

ACUTE MYOCARDIAL INFARCTION SHORTLY AFTER NEGATIVE EXERCISE TEST AND REPERFUSION BY INTRACORONARY THROMBOLYSIS

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A 67-year-old man developed an acute myocardial infarction shortly after normal exercise testing. His clinical history and findings from emergency coronary arteriography suggested that coronary artery spasm followed by intraluminal thrombosis might have been responsible for the myocardial infarction. Although intracoronary thrombolysis two hours after the onset of chest pain provided continued patency of an occluded vessel, serial myocardial perfusion scintigraphies documented myocardial injury, which was probably induced by reperfusion, rather than myocardial salvage.

ACUTE myocardial infarction occurring secondarily to exercise testing is rare.^{1,2} Furthermore, there are only a few case reports of acute myocardial infarction immediately after a normal electrocardiographic response to exercise testing.³⁻⁷ Recently Tuzcu et al⁸ reported a case in which acute myocardial infarction developed shortly after a normal exercise test and early restoration of coronary flow was obtained through percutaneous transluminal coronary angioplasty. Intracoronary thrombolysis in such an instance has not yet been reported. We herein describe a patient who suffered from a nonfatal myocardial infarction shortly after the termination of an exercise test without electrocardiographic abnormalities and in whom intracoronary thrombolysis recanalized acute coronary occlusion. We also evaluated effects of the early restoration of coronary flow on jeopardized myocardium with serial myocardial scintigraphies.

Key words:

Exercise testing
Acute myocardial infarction
Intracoronary thrombolysis
Myocardial perfusion scintigraphy

CASE REPORT

A 67-year-old man, who had been in good health until 2 years previously when he experienced bouts of nonexertional chest pain in the early morning, was referred to another hospital one week later. Selective coronary arteriography revealed no significant stenosis but intravenous injection of ergonovine maleate provoked subtotal occlusions of the proximal circumflex artery and proximal right coronary artery. Thereafter, diltiazem and isonitrate were prescribed to prevent coronary artery spasm and the patient was free from anginal attacks until 3 months previously, when he had two episodes of chest pain at rest. After the addition of nifedipine to the medication, he was again free from angina. He was referred to this hospital for re-evaluation of coronary artery disease.

The patient appeared well. Physical examination, pertinent laboratory studies, chest X-ray, and electrocardiography disclosed no abnormalities. One week later, a treadmill exercise test using Bruce's protocol was performed in the afternoon (14:00). On that day he had taken lunch and postprandial medication including

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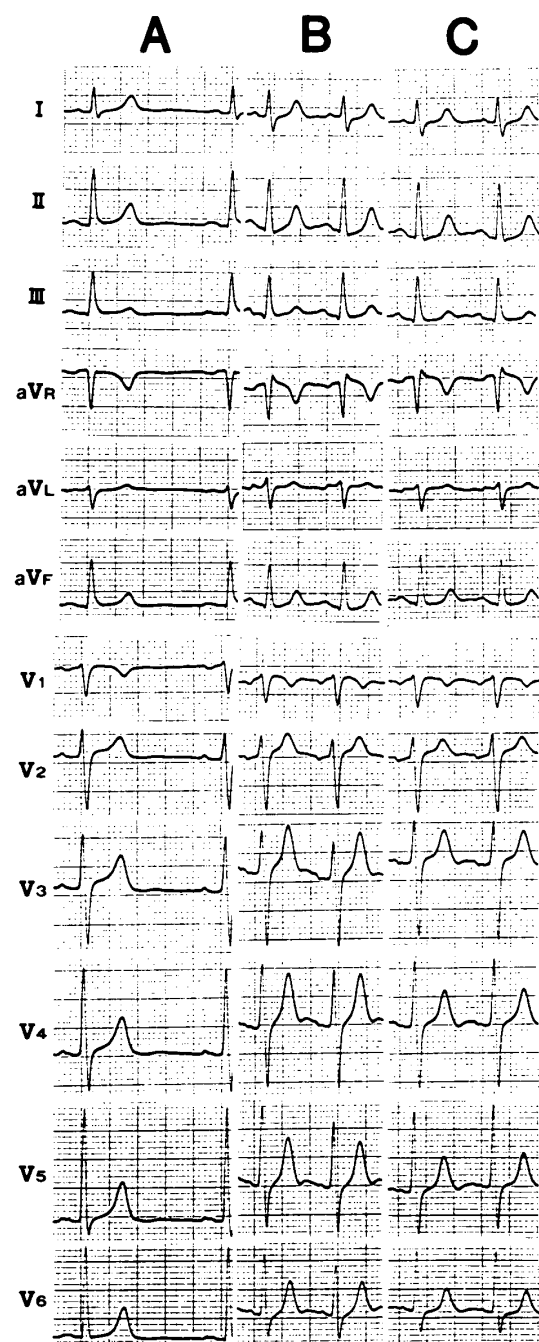


Fig.1. Twelve-lead electrocardiograms recorded during exercise thallium-201 myocardial scintigraphy (10 mm = 1 mV in all leads). (A) Before exercise. (B) Immediately after exercise. (C) Four minutes after exercise. There were no ischemic changes in the ST segments.

diltiazem. A heart rate of 168 beats/min was achieved during stage 4 of the program and a maximum blood pressure of 180/88 mmHg was recorded. The test was stopped because of leg fatigue. There were no ischemic changes in the ST segments at peak exercise or during recovery.

The patient did not complain of chest pain. He remained symptom-free for a period of 2 weeks at which time he was referred to the nuclear cardiology laboratory for exercise thallium-201 myocardial scintigraphy.

On the day of testing the patient had taken neither breakfast nor postprandial medication. At 9:00 he had arrived at our laboratory. The electrocardiogram prior to the test disclosed no abnormalities and was unchanged from the tracing recorded 2 weeks earlier. A multistage exercise test using an upright bicycle ergometer was started at 9:30. The heart rate, systolic pressure, and double product were 144 beats/min, 198 mmHg, and 28512 at peak exercise, respectively. The double product was smaller than that achieved by the treadmill test, 30240. The patient received 3 mCi of thallium-201 intravenously and 1 minute later the test was terminated. The endpoint was leg fatigue and he did not complain of chest pain during the test and early recovery. No electrocardiographic ischemic changes occurred during a 4-minute period following cessation of exercise (Fig. 1). He had increasingly severe chest pain approximately 10 minutes after cessation of exercise while a gamma camera was rotating around him. Sublingual nitroglycerin was administered during imaging but chest pain persisted. The 12-lead electrocardiogram obtained immediately after acquisition of myocardial scintigraphy demonstrated peaking of T waves and ST segment elevation in the leads V₂ to V₅ (Fig. 2A). He was treated with intravenous nitroglycerin as well as sublingual nitroglycerin and nifedipine, but his symptoms persisted and electrocardiographic evidence of acute myocardial infarction developed (Fig. 2B). He was accordingly transported to the catheterization laboratory, where coronary arteriography was performed. The left anterior descending artery was totally occluded proximally without collateral circulation (Fig. 3A). The circumflex and right coronary arteries showed no significant stenosis.

Intracoronary infusion of nitroglycerin (0.5 mg) yielded no restoration of blood flow. Urokinase was subsequently infused into the occluded vessel, which successfully recanalized 2 hours after the onset of chest pain with no substantial residual stenosis (Fig. 3B). However, the recanalization yielded a ventricular arrhythmia, aggravated ST segment elevation (Fig. 4) and chest pain, which was relieved by the administration of morphine sulfate. Left ven-

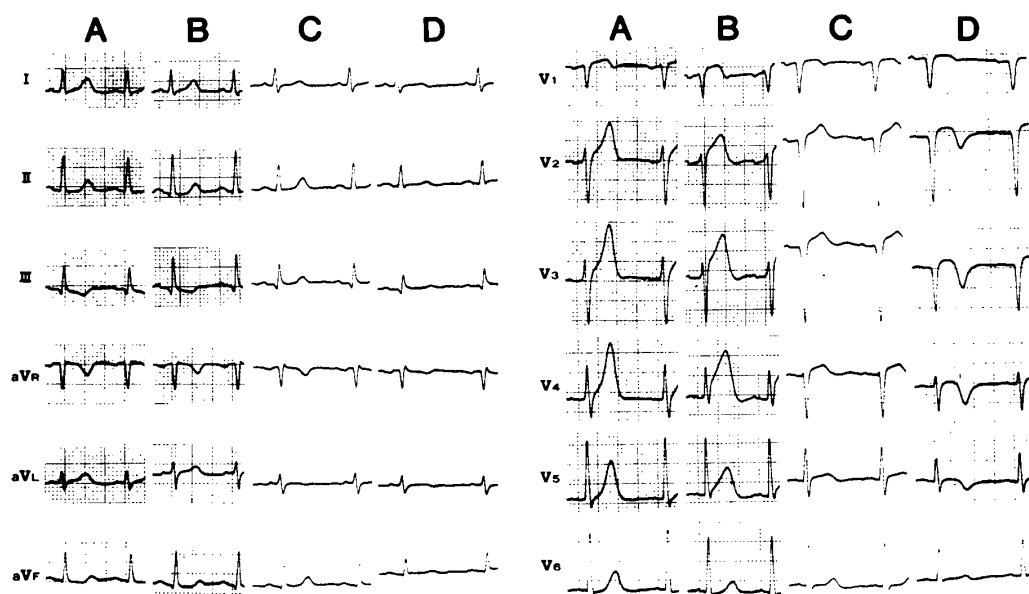


Fig. 2. Serial 12-lead electrocardiograms recorded after the appearance of chest pain (10 mm = 1 mV in all leads). (A) Immediately after acquisition of myocardial scintigraphy. Peaking of T waves and elevation of ST segments are noted in leads V_2 to V_5 . (B) One and one-half hours after the onset of chest pain and immediately before emergency coronary arteriography. Electrocardiographic changes suggest that acute anterior myocardial infarction is developing. (C) Two hours after coronary recanalization. New appearance of QS pattern is noted in leads V_2 and V_3 and the height of the R wave in lead V_4 is markedly reduced. (D) Four weeks after acute myocardial infarction.

triculography in the right anterior oblique projection showed severe hypokinesis of the anterolateral segment and akinesis of the apical segment with an ejection fraction of 59%. The 12-lead electrocardiogram obtained after the recanalization revealed a new appearance of the QS pattern in leads V_2 to V_3 and a markedly reduced height of the R wave in lead V_4 (Fig. 2C).

A stress thallium scan obtained before and at the beginning of chest pain demonstrated a perfusion defect of the apical anterior wall and apex (Fig. 5A). A delayed scan was not performed because of the acute myocardial infarction. The serum creatine kinase level was 44 IU/ml immediately before intracoronary thrombolysis and rapidly rose to 2057 IU/ml 2 hours after the recanalization with a peak value of 2329 IU/ml 8 hours after the onset of chest pain. Four days later he underwent simultaneous dual emission computed tomography with thallium-201 and technetium-99m pyrophosphate. Images with thallium-201 showed perfusion defects in the apex and apical anterior wall and hypoperfusion in the septum (Fig. 5B). Images with technetium-99m pyrophosphate showed localized uptake in the apex, apical anterior wall and septum (Fig. 5E). Namely,

there was a significant overlap of thallium-201 and technetium-99m pyrophosphate in the septum. At no time during the patient's subsequent hospital stay did a recurrent attack or evidence of heart failure develop.

Repeat exercise thallium-201 myocardial scintigraphy was performed 21 days after the attack. There was neither chest pain nor electrocardiographic ischemic changes during exercise and recovery. Emission computed tomography with thallium-201 showed a perfusion defect of the apex, apical anterior wall and septum, in which no redistribution appeared on the delayed scan (Fig. 5C, D). The defect size was larger than that in the scan obtained during the beginning of myocardial infarction as well as that obtained 4 days after the episode (Fig. 6). Repeat coronary arteriography and left ventriculography were subsequently performed 4 weeks after the attack. Coronary arteriography revealed no significant stenosis. The left anterior descending artery had slight irregularity at the portion which had been totally occluded. Left ventriculography in the right and left anterior oblique projections revealed akinesis of the apical and septal segments and severe hypokinesis of the anterolateral segment with an ejection fraction of 52%, which

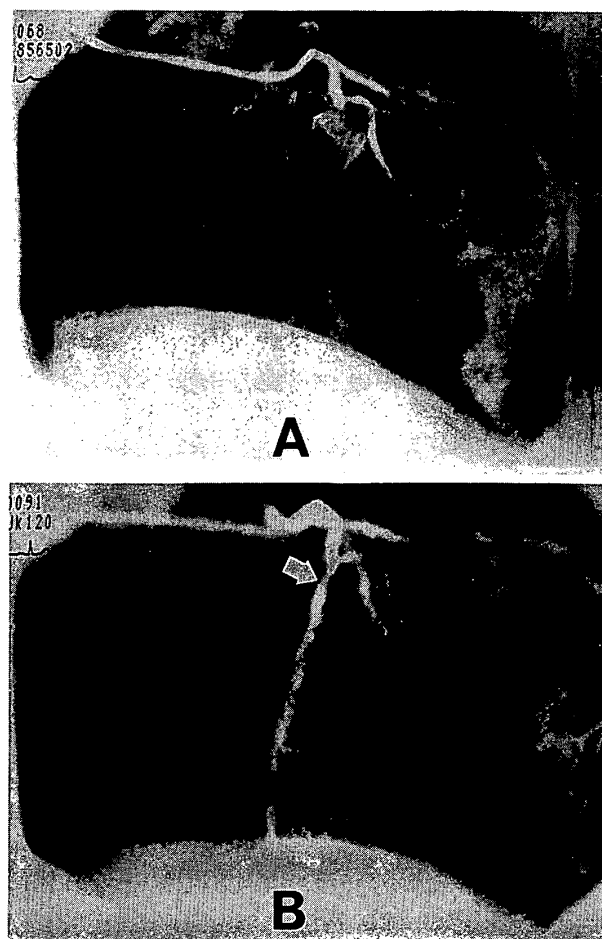


Fig.3. Emergency left coronary arteriograms in the left anterior oblique projection with cranial tilt. (A) After intracoronary infusion of nitroglycerin and before intracoronary infusion of urokinase. Total occlusion of the proximal left anterior descending artery is noted. (B) After intracoronary infusion of urokinase, which recanalized the occluded vessel with no substantial residual stenosis.

was slightly lower than that during the acute phase.

He was discharged from the hospital on the 36th day with no recurrence of chest pain.

DISCUSSION

Myocardial infarction has been reported to be an extremely rare complication of exercise testing when appropriate precautions are employed.^{1,2} Acute myocardial infarction immediately after a negative exercise test may be an even more rare complication. There have been several isolated case reports of nonfatal acute myocardial infarction shortly after a normal electrocardiographic response to exercise test-

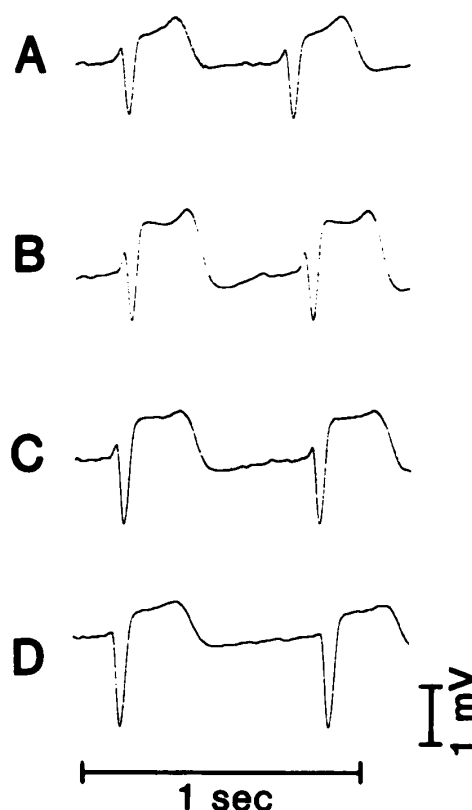


Fig.4. Serial electrocardiograms recorded from a V_3 lead during emergency coronary arteriography with intracoronary thrombolysis (10 mm = 1 mV and paper speed 50 mm/sec in all tracings). (A) Before intracoronary thrombolysis. (B) Immediately after recanalization, which induced aggravation of the ST segment elevation. (C) About 10 minutes after recanalization. (D) At the end of coronary arteriography, when R wave in lead V_3 disappeared.

ing.^{3,5-9} Bruce et al³ described an asymptomatic individual who had an acute anterior myocardial infarction shortly after a normal performance of a maximal exercise test. Coronary arteriography 6 months later revealed only minimal plaque in the left anterior descending artery other than significant stenosis of the circumflex artery. Sweet et al⁹ described a patient with variant angina pectoris who suffered an acute anterolateral myocardial infarction 10 min after discontinuing the stress test. In this case, resting ST-T abnormalities reverted to a normal appearance with exercise. Coronary arteriography 10 months later revealed proximal occlusion of the left anterior descending artery. Brown et al⁵ described a patient with atypical chest pain who sustained an acute inferoapical myocardial infarction within 15 min of a negative treadmill exercise test. Coronary arteriography 4 months

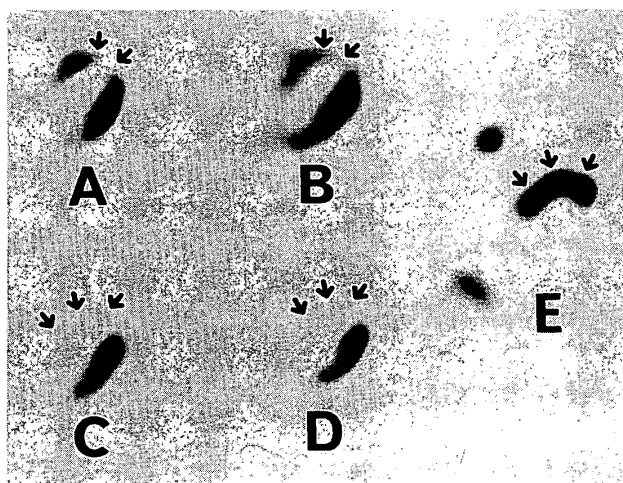


Fig. 5. Serial thallium-201 myocardial scintigrams (A-D) and technetium-99m pyrophosphate scintigram (E). All images are transaxial tomograms at the same level with a 30% background subtraction. (A) Stress thallium-201 image obtained before and at the onset of chest pain. Perfusion defect is noted in the apical anterior wall and apex. (B) Rest thallium-201 image of dual emission computed tomography obtained 4 days later. Stress (C) and delayed (D) thallium-201 images obtained 3 weeks later. (E) Technetium-99m pyrophosphate image of dual emission computed tomography, which is derived from the identical level as the image (B).

later revealed only insignificant stenosis in the circumflex and right coronary arteries. Dash⁶ reported a case of acute coronary occlusion 30 min after negative treadmill stress testing 2 days after successful percutaneous transluminal coronary angioplasty. Nygaard et al⁷ reported a case in which acute coronary occlusion developed 20 min after a normal exercise test 5 days after successful percutaneous transluminal coronary angioplasty. During emergency coronary bypass surgery, a hematoma in the proximal portion of the totally occluded left anterior descending artery was identified. Recently, Tuzcu et al⁸ described a patient in whom acute inferolateral myocardial infarction developed 10 min after a normal exercise test and emergency coronary angioplasty successfully dilated total occlusion in the circumflex artery within 60 min of chest pain. They noted that the absence of perfusion defect in the rest thallium scanning, performed 3 days after the attack, indicated that the patient did not have significant myocardial necrosis. A pyrophosphate study 2 days after the attack showed no abnormal uptake, although the creatine kinase level rose to 1720 IU/ml.

Lintgen⁴ reported a case in whom fatal acute myocardial infarction occurred about 30 min after an exercise test with a normal result. Autopsy findings suggested that hemorrhage into

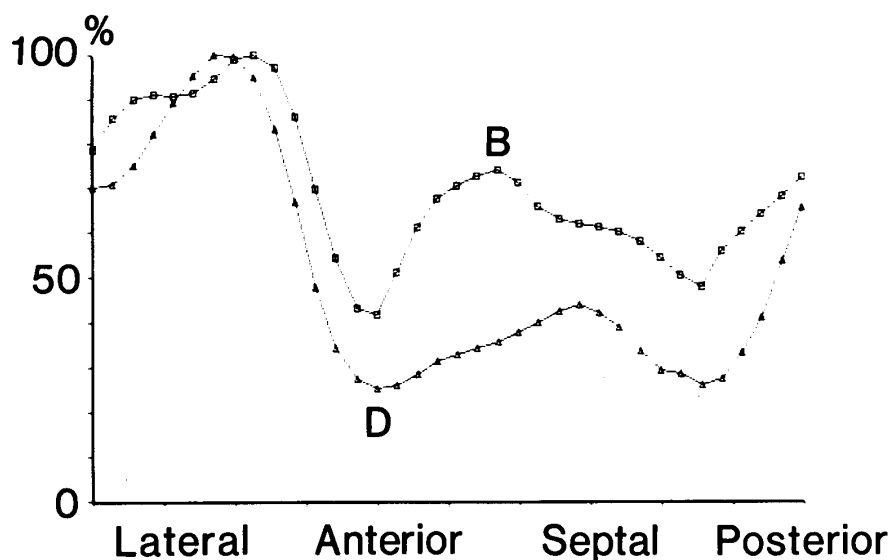


Fig. 6. Relative circumferential profile curves of the peak counts along 36 radii drawn from the center of the left ventricular cavity in thallium-201 transaxial tomograms with no background subtraction. Curve B represents a circumferential profile in Fig. 5B (the rest image obtained 4 days after the onset of infarction). Curve D represents a circumferential profile in Fig. 5D (the delayed image obtained 3 weeks after the onset of infarction). Relative counts of thallium-201 in the anterior and septal regions decreased significantly from curve B to curve D.

intimal atherosclerotic plaque with superimposed, intraluminal clot formation was the cause of coronary artery occlusion. Shea et al¹⁰ described a patient in whom an acute inferior myocardial infarction evolved after a cold pressor test accompanied by chest pain and ST segment elevation. Coronary arteriography 2 months later showed complete occlusion of the right coronary artery.

Three possible mechanisms responsible for acute myocardial infarction immediately following a normal exercise test might be considered:

1. Sudden reduction in cardiac output and coronary perfusion secondary to orthostatic venous pooling in acutely dilated venous capacitance vessels after cessation of exercise may lead to acute coronary insufficiency, particularly while standing after exercise.³ Inversely, the postural change from an upright to supine position immediately after erect exercise may augment preload by abruptly increasing venous return resulting in expansion in left ventricular volume and an increase in left ventricular diastolic pressure. Supine positioning could have therefore potentiated subendocardial ischemia even during recovery in our patient, since he began to complain of chest pain when supine.¹¹ The above mechanisms could indeed cause ischemia during recovery only, but neither is likely to be sufficient for directly developing myocardial infarction.

2. Coronary artery spasm may cause acute myocardial infarction immediately after exercise. It is likely that prolonged coronary artery spasm was the major factor in our patient, since, on the day of testing, he had not taken antianginal drugs in the morning when his angina attacks had occurred. He had indeed performed a treadmill stress test without incident in the afternoon 2 weeks before the onset of myocardial infarction, although the test had induced a higher level of double product than did the second test followed by myocardial infarction. However, since sublingual, intravenous and intracoronary nitroglycerin could not stop chest pain or electrocardiographic abnormalities, it is unlikely that coronary artery spasm alone contributed to the myocardial infarction.

3. Paterson¹² has suggested that unusual work stress may result in the rupture of intimal capillaries with severe and rapid bleeding into a preexistent atherosclerotic plaque and that the resultant massive intimal hematoma may occlude the lumen of a main coronary artery. There was,

in our case, a coronary thrombus which disappeared with intracoronary urokinase. After percutaneous transluminal coronary angioplasty, Nygaard et al⁷ documented extensive coronary dissection in a patient and suggested that the dissection might occur during exercise. We were unable to demonstrate either dissection or formation of an obstructing intimal flap upon coronary arteriography. However, it is likely that the intimal disruption caused by coronary artery spasm may lead to intraluminal clot formation resulting in a total occlusion of the coronary artery.

In our case, we therefore speculated on the following mechanism: coronary artery spasm in the site with little plaque, insufficient to provide detectable ischemia during exercise, might be provoked by exercise testing in the morning with discontinuation of antianginal drugs. Subsequent intimal disruption followed by intraluminal thrombosis might also result in coronary artery occlusion. Is it possible to anticipate and prevent such a rare instance? We could not find any contraindications for exercise testing in our case, since the 12-lead electrocardiogram obtained before exercise was within normal limits and the recent history of the patient showed that his angina attacks had been stable. Furthermore, there were no abnormalities, such as ischemic changes in ST-segment, arrhythmias, or chest pain, to discontinue exercise at a submaximal level. However, it may be pointed out that exercise testing should be performed without stopping all medications. This is likely to concern the problem of whether exercise testing in patients with variant angina should be performed without cessation of medications, even in a stable state. To our knowledge it has not been considered a contraindication to perform exercise testing in patients with variant angina after stopping medications, although consideration of continuing medications until the time of exercise testing should be given in selected patients, even with stable angina pectoris.

In our case, serial scintigraphic findings were available to evaluate effects of early reperfusion on jeopardized myocardium. Serial thallium-201 studies demonstrated a progressive increase in the defect size. The first study performed at the beginning of acute myocardial infarction showed a perfusion defect in the apical anterior wall and apex. The second study performed 4 days later showed hypoperfusion in the septum as well as a defect in the apical anterior wall and apex. The

third study performed 21 days later showed a persistent defect in the septum as well as in the apical anterior wall and apex. It has been known that successful early reperfusion in the acute myocardial infarction is frequently accompanied with improvement of myocardial perfusion which is assessed by serial thallium-201 myocardial scintigraphies.¹³ In our case, however, serial thallium-201 studies revealed aggravation of myocardial damage. Simultaneous dual emission computed tomography with thallium-201 and technetium-99m pyrophosphate demonstrated a significant overlap of thallium-201 and technetium-99m pyrophosphate in the septum, which may reflect successful early recanalization.¹⁴ Nevertheless, the septum had akinesis in the left ventriculography performed 4 weeks later as well as a persistent defect in the last thallium study. It is therefore likely that the early reperfusion in this case would not have provided any beneficial effects on myocardial viability. Rather, reperfusion may have aggravated myocardial damage, namely, coronary thrombolysis might have added reperfusion injury to the initial ischemic damage. It should be noted that the first thallium-201 images obtained before and at the onset of chest pain may show an incomplete feature of acute myocardial infarction because thallium-201 could be almost distributed into the myocardium before the onset of acute myocardial infarction. Thus, it is likely that the increase in defect size from the first study to the second study may not have indicated aggravation of myocardial infarction. At least, the increase in defect size from the second study to the third study may have reflected aggravation of myocardial damage although the recanalized vessel showed continued patency.

This case indicates that acute myocardial infarction may develop immediately after a normal exercise test, probably due to coronary artery spasm followed by intraluminal thrombosis. Also, serial myocardial perfusion imagings with thallium-201 in this case demonstrated that early coronary reperfusion could not salvage the viability of reperfused myocardium.

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