I. Introduction

Despite removal of coronary obstruction by percutaneous coronary intervention (PCI) for the treatment of patients with ST-elevation myocardial infarction (STEMI), impaired myocardial perfusion, known as no-reflow phenomenon, occurs in a significant proportion of those patients. No-reflow phenomenon is caused by shedding of active tissue factor from dissected atherosclerotic plaque, microvascular spasm, thrombus or others. A recent study has reported its incidence rate to be 12%. No-reflow phenomenon is clinically important as it leads to cardiac failure as well as in-hospital and long-term mortality. According to a meta-analysis, there are several agents that improve no-reflow phenomenon. However, so far, there is no standardized therapy for no-reflow phenomenon after the primary PCI in STEMI patients. We herein report a case of no-reflow phenomenon improved by intracoronary nitroprusside injection with a Lumine™ infusion catheter (Gadelius Medical K.K., Tokyo, Japan).

II. Case report

A 66-year-old male was admitted to our hospital for acute myocardial infarction and underwent emergent catheterization. Coronary angiogram showed total obstruction of the distal right coronary artery (RCA). We used an AL2 guiding catheter and passed a coronary guidewire into the RCA. Coronary flow was then slightly restored, and severe stenosis of the distal RCA with massive thrombus was observed. Intracoronal ultrasound revealed that the thrombus was large and diffuse. Firstly, thrombus aspiration was performed. Then, no-reflow phenomenon was observed in the far distal RCA. An infusion catheter (Lumine™) was advanced to the distal RCA and 50 µg nitroprusside was injected. Thrombolysis in Myocardial Infarction (TIMI) flow grade 3 was immediately achieved. Two weeks after the first catheterization, a second catheterization was performed. Coronary angiogram showed no stenosis in the RCA and most of the thrombus disappeared. Left ventriculography showed severe hypokinesis of the inferior wall, but ejection fraction increased to 59%. He was discharged and has been followed as an outpatient at our hospital. We experienced a case of no-reflow phenomenon clearly ameliorated by intracoronary nitroprusside injection with a Lumine™ infusion catheter. This method could be a powerful option to treat no-reflow phenomenon.

KEY WORDS: acute coronary syndrome, myocardial ischemia, nitroprusside, no-reflow phenomenon, percutaneous coronary intervention

Yukiko Sugawara, Takayuki Ohwada, Kenichi Watanabe, Takayuki Sakamoto, Kazuhiko Nakazato, and Yasuchika Takeishi

No-reflow phenomenon is a condition in which blood flow to the ischemic myocardium is significantly reduced despite percutaneous coronary intervention. So far, a standard treatment to improve this condition has not been established. We here report an interesting case that illustrates an effective treatment for no-reflow phenomenon. A 66-year-old male was admitted to our hospital for acute myocardial infarction and underwent emergent catheterization. Coronary angiogram showed total obstruction of the distal right coronary artery (RCA). We used an AL2 guiding catheter and passed a coronary guidewire into the RCA. Coronary flow was then slightly restored, and severe stenosis of the distal RCA with massive thrombus was observed. Intravascular ultrasound revealed that the thrombus was large and diffuse. Firstly, thrombus aspiration was performed. Then, no-reflow phenomenon was observed in the far distal RCA. An infusion catheter (Lumine™) was advanced to the distal RCA and 50 µg nitroprusside was injected. Thrombolysis in Myocardial Infarction (TIMI) flow grade 3 was immediately achieved. Two weeks after the first catheterization, a second catheterization was performed. Coronary angiogram showed no stenosis in the RCA and most of the thrombus disappeared. Left ventriculography showed severe hypokinesis of the inferior wall, but ejection fraction increased to 59%. He was discharged and has been followed as an outpatient at our hospital. We experienced a case of no-reflow phenomenon clearly ameliorated by intracoronary nitroprusside injection with a Lumine™ infusion catheter. This method could be a powerful option to treat no-reflow phenomenon.

KEY WORDS: acute coronary syndrome, myocardial ischemia, nitroprusside, no-reflow phenomenon, percutaneous coronary intervention
Construction of the right coronary artery (RCA) with haziness (Fig. 2), and PCI was performed. We used an AL2 guiding catheter and advanced a coronary guidewire to the RCA. Blood flow to the distal RCA was observed immediately after the guide wire passed through the lesion. Intravascular ultrasound (IVUS) showed large and diffuse thrombus in the segment 3 of RCA. We tried to aspirate the thrombus with an aspiration catheter (Thrombuster III GR-a, Kaneka Medix Co., Tokyo, Japan), but could not remove the blood clot effectively (Fig. 3). In addition, blood flow to the distal RCA disappeared again during this manipulation. We, therefore, inserted another wire into the posterior descending artery using a double-lumen microcatheter (Sasuke, Asahi Intecc Co. Ltd., Aichi, Japan), and the posterior descending artery and atrioventricular nodal artery were dilated by balloon (Douvan Kamui 2.0×15 mm, Asahi Intecc Co. Ltd.). However, coronary blood flow was not recovered. Then, a Lumine™

Fig. 1  A 12-lead electrocardiogram.
A 12-lead electrocardiogram on admission showed ST elevation in inferior leads, ST depression in leads I, aVL, and V2-V4, and negative T in leads I and aVL. 10 mm=1 mV.

Fig. 2  Control coronary angiogram.
Control coronary angiogram showed total obstruction of the distal RCA with haziness.
a: left anterior oblique (LAO) view.
b: right anterior oblique (RAO) view.
infusion catheter was advanced to the distal RCA, and 50 µg nitroprusside was injected directly into the coronary artery through a Lumine™ infusion catheter. After nitroprusside injection, the Thrombolysis in Myocardial Infarction (TIMI) flow grade 3 was achieved (Fig. 4). However, massive thrombus in the RCA (segment 3) was still observed by IVUS (Fig. 5). We did not use a coronary stent because the diameter of RCA was too large to achieve good stent strut apposition. An intra-aortic balloon pump (IABP) was inserted and anticoagulant therapy with continuous intravenous infusion of heparin was continued. On the 3rd hospital day, the IABP was removed. The maximum creatine kinase level was 2,553 U/L. After 2 weeks from the first catheterization, a second catheterization was performed (Fig. 6). Coronary angiogram showed no stenosis in the RCA and most of the thrombus disappeared. Left ventriculography showed severe hypokinesis in the inferior wall, but global ejection fraction was recovered to 59%. He was discharged and has been followed up as an outpatient at our hospital.

III. Discussion

We experienced a case of no-reflow phenomenon that occurred immediately after aspiration maneuver for coronary thrombus in the RCA in a STEMI patient. We successfully managed this situation with intracoronary nitroprusside injection via a Lumine™ catheter.

There is no established treatment with universally accepted evidence for no-reflow phenomenon, and several pharmacological therapies (adenosine, anisodamine, diltiazem, nicorandil, nitroprusside, urapidil, and verapamil) have been reported. The results of meta-analyses have showed that intracoronary nitroprusside injection is beneficial in preventing no-reflow/slow-flow phenomenon and in improving TIMI flow grade and left ventricular ejection fraction. It also likely reduces adverse reactions in patients after PCI and rehospitalization due to cardiovascular events. As nitroprusside leads to coronary hyperemia by dilatation of coronary microvessels, intracoronary nitroprusside is likely to have a beneficial effect on the treatment and prevention of no-reflow phenomenon. In particular, Zhao et al. showed better outcome after selective intracoronary nitroprusside infusion using thrombectomy catheter for no-reflow phenomenon.

In our case, we used a Lumine™ catheter, which has 12 micro-holes in the tip to inject drugs directly into the distal lesion of coronary artery. We considered that, in the no-reflow/slow-
flow phenomena, the drugs cannot reach distal micro vessels efficiently from the guiding catheter and that there is a risk of lowering systemic blood pressure when the nitroprusside leak out of coronary artery into the aorta. We were able to inject nitroprusside into the distal vessels effectively and safely by using the Lumine™ catheter. To our knowledge, there has been no report of using a Lumine™ catheter used in treatment for no-reflow phenomenon.

An animal study demonstrated that, after prolonged myocardial ischemia, IABP assistance started just 10 min before reperfusion increased coronary blood flow and limited infarct size and extent of the no-reflow phenomenon. In the present case, we used an IABP after PCI, which might have contributed to the angiographically successful result in the second catheterization. The recent study showed IABP did not improve outcomes in STEMI patients with cardiogenic shock. Although the benefit of IABP in patients with AMI has yet been controversial, in this particular case, we used IABP for improving coronary blood flow to avoid the recurrence of thrombus formation.

The TOTAL trial, a large randomized trial on primary PCI with or without routine manual thrombectomy, did not show any benefit for the routine use of thrombectomy. This trial also suggested that a maneuver of thrombectomy might be slightly harmful, with concerns of increasing the risk of stroke. The mechanism of stroke is that the aspirated thrombus causes embolization of the brain. Thrombectomy is probably beneficial for patients with very large thrombus, but this has not been robustly proven with randomized controlled evidence. In the ESC guideline (2017), routine thrombus aspiration is not recommended. As it was reported that STEMI patients with a greater residual thrombus burden after aspiration thrombectomy had worse microvascular function and larger myocardial damage than patients with a smaller residual thrombus burden, thrombectomy should be chosen carefully. In the present case, we repeated thrombus aspiration, but could not remove the blood clot effectively. Furthermore, through this maneuver, coronary blood flow was interrupted again. We considered that this situation occurred by impaired blood flow in the microvessels rather than thrombus obstruction at the epicardial coronary lesion. So, we challenged the powerful vasodilation and blood flow recovery by intra-coronary nitroprusside injection.

Finally, our patient achieved TIMI flow grade 3 by nitroprusside injection via the Lumine™ infusion catheter, following IABP support and intravenous heparin administration for 3 days. No thrombus was detected in the RCA 2 weeks after the first catheterization.

IV. Conclusion

Intracoronary nitroprusside injection with the Lumine™ infusion catheter may be useful for treatment of no-reflow phenomenon during PCI for STEMI.

Conflicts of interests
None.

References
1) Bonderman D, Teml A, Jakowitsch J, et al: Coronary no-reflow is
caused by shedding of active tissue factor from dissected atherosclerotic plaque. Blood 2002; 99: 2794–2800

2) Jaffe R, Charron T, Puley G, et al: Microvascular obstruction and the no-reflow phenomenon after percutaneous coronary intervention. Circulation 2008; 117: 3152–3156

3) Piana RN, Paik GY, Moscucci M, et al: Incidence and treatment of ‘no-reflow’ after percutaneous coronary intervention. Circulation 1994; 89: 2514–2518

4) Eekhout E, Kern MJ: The coronary no-reflow phenomenon: a review of mechanisms and therapies. Eur Heart J 2001; 22: 729–739

5) Celik T, Balta S, Mikhalidis DP, et al: The relation between no-reflow phenomenon and complete blood count parameters. Angiology 2017; 68: 381–388

6) Magro M, Nauta ST, Simsek C, et al: Usefulness of the SYNTAX score to predict "no-reflow" in patients treated with primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. Am J Cardiol 2012; 109: 601–606

7) Ndrepepa G, Tiroch K, Fusaro M, et al: 5-year prognostic value of no-reflow phenomenon after percutaneous coronary intervention in patients with acute myocardial infarction. J Am Coll Cardiol 2010; 55: 2383–2389

8) Niu X, Zhang J, Bai M, et al: Effect of intracoronary agents on the no-reflow phenomenon during primary percutaneous coronary intervention in patients with ST-elevation myocardial infarction: a network meta-analysis. BMC Cardiovasc Disord 2018; 18: 3

9) Bai S, Fu X, Gu X, et al: Intracoronary administration of different doses of anisodamine in primary percutaneous coronary intervention: protective effect in patients with ST-segment elevation myocardial infarction. Coron Artery Dis 2016; 27: 302–310

10) Pi SF, Liu YW, Li T, et al: Effect of sequential nicorandil on myocardial microcirculation and short-term prognosis in acute myocardial infarction patients undergoing coronary intervention. J Thorac Dis 2019; 11: 744–752

11) Zhang H, Tian NL, Hu ZY, et al: Three hours continuous injection of adenosine improved left ventricular function and infarct size in patients with ST-segment elevation myocardial infarction. Chin Med J (Engl) 2012; 125: 1713–1719

12) Peng Y, Fu X, Li W, et al. Effect of intracoronary anisodamine and diltiazem administration during primary percutaneous coronary intervention in acute myocardial infarction. Coron Artery Dis 2014; 25: 645–652

13) Zhao S, Qi G, Tian W, et al: Effect of intracoronary nitroprusside in preventing no reflow phenomenon during primary percutaneous coronary intervention: a meta-analysis. J Interv Cardiol 2014; 27: 356–364

14) Su Q, Li L, Naing KA, et al: Safety and effectiveness of nitroprusside in preventing no-reflow during percutaneous coronary intervention: a systematic review. Cell Biochem Biophys 2014; 68: 201–206

15) Pasceri V, Pristipino C, Pelliccia F, et al: Effects of the nitric oxide donor nitroprusside on no-reflow phenomenon during coronary interventions for acute myocardial infarction. Am J Cardiol 2005; 95: 1358–1361

16) Pierrakos CN, Bonios MJ, Drakos SG, et al: Mechanical assistance by intra-aortic balloon pump counterpulsation during reperfusion increases coronary blood flow and mitigates the no-reflow phenomenon: an experimental study. Artif Organs 2011; 35: 867–874

17) Patel MR, Smalling RW, Thiele H, et al: Intra-aortic balloon counterpulsation and infarct size in patients with acute anterior myocardial infarction without shock: the CRISP AMI randomized trial. JAMA 2011; 306: 1329–1337

18) Jolly SS, Cairns JA, Yusuf S, et al: Randomized trial of primary PCI with or without routine manual thrombectomy. N Engl J Med 2015; 372: 1389–1398

19) Ibanez B, James S, Agewall S, et al: 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2018; 39: 119–177

20) Higuma T, Soeda T, Yamada M, et al: Does residual thrombus after aspiration thrombectomy affect the outcome of primary PCI in patients with ST-segment elevation myocardial infarction?: An optical coherence tomography study. JACC Cardiovasc Interv 2016; 9: 2002–2011