG PET imaging showed normal uptake on 3-month follow up (C, D).

systolic contraction. Additionally, the discrepancy between MIBI SPECT and ^{13}N-NH_3 PET images observed in this case may reflect the time duration of two images, in which MIBI SPECT was acquired 2 weeks earlier.

This was an interesting case in which we were able to observe the time course of changing myocardial metabolism following repetitive myocardial stunning.

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