Recovery of Perfusion, Glucose Utilization and Fatty Acid Utilization in Stunned Myocardium

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We describe the clinical features and results of cardiac catheterization, PET ([^{13}N]ammonia, ^{18}F-fluorodeoxyglucose (FDG)) and SPECT [^{123}I-labeled 15-(p-iodophenyl)-3-R,S-methylpentadecanoic acid (BMIPP)], in a patient with acute myocardial infarction successfully treated with intracoronary thrombolytic therapy. We compared the clinical and electrocardiographic changes with the myocardial glucose and fatty acid metabolism in stunned myocardium over a period of several months. The patient we studied illustrates the features of stunned myocardium. In the subacute phase, there was a concordant depression of myocardial [^{13}N]ammonia and FDG uptake, and the metabolic abnormalities persisted even after regional wall motion at rest had returned to normal. The electrocardiographic recovery of deep negative T waves appeared to be related to the metabolic recovery in regions of stunned myocardium in this patient.

Key Words: PET; fluorine-18-fluorodeoxyglucose; iodine-123-BMIPP; stunned myocardium

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Stunned myocardium is defined as reversible left ventricular contractile dysfunction in the setting of acute ischemia followed by reperfusion (*1*). In experimental studies, prolonged metabolic abnormalities have been demonstrated in stunned myocardium (*2,3*). Recently, it has become possible to evaluate myocardial glucose and fatty acid utilization in humans using ^{18}F-fluorodeoxyglucose (FDG) (*4,5*) and ^{123}I-labeled 15-(p-iodophenyl)-3-R,S-methylpentadecanoic acid (BMIPP) (*6*). We describe the clinical course and the metabolic changes observed in stunned myocardium in a patient with acute myocardial infarction treated successfully by intracoronary thrombolytic therapy.

CASE REPORT

On September 12, 1995, a 61-yr-old man was admitted to our hospital complaining of severe chest pain. The electrocardiogram (ECG) revealed marked ST segment elevations in the precordial leads (Fig. 1A) with ventricular fibrillation. After sinus rhythm was restored using electric defibrillation, the patient was transferred to the cardiac catheterization laboratory. Coronary angiography revealed 90% stenosis in the proximal left anterior descending artery (LAD) accompanied by residual thrombotic filling defect. Percutaneous transluminal coronary recanalization (PTCR) using tissue-plasminogen activator was performed successfully and resulted in a stenosis of less than 50% in the proximal LAD (Fig. 2A). The ST segment elevations on the ECG returned to the baseline immediately after PTCR, and T waves inverted in the precordial leads (Fig. 1B). However, left ventriculography (LVG) revealed akinesis in the anterior, septal and apical segments. Regional ejection fractions of the anterior and apical segments measured by the method of Gelberg et al. (*7*) were 20% and 15%, respectively (Fig. 2B). There was no subsequent clinical evidence of reinfarction. The serum levels of total creatine kinase (normal 24–195 IU/liter) and myosin light chain I (normal < 2.5 ng/ml) peaked at 586 IU/liter (20 hr after onset) and 4.0 ng/ml (3 days after onset), respectively. On the 32nd day after onset, cardiac catheterization was repeated. At this time, the negative T waves in the precordial leads became deep, but no Q waves were present (Fig. 1C). Coronary angiography showed no significant luminal narrowing. Regional ejection fraction of the anterior and apical segments improved to 47% and 48%, respectively (Fig. 2C). On the 134th day after onset, deep negative T waves were no longer observed in the precordial leads (Fig. 1D), and the patient again underwent cardiac catheterization. LVG at that time revealed normal wall motion.

PET and BMIPP Studies

PET studies at rest were performed on the 8th, 36th and 142nd days after onset. Before each PET study, the patient fasted overnight. Myocardial blood flow was assessed with [^{13}N]ammonia, and exogenous glucose utilization was assessed with FDG. After the patient was positioned in the whole-body tomograph (ADVANCE, GE, Milwaukee, WI), a transmission scan was acquired for 20 min. Static PET images were acquired over a duration of 10 min beginning at 10 min after the intravenous bolus administration of [^{13}N]ammonia (20 mCi). FDG (10 mCi) was then injected intravenously, and static images were acquired over a duration of 10 min beginning at 60 min after the injection (*8*). From a series of transeverese slices, oblique tomograms parallel to the long- and short-axis of the left ventricle were also reconstructed for comparison with the SPECT images.

BMIPP imaging was performed on the same day as the PET study. SPECT images were acquired at rest, 30 min after administration of 111 MBq (3 mCi) BMIPP using a three-headed SPECT camera with high-resolution, parallel-hole collimators (Toshiba GCA-9300A/HG, Tokyo, Japan). A total of 90 projection images were obtained over 360° in 4° increments, with 20 sec per view. Data were recorded in 128 × 128 matrices and stored on a magnetic disk. The energy discrimination window was centered on 159 keV with a 20% window. After transaxial tomograms were reconstructed using Butterworth and ramp filters, short- and vertical long-axis tomograms were obtained. The parameters of the Butterworth filter were 8th order, and the cutoff frequency was 0.14 cycles/pixel (*9*). Although ^{201}TI is a good marker of myocardial perfusion and viability, it was not used in this patient.

Regional [^{13}N]ammonia uptake and BMIPP uptake were calculated in the region of interest (ROI) in a bull's-eye polar map and expressed relative to the ROI with maximal (=100%) tracer uptake. FDG uptake was measured as the percent of the injected dose per 100 ml of tissue (% ID/100 ml) in the ROI in a bull's-eye polar map. The normal upper limit of this value was approximately

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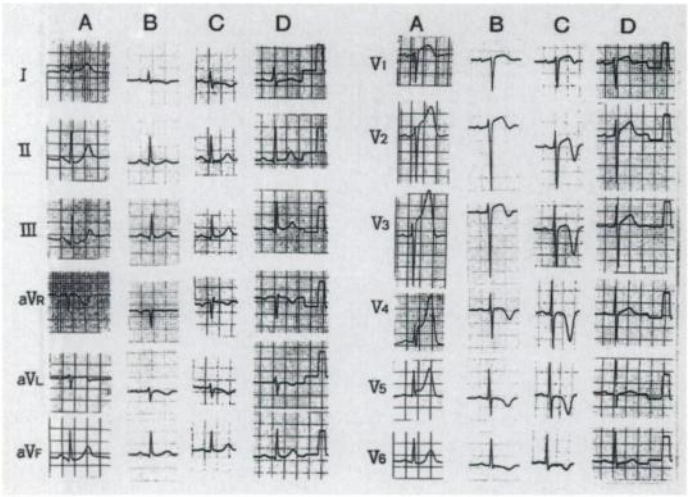

FIGURE 1. A 61-yr-old man with acute myocardial infarction. Serial electrocardiograms. (A) ECG demonstrated anterior ST segment elevations at admission. (B) Immediately after successful PTCR, the ST segment elevations on the ECG returned to baseline, and T waves inverted in the precordial leads. (C) On the 32nd day after the onset, prominent deep T waves in the precordial leads were present, but no Q waves were detected. (D) About 5 mo later, ECG was normal. Prominent deep T waves in the precordial leads were not observed.

0.6% ID/100 ml in the anterior region and 0.7% ID/100 ml in the lateral and inferior regions (*10*).

RESULTS

The [^{13}N]ammonia PET study showed reduced regional myocardial perfusion in the anterior region on the 8th day. However, regional myocardial perfusion became normal by the 36th day. The percent [^{13}N]ammonia uptake in the anterior ROI improved from 55% to 86%. On the other hand, the FDG-PET study showed diffusely increased uptake in the left ventricular myocardium on both the 8th and 36th days. The FDG uptake in the anterior, lateral and inferior ROIs ranged from 0.7% - 1.2% ID/100 ml on the 8th day, and from 1.0% - 1.3% ID/100 ml on the 36th day. In addition, FDG uptake in the anterior ROI was 58% lower than the remote region on the 8th day, but increased to 87% on the 36th day. On the 142nd day, FDG uptake in all three ROIs decreased below 0.6% ID/100 ml. Plasma glucose, serum-insulin and nonesterified fatty acid levels were not significantly changed among three PET studies.

BMIPP uptake in the anterior region was lower than that in the remote region on both the 8th and 36th days. On the 142nd day, BMIPP uptake was normal. The percent BMIPP uptake in the anterior ROI was 41% on the 8th day and 65% on the 36th day, which improved to 90% on the 142nd day (Fig. 3).

DISCUSSION

The pattern of myocardial perfusion and FDG uptake in stunned myocardium has not been clearly demonstrated. On the 8th day after the onset of a severe ischemic event, the region of stunned myocardium exhibited a concordant depression of myocardial [^{13}N]ammonia and FDG uptake despite functional recovery after revascularization. The PET study underestimated myocardial viability at this time. The reasons for this underestimation are not clear, although it is possible that the concordant depression of myocardial perfusion and FDG uptake may reflect decreased count recovery caused by wall motion abnormality and the partial volume effect (*11*).

We also documented the time course of recovery in regional myocardial wall motion, glucose utilization and fatty acid utilization (assessed with BMIPP) in stunned myocardium. On the 8th day after onset, glucose and fatty acid utilization were lower in stunned myocardium compared with remote, normal myocardium. One month later, regional myocardial [^{13}N]ammonia uptake and wall motion in stunned myocardium had already returned to normal, while fatty acid utilization remained impaired in that region. In contrast, glucose utilization in stunned myocardium increased despite the fasting condition, showing a relatively homogeneous image of the left ventricle at this time. From these observations, we speculate that glucose was used to supplement the fatty acid utilization, which remained depressed resulting in normal wall motion at rest. About 5 mo later, fatty acid utilization returned to normal, and glucose utilization significantly decreased both in stunned and normal myocardium.

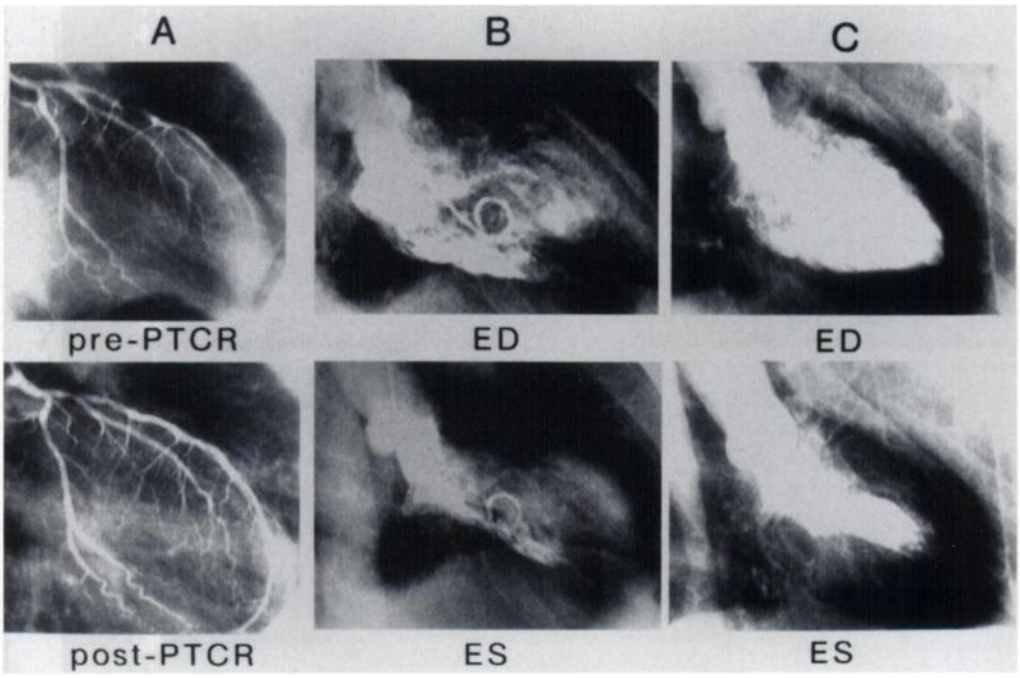

FIGURE 2. Coronary angiography before and after PTCR, and serial left ventriculography images. (A) The pre-PTCR angiogram (upper) showed 90% stenosis of the proximal left anterior descending artery accompanied by residual thrombotic filling defect, which improved to less than 50% of in the luminal diameter after PTCR (lower). (B) Left ventriculography in 30° right anterior oblique projection at the time of emergency cardiac catheterization showed regional asynergy in the anterior and apical segments. (C) Left ventriculography on the 32nd day after onset showed marked improvement of regional asynergy. ED = end-diastole; ES = end-systole.

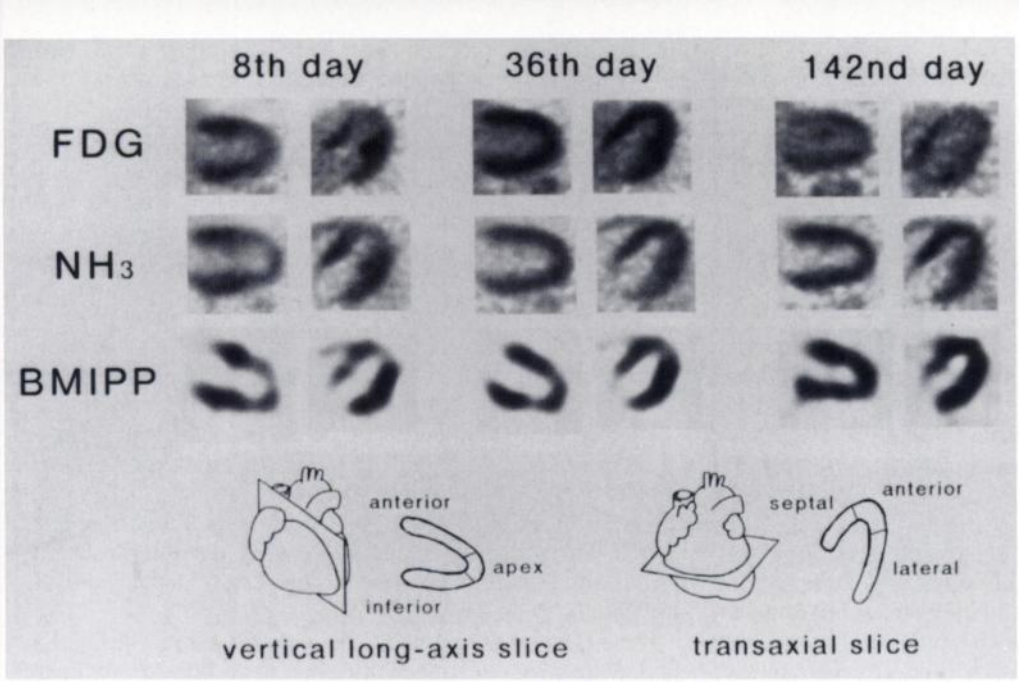

FIGURE 3. PET and BMIPP images (vertical long-axis and transaxial slices through the midleft ventricle), and the schema of myocardial segments of PET and BMIPP images. On the 8th day after onset, FDG uptake in the anterior and septal regions were relatively lower than that in the remote region. This relative reduction in FDG uptake was not observed on the 36th day. About 5 mo later, FDG uptake in the left ventricular myocardium significantly decreased. Nitrogen-13-ammonia uptake decreased in the anterior and septal regions on the 8th day, but this decreased uptake improved in the chronic phase. BMIPP uptake in the anterior and septal regions were relatively lower than that in the remote region on the 8th and 36th days, but improved at 5 mo after onset.

CONCLUSION

Metabolic abnormalities in stunned myocardium are sustained despite recovery from functional impairment; recovery from these abnormalities requires considerable time. The time course of the electrocardiographic recovery of deep negative T waves appeared to be related to the recovery of impaired energy metabolism in stunned myocardium in this patient.

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Acute Myocardial Infarction Followed by Technetium-99m-Sestamibi SPECT Imaging and Pathologic Correlation

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A 79-yr-old man received thrombolytic therapy for acute myocardial infarction after injection with ^{99m}Tc-sestamibi and died shortly thereafter. Postmortem in situ SPECT imaging of the heart was performed. The heart was then removed and sectioned into short-axis slices, which were placed directly on the SPECT camera face for imaging, and examined by routine gross and microscopic pathologic methods. Pathologic findings were consistent with a small acute inferoseptal myocardial infarction, as demonstrated on both SPECT imaging of the intact heart and imaging of the heart slices. This case report provides further evidence of the validity of SPECT sestamibi imaging for the determination of myocardium at risk during acute myocardial infarction.

Key Words: myocardial infarction; technetium-99m-sestamibi; thrombolytic therapy; SPECT

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The amount of myocardial salvage after acute infarction is a useful endpoint in the assessment of cardiovascular therapies (*1*). The assessment of myocardial salvage requires an accurate