Jikeikai Med J 2003 ; 50 : 189-94

Case Report

Unsuccessful Reperfusion Due to No-reflow Phenomenon in Acute Inferior Myocardial Infarction : A Case Report with Postmortem Examination

Tetsuya ISHIKAWA[1,3], Masaaki SUZUKI[2], Tetsuji TSURUSAKI[1], Yasuyuki TANAKA[1], Makoto MUTOH[3], Satoru YOSHIDA[1], Takahiro SHIBATA[1], Makio KAWAKAMI[2], and Seibu MOCHIZUKI[1]

[1]*Division of Cardiology, Department of Internal Medicine, The Jikei University School of Medicine*
[2]*Department of Pathology, The Jikei University School of Medicine*
[3]*Division of Cardiology, Saitama Cardiovascular and Respiratory Center*

ABSTRACT

A 70-year-old man with a subacute inferior myocardial infarction (MI) underwent emergency percutaneous coronary intervention because of recurrent inferior MI with cardiogenic shock. All three coronary arteries, particularly the large, dominant right coronary artery, had diffuse, severe sclerotic changes. Intra-aortic balloon pumping could not be performed owing to moderate aortic regurgitation. Thrombectomy with a Rescue™ catheter could not be done because of the tortuousness and stenosis of the proximal right coronary artery. The no-reflow phenomenon developed along with reperfusion injury immediately after balloon angioplasty at the culprit site (# 3), which disrupted the atheromatous plaque ; the no-reflow phenomenon could not be relieved despite several interventions. Histopathologically, an extensive inferoposterior region, from the base to the apex, was exposed to multiple phases of ischemia, and multiple atheromatous plaques obstructed the arterioles within the area of acute infarction. In addition, old ischemia was recognized in the anteroseptal wall. Because of these underlying problems, the cardiogenic shock induced by global ischemia could not be relieved and resulted in death. Thus, reperfusion might be unsuccessful in cases of acute MI owing to multiple pre-existing problems.

(Jikeikai Med J 2003 ; 50 : 189-94)

Key words : myocardial infarction, percutaneous coronary intervention, no-reflow phenomenon

INTRODUCTION

Early restoration of epicardial coronary flow is essential for recovery from acute myocardial infarction (MI), and reperfusion with emergency percutaneous coronary intervention (PCI) is successful in 95% of cases[1]. However, several factors indicate a decrease likelihood of successful reperfusion in cases of acute MI[2-4].

We report autopsy findings in a case of unsuccessful reperfusion after acute MI with multiple underlying problems.

CASE REPORT

A 70-year-old man was admitted on March 12,

Received for publication, August 23, 2003
石川 哲也, 鈴木 正章, 鶴崎 哲士, 田中 康之, 武藤 誠, 吉田 哲, 芝田 貴裕, 河上 牧夫, 望月 正武
Mailing address : Tetsuya ISHIKAWA, Division of Cardiology, Department of Internal Medicine, The Jikei University School of Medicine, 3-25-8, Nishi-Shimbashi, Minato-ku, Tokyo 105-8461, Japan.

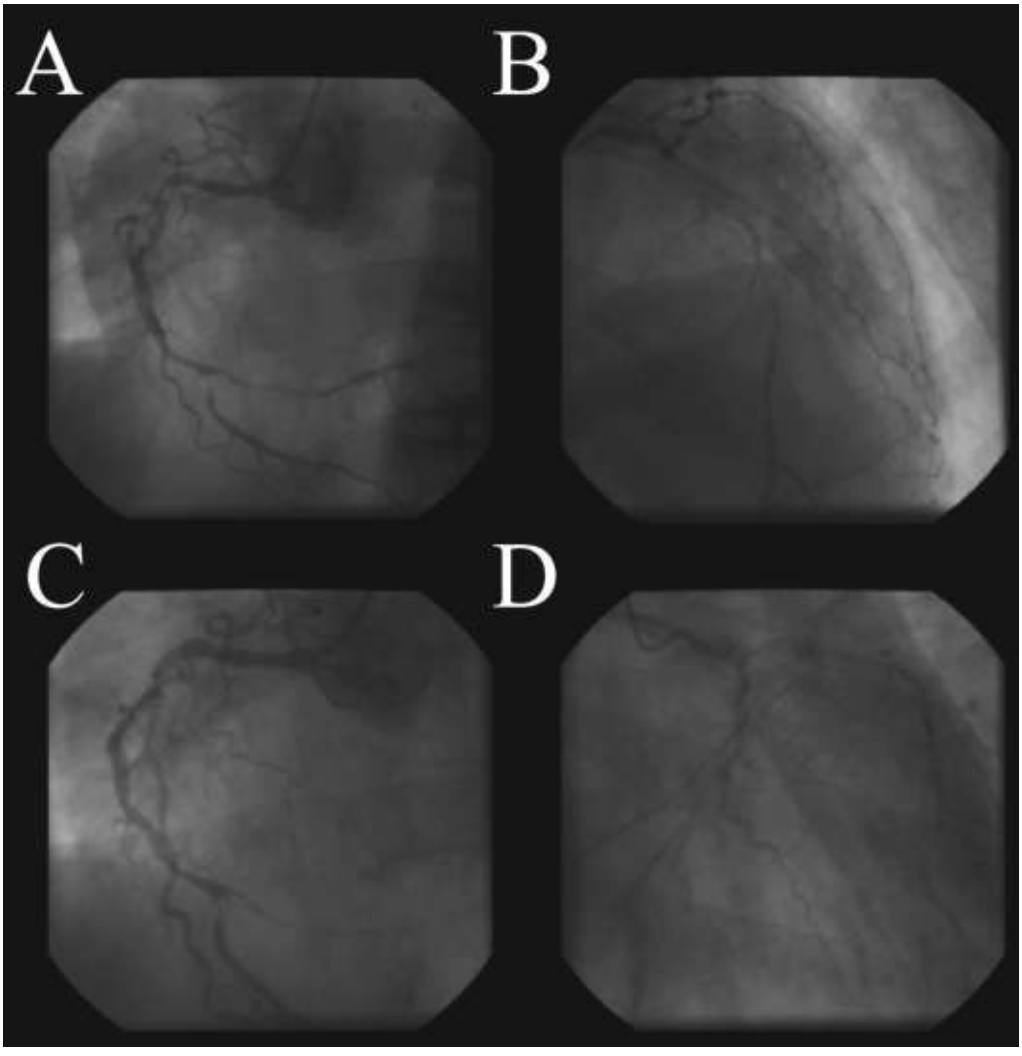

Fig. 1. Coronary angiogram performed at the recurrence of AMI with candiogenic shock
(A) RCA before PCI in LAO view. (B) LAD of LAO cranial view. (C) Established no-reflow phenomenon despite several interventions. No-reflow developed at the culprit lesion. (D) Circumflex artery of LAO caudal view.

2002, because of epigastralgia of 12 hours' duration. Chest X-ray films and ST-segment elevations in electrocardiographic limb leads II, III, and aV_f indicated inferior acute MI complicated by congestive heart failure (CHF) (Killip classification III). The patient's history included untreated diabetes mellitus (DM), hypertension, and hyperlipidemia. Because the optimal time for reperfusion therapy was passing, oral aspirin, nicorandil, intravenous heparin, and nitroglycerin were quickly administered without cardiac catheterization.

The following day the patient was transferred to the coronary care unit because of worsening CHF. Cardiac ultrasonography revealed widespread akinesis from the base to the apex of the inferoposterior wall, dyskinesis of the upper posterior portion of the inferoposterior wall, and a symmetric thickness of the wall of the left ventricle (LV) of 15 mm. In addition, the anteroseptal and lateral walls were hypokinetic and the ejection fraction (EF) of the LV was 34%. Moderate aortic regurgitation was observed. Hemodynamic montioring with a Swan-Ganz catheter revealed a Forrester subset IV with a cardiac index of 1.7 and a pulmonary capillary wedge pressure of 24 mmHg. The clinical diagnosis was inferior acute MI, acute, severe CHF, renal insufficiency

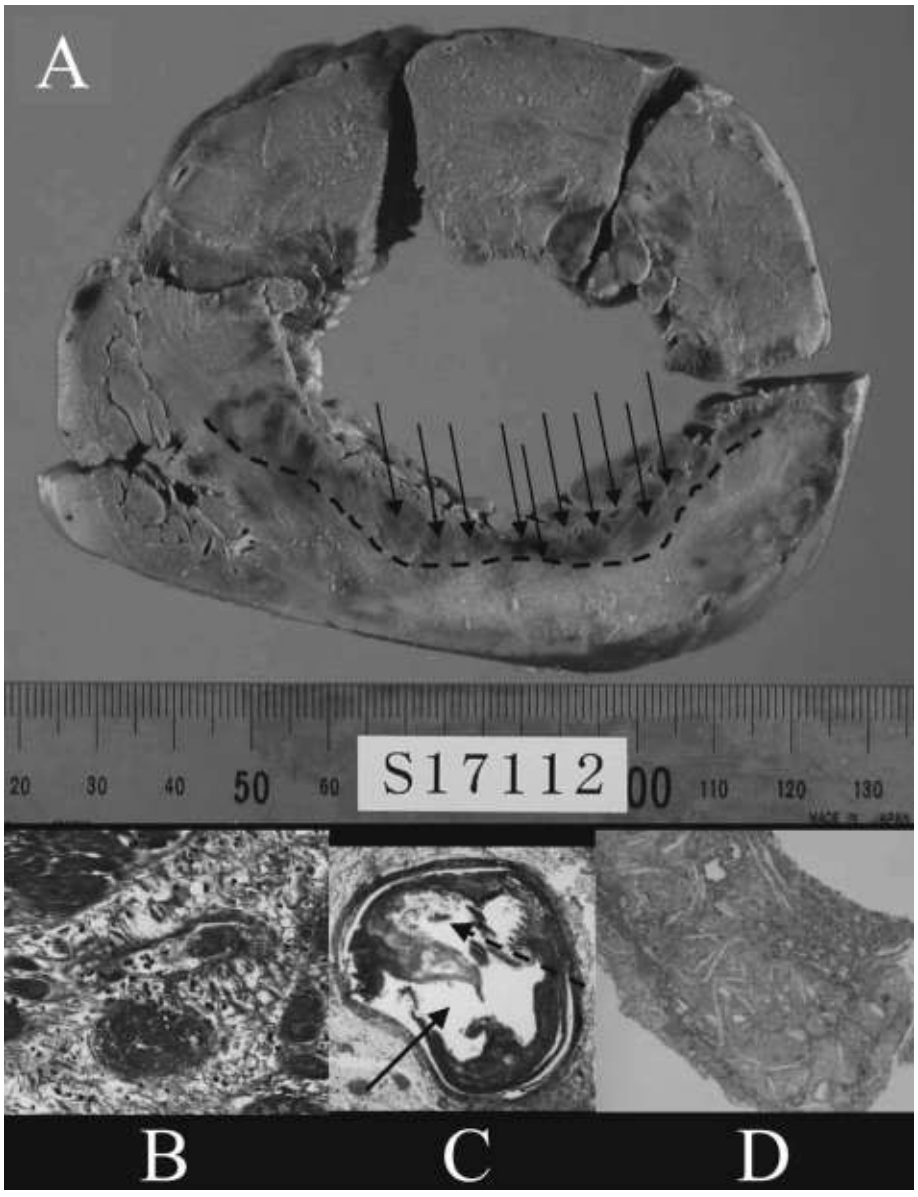

Fig. 2. Histopathologic assessment of ischemic heart.
(A) Horizontal sectional view at the mid-portion of the heart. Infarction in broad posteroinferior wall with matured scar, and hemorrhage with basal aneurysm (hemorrhage could be recognized along the dashed line). Arrows indicate the scattered plugged atherothrombi, as shown in (B). (B) Arterioles plugged by atherothrombus in the infarcted area of the RCA territory (hematoxylin stain, ×40). (C) Horizontal sectional view of stented segment (#3) assessed after the stent had been removed. (hematoxylin stain, ×40). In the area indicated by arrow (lower side), the stent had been implanted but could not be completely dilated. In the area indicated by dashed arrow (upper side), there would be an atheroma. (D) Atherothrombus collected from the struts of implanted stents.

(serum creatine kinase=1.4 mg/dl), DM, hypertension, and congestive liver damage. Thus, treatment was started with heparin, nitroglycerin, nicorandil, furosemide, dobutamine, human atrial natriuretic peptide, and olprinone. The serum level of creatine kinase peaked at 4,800 U/l. The CHF had gradually resolved by 9 days after onset, and cardiac rehabilitation was started.

The following night (10 days after onset), however, the patient suddenly complained of severe

dyspnea with additional ST-segment elevations in limbs leads II, III, and aVf and ST-segment depression in lead V_{4-6}. A second inferior acute MI was suspected, and emergency coronary angiography was performed. Intra-aortic balloon pumping (IABP) could not be performed because of the known moderate aortic regurgitation. There was an eccentric 99% stenosis at the proximal right coronary artery (RCA) (#1), and the coronary flow was Thromobolysis in Myocardial Infarction grade II (Fig. 1A). There were also 90% stenotic organic lesions at the mid-portion of the left anterior descending artery (LAD) (#7) (Fig. 1B). In addition, there were 99% and 100% stenotic lesions at #13 and #14 of the circumflex artery Fig. 1D). We used a 7-French JR 4.0 Neat as the guide catheter and a TGV intermediate as the guide wire. Although the guide wire crossed the stenotic lesions, the tortuousness and the stenosis of the proximal RCA (Fig. 1A) indicated that thrombectomy with a Rescue™ catheter would not be successful. Thus, balloon angioplasty was performed. Immediately after the balloon (MAXMUM, 3.0×20 mm) had been deflated, anterior chest pain became severe and the ST segments in leads of II, III, aV_f became further elevated. Convulsions occurred subsequent to ventricular tachycardia, but the rhythm returned to sinus tachycardia after a direct countershock at 150 J. A no-reflow phenomenon was established (Fig. 1C). Repeated intracoronary administration of isosorbide dinitrate and nicorandil, repeated ballooning, intracoronary thrombolysis with tisokinase, and implantation of two stents (Multi-Link, 3.0×15 mm) at the ballooning site were unable to suppress the atherothrombus and restore coronary flow.

Hemodynamic monitoring with a Swan-Ganz catheter revealed a Forrester subset IV (cardiac index=1.7, pulmonary capillary wedge pressure=32 mmHg). After these procedures, an endothracheal tube was inserted and treatment with the drugs given at admission was started again. However, frequent ventricular tachycardia, i.e., electrical storm, persisted despite repeated direct countershock and the administration of nifekalant, ultimately resulting in cardiac arrest.

A postmortem examination was performed 21 hours later. The heart weighed 715 g, and the LV wall was thickened symmetrically to 15 mm, representing concentric hypertrophy (Fig. 2A). A ventricular aneurysm in high posterior (about 45 mm×45 mm), hemorrhage within an extensive transmural infarction, and an old mural infarction were found in the territory of the dominant RCA. Histopathologic examination of the infarcted area revealed few recognizable intact cardiomyocytes owing to multiple old mural MIs with mature fibrous scars and extensive recent MIs from the middle to the epicardium, infiltrated with lymphocytes, macrophages, hemorrhages, and early fibrosis. In addition, an acute phase of infarction with neutrophilic infiltration of multiple shedded, plugged atherothrombi (Fig. 2B) was observed as a white region in the middle area of the inferoposterior wall. In the internal half of the myocardium, a hyperacute phase of MI with wavy fibers and nuclear shrinkage without neutrophilic infiltration was found. Acute infarction of the right ventricle was also found. In the territory of the LAD, multiple old fibrous mural scars and small apical aneurysms with thrombus were recognized. Hyperacute ischemic damage was also found in the epicardium, and a recent phase of MI was seen in the internal half of myocardium. In all three major coronary arteries, significant stenosis consisting of atheroma and calcification was found, indicating that the stents did not fully dilate circularly (Fig. 2C). The proximal RCA was almostly completely occluded. The atheromatous gels on the stent strut were atheroma with fibrin, cholestin, and white thrombus (Fig. 2D) and were also found in arterioles (Fig. 2B).

DISCUSSION

Emergency PCI was unsuccessful against recurrent inferior acute MI in this patient with severe underlying disease, resulting in death. After postmortem evaluation of the multiple underlying factors of unsuccessful reperfusion of acute MI, we concluded that because of undelying disease not all cases of acute MI can be successfully treated. Therefore, a new treatment would need to be developed for each

factor. The adverse factors were cardiogenic shock[2], previous myocardial infarction (re-infarction) with LV dysfunction[2], multivessel coronary artery disease[2], organic morphologic abnormalities in ischemia-related arteries[3], and the no-reflow phenomenon[4].

The multivessel coronary artery disease with organic morphologic abnormalities and the LV dysfunction with silent MI developed owing to the patient's coronary risk factors, so these factors could not be reduced. To maintain hemodynamic conditions, IABP is used first to resolve coronary ischemia and support cardiac output, which relieves the global ischemia[5]. However, in this patient, IABP could not be performed because of moderate aortic regurgitation. Coronary artery bypass graft was also considered for revascularization, but the inability to use IABP meant that coronary artery bypass graft also could not be performed owing to the poor hemodynamic status. Therefore, the RCA was revascularized with PCI. However, this procedure was unsuccessful owing to the no-reflow phenomenon (Fig. 1C), which induced acute ischemia in the old MI in a broad region of the inferoposterior wall (Fig. 2A). This additional damage by the old and recent MIs caused extensive, irreversible damage to the inferoposterior wall. Moreover, remote ischemia was observed in multiple regions (Fig. 2A). In patients who have cardiogenic shock and three diseased coronary vessels, both ischemia in the culprit region and remote ischemia would be induced and cause hemodynamic conditions to deteriorate. Therefore, the main reasons treatment failed in this patient were the inability to use IABP and the development of the no-reflow phenomenon.

Because development of the no-reflow phenomenon is the main reason for unsuccessful PCI, recently both thrombectomy and distal protection device have been used. However, thrombectomy with the Rescue™ catheter would have failed in our patient because of the amount of atherothrombus and the morphologic problems found on angiography (Fig. 1A) and on postmortem examination (i.e., stenosis and tortuousness at the proximal RCA; Fig. 2C). The no-reflow phenomenon in this patient developed as a result of ischemic burdens plugging the distal arterioles and manifested as reperfusion injury (Fig. 2B & D), multiple coronary risk factors (hypertension, DM, hyperlipidemia, smoking) that decreased the coronary flow reserve, and the antecedent broad ischemia that induced microvascular dysfunction. Recent histopathologic studies have revealed that the no-reflow phenomenon after PCI is largely iatrogenic[6]. This concept is supported by the identical atheromatous gels in the arterioles in the RCA territory (Fig. 2B) and on the stent strut (Fig. 2D) and by the reperfusion injury induced immediately after the balloon was deflated. However, as mentioned above, the no-reflow phenomenon in our patient could not be prevented or relieved.

Thanks to advances in reperfusion techniques, epicardial coronary flow is now restored in the ischemia-related artery in 95% of cases[1], reducing the incidence of fatal acute MI in hospitals[1,2]. However, in cases of cardiogenic shock[2], complicating morphologic changes (atherosclerotic changes and tortuousness)[3], the inability of thrombectomy to relieve the no-reflow phenomenon[4,6], and multivessel coronary artery disease[2] that induces remote ischemia contribute to the worst outcome, death. Thus, PCI may still be unsuccessful, as in the present patient with adverse underlying factors, so new treatments must be developed.

Acknowledgement: This study was supported in part by a Ueda Memorial Foundation grant to T.I..

References

1. Stone GW, Grines CL, Cox DA, Garcia E, Tcheng JE, Griffin JJ, et al. Comparison of angioplasty with stenting, with or without abciximab, in acute myocardial infarction. N Engl J Med 2002; 346: 957-66.
2. Bedotto JB, Kahn JK, Rutherford BD, McConahay DR, Giorgi LV, Johnson WL, et al. Failed direct coronary angioplasty for acute myocardial infarction: in-hospital outcome and predictors of death. J Am Coll Cardiol 1993; 22: 690-4.
3. Myler RK, Shaw RE, Stertzer SH, Hecht HS, Ryan C, Rosenblum J, et al. Lesion morphology and coronary angioplasty: current experience and analysis. J Am Coll Cardiol 1992; 19: 1641-52.
4. Morishima I, Sone T, Okumura K, Tsuboi H, Kondo J,

Mukawa H, et al. Angiographic no-reflow phenomenon as a predictor of adverse long-term outcome in patients treated with percutaneous transluminal coronary angioplasty for first acute myocardial infarction. J Am Coll Cardiol 2000; 36: 1201–9.
5. Brodie BR, Stuckey TD, Hansen C, Muncy D. Intraaortic balloon counterpulsation before primary percutaneous transluminal coronary angioplasty reduces catheterization laboratory events in high-risk patients with acute myocardial infarction. Am J Cardiol 1999; 84: 18–23.
6. Kotani J, Nanto S, Mintz GZ, Kitakaze M, Ohara T, Morozumi T, et al. Plaque gruel of atheromatous coronary lesion may contribute to the no-reflow phenomenon in patients with acute coronary syndrome. Circulation 2002; 106: 1672–7.