Histopathological Findings of the No-reflow Phenomenon Following Coronary Intervention for Acute Coronary Syndrome

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SUMMARY

Although no-reflow phenomenon may occur in patients that experience reperfusion after ischemia, there have been no reports describing the postmortem findings in these patients. We describe the findings of an autopsy in a 56-year-old man who experienced acute coronary syndrome with no-reflow phenomenon after coronary intervention. Macroscopic study demonstrated myocardial infarction with diffuse hemorrhage, and microscopic analysis revealed vascular damage and microembolization in the no-reflow area. In conclusion, coronary microembolization and damage to the small coronary artery may contribute to the pathogenesis of no-reflow phenomenon following coronary intervention in humans. (Int Heart J 2005; 46: 327-332)

Key words: Autopsy, Microembolization, No-reflow phenomenon, Necrotizing arteritis, Percutaneous coronary intervention

PERCUTANEOUS coronary intervention (PCI) is the most common strategy for treatment of acute coronary syndrome. No-reflow phenomenon is a well recognized consequence of coronary reperfusion after ischemia and carries important prognostic implications. Several mechanisms have been postulated as possible etiologies of the no-reflow phenomenon. However, there has been only one report that describes the postmortem findings in patients with no-reflow phenomenon after PCI. We report findings of an autopsy in a 56-year-old man who experienced acute coronary syndrome with no-reflow phenomenon after coronary intervention.

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CASE REPORT

A previously healthy 56-year-old man presented with acute onset of severe chest pain at 10 PM on May 24, 2003. He was transported to the nearest hospital at 11 PM, at which an ECG examination showed ST segment elevation in leads I, aVL, and V1 through V4, consistent with an acute anterolateral wall myocardial infarction. The patient was transferred to our hospital for further evaluation and treatment and arrived at 0 AM on May 25. Shortly after arrival in our emergency room, he experienced cardiopulmonary arrest. Resuscitation efforts were initiated, and a ventricular tachycardia rhythm was established with low blood pressure. The patient was immediately transported to the cardiac catheterization laboratory, where coronary arteriography revealed a total occlusion of the main trunk in the left coronary artery (LAD). Coronary balloon angioplasty of the LAD

![Figure 1](image1.png)

**Figure 1.** A: Coronary angiography showed total obstruction in main trunk of the left coronary artery. B: Although the occlusion of the left coronary artery was changed into 50% stenosis after coronary intervention, no-reflow phenomenon was seen at a distal site in the left coronary artery.

![Figure 2](image2.png)

**Figure 2.** Coronary section of the autopsy heart. Left ventricle (LV) showed concentric hypertrophy. Diffuse myocardial hemorrhage was seen in the anteroseptal and lateral walls of LV.
Figure 3. Myocardial coagulation necrosis with massive hemorrhage (A) and contraction band necrosis (B) were seen in the infarcted area of the LV (hematoxylin and eosin staining, original magnification, × 40).

Figure 4. A: Microscopic appearance of the stenotic artery. There was an atheromatous rupture with hemorrhage and fibrinous exudation. (No thrombosis is seen due to PCI). (Azan staining, original magnification, × 2). B: A small artery in the infarcted myocardium showed necrosis of the vascular wall, detachment of endothelial cells, and intramural fibrinous exudate (hematoxylin and eosin staining, original magnification, × 20). C: There was microembolization consisting of cell debris within the capillary vessels in the myocardium (hematoxylin and eosin staining, original magnification, × 40). D: Thrombus was seen in the small coronary artery in the myocardium (phosphotungstic acid-hematoxylin staining, original magnification, × 40).

was subsequently performed. Although angioplasty relieved the obstruction, no-reflow phenomenon to the distal LAD was present (Figure 1). The patient died two days after the infarction on May 26, 2003.
An autopsy was performed. The heart, weighing 545 g, displayed concentric hypertrophy of the left ventricle (LV), and diffuse myocardial hemorrhage was seen in the anteroseptal and lateral walls of the LV (Figure 2). Microscopic analysis showed 1) myocardial coagulation necrosis with massive hemorrhage and contraction band necrosis in the infarcted area of the LV (Figure 3), 2) an atherosclerotic stenosis with atheromatous rupture in the main trunk of the LAD (Figure 4), and 3) mural necrosis of small coronary arteries (necrotizing arteritis) andobliterative microembolization with cellular debris of the arterioles present in the no-reflow area of the myocardium (Figure 4).

**DISCUSSION**

Investigators have postulated that the mechanisms of the no-reflow phenomenon included capillary plugging by leukocytes or erythrocytes, endothelial cell swelling and protrusion, perivascular edema, vascular dysfunction after reperfusion, small vessel spasm, and compression of the microvascular bed due to myocardial cell swelling or contracture.\(^1,4-6\) Clinically, myocardial contrast echocardiography and contrast-enhanced magnetic resonance imaging are particularly helpful in identifying a no-reflow zone.\(^2,3\) However, they cannot show the mechanisms of the no-reflow phenomenon. Thus, histopathological study is important to elucidate its mechanism in humans.

Mechanical compression of the microvascular bed in the myocardium may be induced by reperfusion injury which includes massive hemorrhage in the myocardium and contraction band necrosis. However, Reffelmann and Kloner\(^3\) stated that mechanical compression is not the primary mechanism of no-reflow although it contributes in some situations. Moreover, previous reports suggested that the pathogenesis of the no-reflow phenomenon after PCI to an atherosclerotic coronary artery may differ from the no-reflow phenomenon obtained using animal models in which a normal coronary artery was occluded, as the importance of microembolization has been recognized in atherosclerotic vascular disease.\(^7-9\) Saber, et al\(^{10}\) reported that coronary microembolization was observed in patients following angioplasty or thrombolytic therapy in an autopsy study. However, they did not mention whether these patients had no-reflow phenomenon or not. There is only one case report of the postmortem outcome of no reflow phenomenon in a patient treated with rotational atherectomy, and it showed that atherothrombi were seen in myocardial arterioles in the patient.\(^11\) Recently, Kotani, et al\(^{12}\) demonstrated that microscopic analysis of the aspirate at the time of no-reflow detected plaque elements, including foam-shaped macrophages, aggregate platelets, cholesterol crystals, and thrombi. In the present case, obliterative microembolization was frequently observed in the arterioles in the no-reflow area.
of the myocardium. These data suggest that coronary microembolization is an important mechanism of no-reflow phenomenon in acute coronary syndromes with PCI.

This is the first report to demonstrate damage to small arteries, including vessel wall necrosis, endothelial damage, and intramural fibrinous exudate (fibrin thrombus), in patients with no-reflow phenomenon after PCI. While ischemia can cause progressive injury to the endothelium and vascular smooth muscle, reperfusion can inflict additional and severe injury to the microcirculation; progressive damage to the vasculature causes an expanding zone of no-reflow and deterioration of coronary flow reserve during the phase of reperfusion. Vascular damage induced by both ischemia and reperfusion may be also related to thrombus formation in the vessel lumen to contribute to no-reflow phenomenon. While a compromised atheroma may cause vascular damage and obliteration in more distal vessels, atheromatous elements such as cholesterol clefts and foam cells were inconspicuous in the microcirculation of the myocardium in the present case.

Treatment strategies to reduce the incidence of no-reflow phenomenon after PCI in acute coronary syndrome are under development. Although there have been reports that distal protection devices may be effective in preventing distal embolization, inhibition of vascular damage may also be required to prevent no-reflow phenomenon after coronary reperfusion.

In conclusion, coronary microembolization and damage to the small coronary artery may contribute to the pathogenesis of no-reflow phenomenon following coronary intervention in humans.

REFERENCES


