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【 CASE REPORT 】

Multiple Life-threatening Coronary Artery Spasms after Percutaneous Coronary Intervention for Acute Coronary Syndrome

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Abstract:
A 69-year-old man who had been hospitalized with acute coronary syndrome (ACS), underwent urgent percutaneous coronary intervention. In the subacute phase, he developed sudden chest pain and hemodynamic deterioration, and urgent coronary angiogram showed multiple coronary artery spasms. The discontinuation of beta-blocker treatment and the administration of a calcium antagonist helped prevent angina attacks. In Japanese patients who tend to have coronary artery spasm, the routine administration of beta-blockers for post-ACS patients with a preserved left ventricular systolic function should be considered carefully.

Key words: multiple coronary artery spasm, life-threatening, acute coronary syndrome, calcium channel blocker, beta-blocker

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Introduction

Coronary artery spasms have been shown to cause life-threatening cardiac events (1-3). Beta-blockers have long been the standard treatment for prevention of cardiac events after acute coronary syndrome (ACS), however the administration of beta-blockers may induce coronary artery spasm. In this era of coronary revascularization for ACS, whether or not beta-blockers are associated with a reduced mortality in patients with a preserved left ventricular systolic function (LVSF) is unclear. We herein report the case of a 69-year-old man who developed beta-blocker induced multiple life-threatening coronary artery spasms after ACS.

Case Report

A 69-year-old man with no history of coronary artery disease was admitted to our hospital with acute chest pain. His coronary risk factors included hypertension, being a current smoker, and obesity, and he had been treated with antihypertensive drugs (amlodipine, valsartan, and eplerenone) for about nine years.

His electrocardiogram (ECG) showed ST-segment elevations in leads V1-V5 (Fig. 1A). He was diagnosed with ST-elevation anteroseptal myocardial infarction, and urgent coronary angiogram was performed. The initial angiogram revealed the culprit lesion in the proximal portion of the left anterior descending artery (LAD) and thrombolysis in myocardial infarction 2 flow of the LAD (Fig. 2A and B). There were no lesions in the right coronary artery (RCA) or left circumflex artery (LCx).

Aspiration thrombectomy was performed, and small red thrombi were aspirated. Intravascular ultrasound (IVUS) showed a ruptured plaque containing a large necrotic core within the lesion (Fig. 3A). Left main coronary artery (LMCA)/LAD crossover stent implantation was conducted with a 3.0×28-mm everolimus-eluting stent (Xience Alpine, Abbott Vascular, Santa Clara, USA) at 18 atm, followed by kissing-balloon inflation (KBI). IVUS performed after KBI showed stent malapposition at the proximal edge of the stent; therefore, post-dilatation was conducted with a 3.25×

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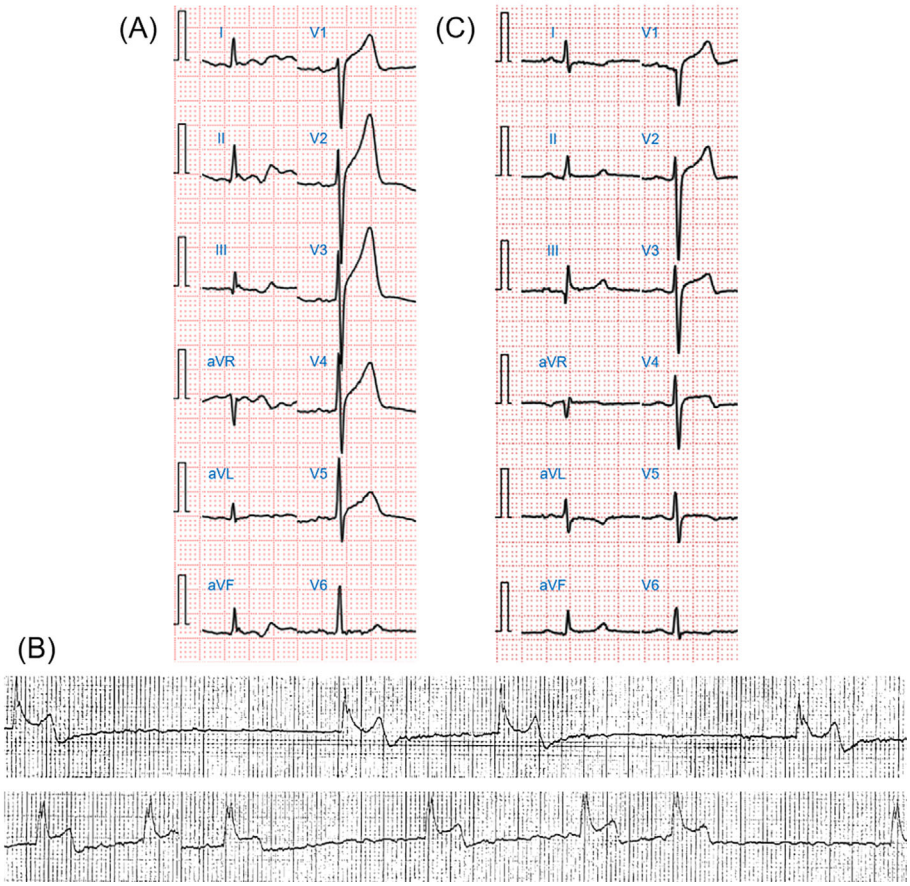

Figure 1. **(A) A 12-lead electrocardiogram showed ST-segment elevation in leads V1-V5, which was suggestive of left anterior descending coronary artery disease. (B) Electrocardiographic monitoring showed atrial fibrillation with bradycardia and an ST-elevation in lead II. (C) A 12-lead electrocardiogram obtained after cardiopulmonary resuscitation showed mild ST-segment elevation in leads V1-V5.**

13-mm non-compliant balloon (KUNAI, ASAHI Intecc, Nagoya, Japan) at 22 atm. The final angiogram showed good results (Fig. 2C and D).

After the procedure, the patient's peak creatine phosphokinase (CPK) level was 1,158 IU/L, and echocardiography revealed an ejection fraction of 55% with hypokinesis of the anteroseptal wall. Aspirin (100 mg/day), prasugrel (3.75 mg/day), rosuvastatin (2.5 mg/day), eplerenone (50 mg/day), lisinopril (10 mg/day), and bisoprolol (2.5 mg/day) were orally administered. Amlodipine, which the patient had been taking before their admission, was discontinued because normotension was observed after the procedure. In the early morning on the second day after admission, the patient complained of sudden chest pain, and electrocardiographic monitoring showed brady atrial fibrillation with ST-elevation in lead II (Fig. 1B). He did not exhibit spontaneous respiration, and his carotid pulse could not be palpated; therefore, cardiopulmonary resuscitation (CPR) was started. After several minutes of CPR, he regained consciousness. After CPR, the patient's ECG showed mild ST-segment elevation (Fig. 1C); therefore, urgent coronary angiogram was performed under a suspicion of subacute stent thrombosis. However, the coronary angiogram did not show significant stenosis (Fig. 4A and B).

IVUS was carried out; however, only mild in-stent plaque protrusion was observed (Fig. 3B). When we were about to finish the procedure, the patient complained of sudden chest pain again. His ECG showed ST-segment elevation in leads II, III, and aVF. Angiogram of the RCA revealed severe spastic changes in the middle and distal portions of the RCA (Fig. 4C). The spastic changes and chest pain were improved by the intracoronary injection of isosorbide dinitrate (Fig. 4D). However, the patient soon complained of chest pain again, and angiogram of the left coronary artery (LCA) revealed spastic changes in the LAD and LCx, which were improved by the intracoronary injection of isosorbide dinitrate (Fig. 4E and F). We finished the angiogram after observing the patient's electrographic changes and symptoms for several minutes. After the angiogram, the beta-blocker treatment was discontinued, and low-dose calcium antagonist treatment (2.5 mg/day amlodipine) was administered. To this day, the patient's coronary spastic angina has not recurred.

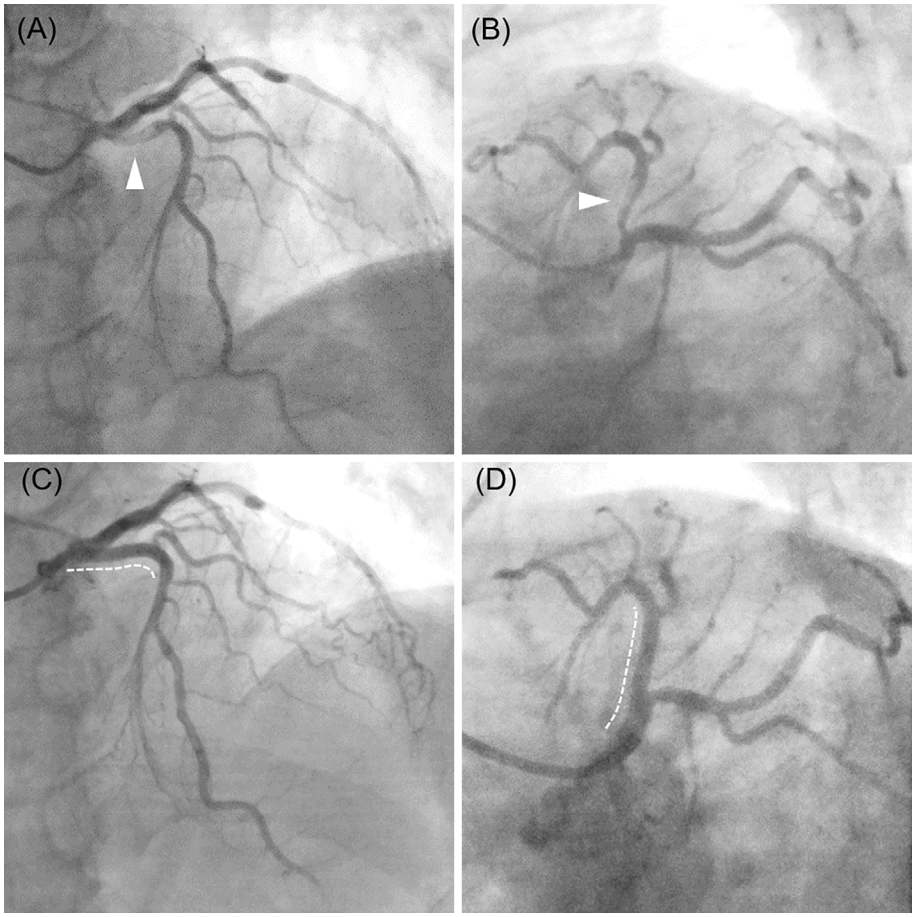

Figure 2. **Coronary angiogram at the first procedure. (A, B) Left coronary angiogram showed the culprit lesion in the proximal portion of the left anterior descending artery (LAD) (white arrows), whereas no significant stenosis was detected in the left circumflex artery. (C, D) The final coronary angiogram showed appropriate stent expansion (white broken lines).**

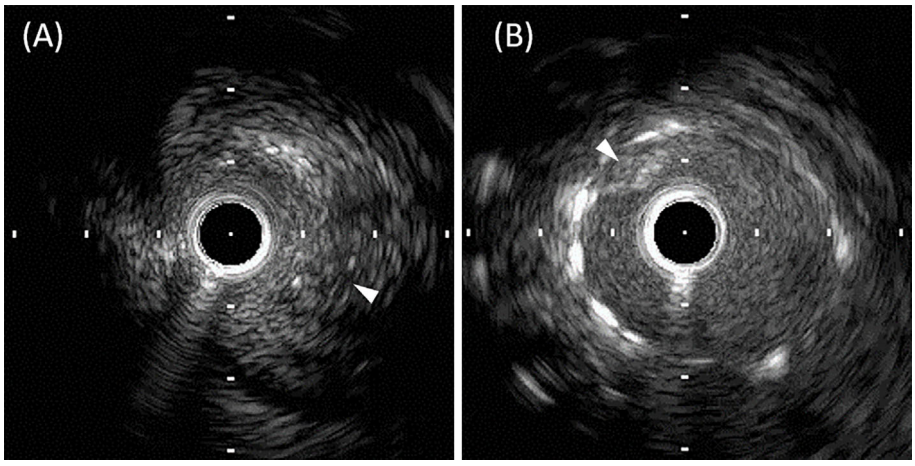

Figure 3. **Intravascular ultrasound (IVUS). (A) IVUS after aspiration thrombectomy showed a ruptured plaque containing a large necrotic core within the lesion (white arrow). (B) IVUS showed mild in-stent plaque protrusion (white arrow).**

Discussion

Coronary artery spasms have been shown to cause angina, myocardial infarctions, and arrhythmia (1-3). Multiple coronary artery spasms might cause more significant myocardial ischemia and be more life-threatening than a single coronary artery spasm (4-6). This report presents a case in which

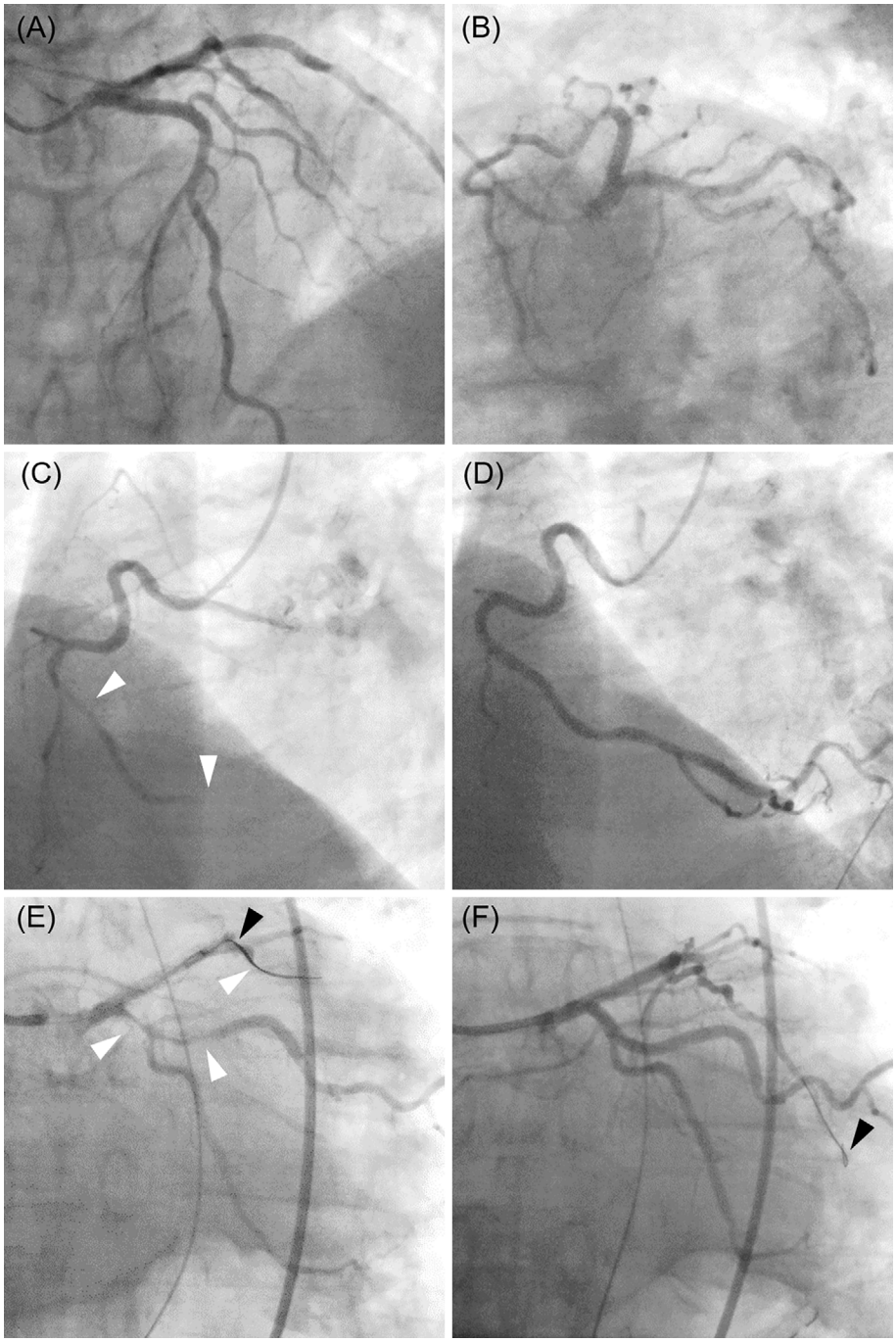

Figure 4. **Coronary angiogram after cardiopulmonary resuscitation. (A, B) No significant stenosis or stent thrombosis was detected on left coronary angiogram. (C, D) Right coronary angiogram showed multiple severe coronary spasms in the middle and distal portions of the artery (white arrows), and the spasms improved after the intracoronary injection of isosorbide dinitrate. (E, F) Left coronary angiogram showed multiple severe coronary artery spasms in the proximal and middle portions of the left circumflex artery and the distal portion of the left anterior descending artery (LAD) (white arrows), and the spasms improved after the intracoronary injection of isosorbide dinitrate. A guidewire was passed into the LAD to allow the implanted stents to be observed on intravascular ultrasound (black arrows).**

multiple life-threatening coronary artery spasms without organic stenosis occurred after percutaneous coronary intervention (PCI) for ACS. Repeated coronary angiogram showed severe coronary artery spasms in the RCA and LCA (at slightly different times), and these events resolved after the intracoronary injection of isosorbide dinitrate.

There have been several reports regarding severe coronary artery spasms associated with life-threatening events after the implantation of drug-eluting stents (DESs) (7, 8). Hypersensitivity reactions to stent components (e.g. coated poly-

mers, drugs, and metal) and endothelial dysfunction have been recognized as important factors influencing the occurrence of coronary artery spasms (9-11). Most reports on this topic have described coronary artery spasms occurring in stent-implanted vessels or in proximal or distal stent segments (7, 12). In the current case, all spasm sites were located away from the stenting site (LMCA to the proximal LAD); therefore, we believe that the multiple coronary artery spasms encountered in this case were not associated with DES implantation.

Pristipino et al. evaluated the racial differences in coronary constrictor responses between Japanese and Caucasian patients who had recently suffered myocardial infarctions (13). They showed that, in the early phase of ACS, Japanese patients exhibited a three-fold greater incidence of coronary spastic responses (in both the infarct-affected and non-infarct-affected arteries) to the intracoronary acetylcholine provocation test than Caucasians, as well as a significantly higher incidence of multiple coronary artery spasms (13).

In the current case, after coronary artery spasms were detected, the discontinuation of beta-blocker treatment and the administration of a calcium antagonist helped prevent angina attacks. We consider that the multiple life-threatening coronary artery spasms encountered in our case were caused by the administration of a beta-blocker in addition to the coronary artery spastic tendency seen in Japanese people. There is also a possibility that the administration of a calcium antagonist as anti-hypertensive therapy before the patient's admission accidentally prevented coronary artery spasms.

In this case, the patient's peak CPK level was mildly elevated, and echocardiography revealed that his LVSF had been preserved. In this era of coronary revascularization for ACS, whether or not beta-blockers are associated with a reduced mortality in patients with a preserved LVSF is unclear. Beta-blockers have long been the standard treatment for ACS; however, most studies evaluating the effects of beta-blockers on ACS were carried out several decades ago, at a time when coronary revascularization was not performed and when the currently used secondary prevention drugs, such as statins and renin angiotensin aldosterone system blockers, were not administered sufficiently often (14, 15). A recent cohort study, in which 52.8% of the included patients exhibited ST-elevation acute myocardial infarctions and 45.9% of the patients underwent coronary revascularization, evaluated the efficacy of beta-blocker treatment in patients with a preserved LVSF and showed that the use of beta-blockers was not associated with an improved survival (16). Furthermore, a meta-analysis that included patients with a preserved LVSF who underwent PCI did not obtain evidence to support the routine use of beta-blockers in ACS patients who undergo PCI (17).

The Japanese beta-blockers and calcium antagonists myocardial infarction (JBCMI) study compared the effects of beta-blockers on cardiovascular events with those of calcium antagonists in Japanese post-ACS patients who underwent coronary revascularization and showed that there was no significant difference in the incidence of cardiovascular mortality between the two groups (18). However, the incidence of coronary artery spasm was significantly higher in the beta-blocker group than in the calcium antagonist group (18). The current Japanese guideline shows the importance of beta-blocker for ischemic heart disease; however, the administration of beta-blockers to low-risk ACS patients who have undergone coronary revascularization remains controversial (19).

In daily clinical practice, we sometimes experience cases of coronary artery spasm caused by beta-blockers; however, there have been few reports about multiple life-threatening coronary artery spasms induced by beta-blocker treatment after PCI for ACS.

Based on the abovementioned points, we consider that the routine administration of beta-blockers to post-ACS Japanese patients with a preserved LVSF who have undergone appropriate PCI should be considered carefully, and that the administration of calcium antagonists to Japanese ischemic heart disease patients is very important.

Author's disclosure of potential Conflicts of Interest (COI).
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