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Case Report

Rapidly Progressive Stenosis of the Left Main Trunk Ostium Starting 21 Months After Stent Implantation

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Rapidly progressive in-stent restenosis (ISR) after stent deployment from the left main trunk (LMT) to the left anterior descending artery (LAD) without plaque at the LMT ostium has not been reported. A 60-year-old Japanese man with a history of scleroderma, pulmonary fibrosis, and type 2 diabetes developed acute myocardial infarction of the right coronary artery (RCA) and was treated by emergency percutaneous coronary intervention (PCI) for RCA. Nine days later he underwent PCI from the LMT to the LAD. Follow-up coronary angiography (CAG) at 9 and 21 months post-PCI did not reveal ISR in any lesion, but the patient experienced cardiac arrest at 25 months post-PCI. Emergency CAG after resuscitation revealed ISR of the LMT ostium; emergency PCI was conducted. The development of ISR at the ostium of the LMT although the patient was free of plaque 4 months before is extremely unusual. This rare ISR of the LMT ostium progressed rapidly after follow-up CAG revealed no ISR at 21 months post-stent implantation.

Key words: left main trunk, in-stent restenosis, cardiopulmonary arrest

Since the advent of drug-eluting stents, the performance of a percutaneous coronary intervention (PCI) for the left main trunk (LMT) has also become safe and effective. Rapidly progressive in-stent restenosis (ISR) after stent deployment from the LMT to the left anterior descending artery (LAD) without plaque at the LMT ostium has not been reported before, to the best of our knowledge. We describe the case of a patient who underwent a PCI from the LMT to the left anterior descending artery (LAD) and had no restenosis according to follow-up coronary angiography (CAG) conducted 21 months later. However, 4 months after the PCI he experienced cardiopulmonary arrest (CPA), and CAG revealed obvious ISR at the LMT ostium.

Case Report

We present the case of a 60-year-old Japanese man with a medical history that included scleroderma, pulmonary fibrosis, and type 2 diabetes mellitus (DM). He had a history of occasional drinking but no history of smoking. His family history of ischemic heart disease was unremarkable. His job was an office worker. He had no allergies. He was taking the following medica-

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tions: aspirin 100 mg, esomeprazole 20 mg, isosorbide mononitrate 40 mg, rosuvastatin 2.5 mg, vildagliptin 50 mg, azathioprine 50 mg, prednisolone 5 mg, trimethoprim-sulfamethoxazole combination, and clarithromycin 200 mg.

The patient had undergone a PCI for the right coronary artery (RCA) elsewhere for an acute inferior myocardial infarction. A Resolute™ Integrity drug-eluting stent 3.0×38 mm (Medtronic, Minneapolis, MN, USA) was implanted into segment 3 of the RCA. Nine days later, residual stenosis was treated by a second coronary angioplasty. Stenosis was severe at segments 6, 7, and 8 of the LAD, and at the first diagonal branch (DB) and high lateral (HL) branches (Fig. 1A, B).

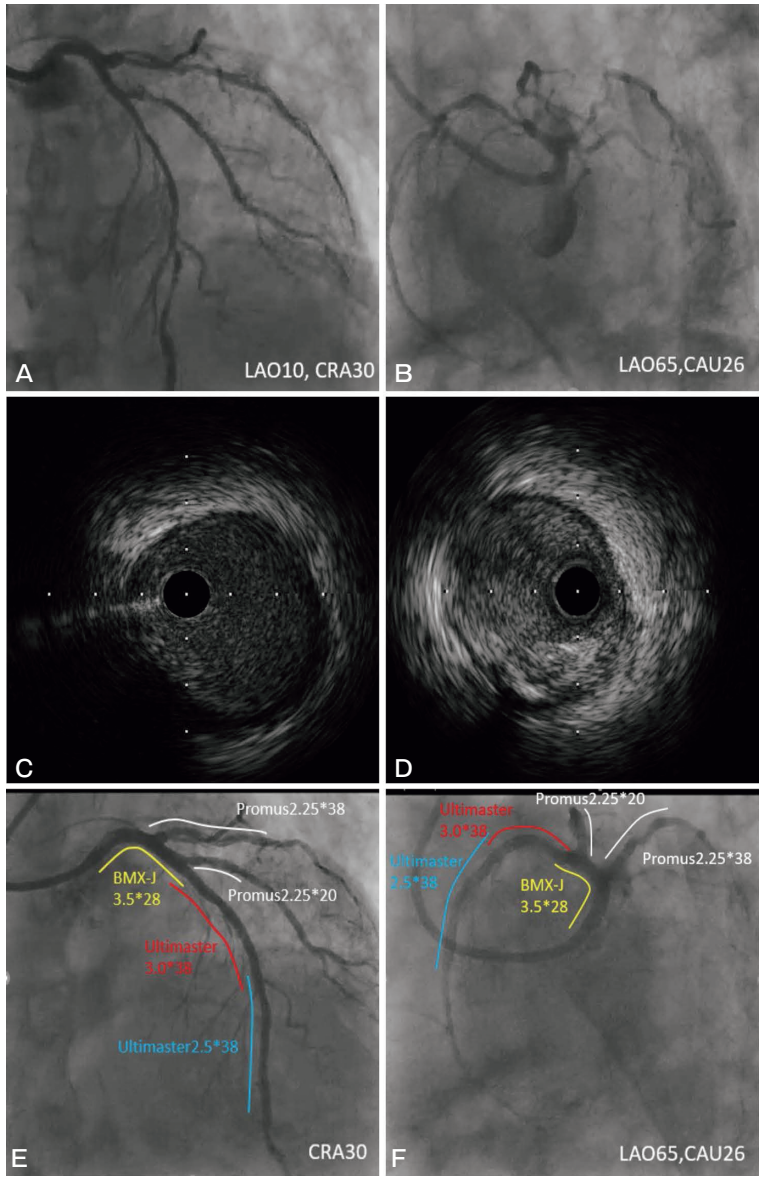

Fig. 1 **A**, Angiography findings of the left coronary artery (LCA) before the initial percutaneous coronary intervention (PCI); **C**, Intravascular ultrasound (IVUS) showed that plaque was not evident in the left main trunk (LMT) ostium; **D**, IVUS showed a moderate amount of plaque at the left anterior descending artery (LAD) ostium. Final angiography of the initial LCA PCI. Diagonal branch; (DB), Promus Element, 2.25×20 mm (Boston Scientific, Natick, MA, USA); Distal LAD, Ultimaster, 2.5×38 mm (Terumo); High lateral (HL), Promus Element, 2.25×38 mm (Boston Scientific); LMT ostium to the LAD, BMX-J, 3.5×28 mm (Terumo); Mid-LAD, Ultimaster, 3.0×38 mm (Terumo) (**E**, **F**).

Intravascular ultrasound (IVUS) showed no plaque in the LMT ostium (Fig. 1C). The Syntax score was 25.

A 3.5×28-mm BMX-J drug-eluting stent (Terumo, Tokyo) was deployed from the LMT ostium to the LAD, due to a moderate amount of plaque at the LAD ostium (Fig. 1D). The stent was placed with the minor curvature side of the LMT. Other stents were implanted at the mid- to distal LAD, DB, and HL branch (Fig. 1E, F).

Follow-up CAG at 9 and 21 months revealed no stent restenosis (Fig. 2). A type Mitsudo catheter was used, and there was no particular problem with the procedure during the follow-up CAG. The patient had no symptoms of angina, and his scleroderma was stable. However, at 25 months after the PCI, the patient experienced a cardiopulmonary arrest (CPA) and collapsed at work. His pulse returned soon after cardiopulmonary resuscitation and the application of an automated external defibrillator (AED). He was transferred to a hospital and then to our institution under a diagnosis of suspected cardiac events.

Cardiac arrest occurred again upon the patient's arrival, but his heart started beating with intravenous epinephrine. Twelve-lead electrocardiography revealed ST depression in leads I, aVL, and V3–V6, as well as ST elevation in the aVR lead (Fig. 3A). Echocardiography showed diffuse severe hypokinesis of the left ventricle (left ventricular ejection fraction [LVEF] 20%), particularly in the anterior-anteroseptal region. Emergency CAG after resuscitation revealed ISR at the LMT ostium (Fig. 3B), which we suspected was the culprit lesion of the ACS. There was no significant stenosis in the RCA and no collateral from the RCA to the LCA.

An intra-aortic balloon pump (IABP) was inserted before the PCI was started, because the patient's hemodynamics were unstable. After a SION® blue guidewire (Asahi Intecc, Aichi, Japan) was passed through the stenosis, we inflated a 2.0×15-mm Sapphire II Pro balloon (OrbusNeich, Shatin New Town, Hong Kong) to 12 atm (Fig. 3C). IVUS using an Altaview instrument (Terumo) showed that the stent was fully expanded to 4 mm, and that intimal thickening was a major factor associated with the development of the stenosis (Fig. 3D). The neointima was homogeneous and consisted of fibrous plaques.

We then attempted to dilate the LMT ostium with a non-compliant 4.0×10-mm NC Kamui balloon (Asahi Intecc), but the balloon slipped and could not be expanded at the lesion. We then changed to a non-slip,

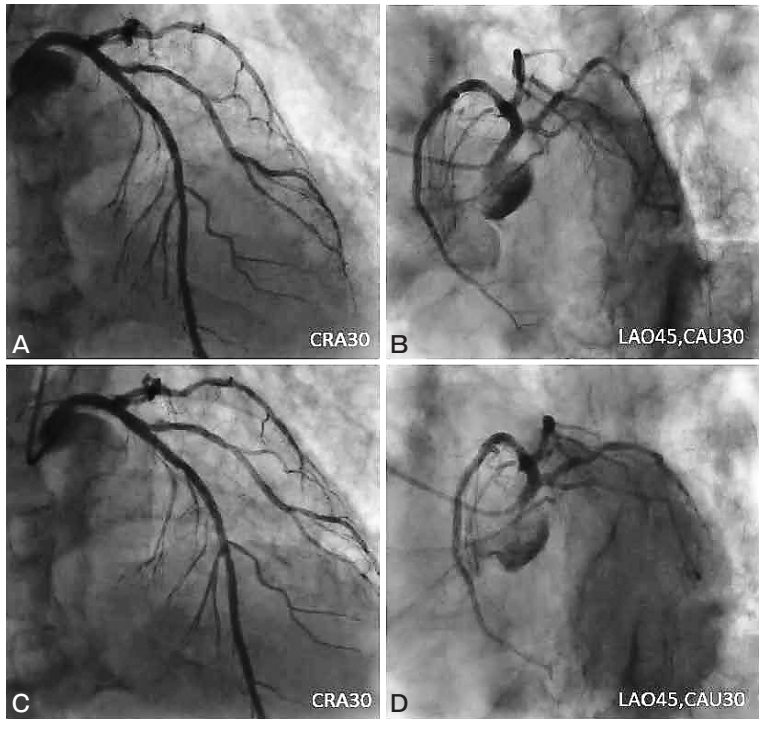

Fig. 2 Follow-up coronary angiography (CAG) at 9 months (A, B) and at 21 months after the initial PCI (C, D).

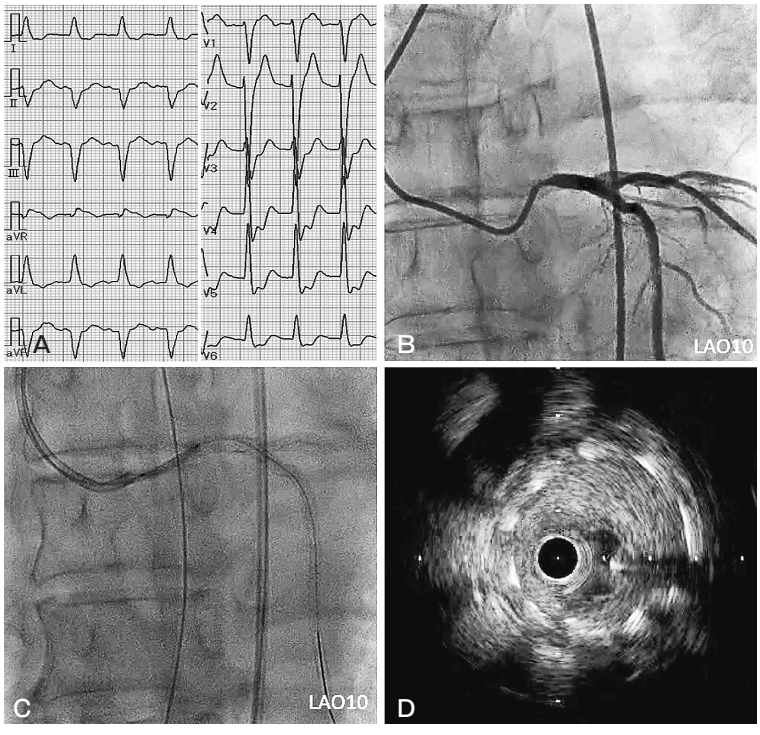

Fig. 3 A, Electrocardiogram findings upon admission; B, Emergency CAG after resuscitation; C, Pre-dilation of LMT with a 2× 15-mm balloon at 12 atm; D, IVUS showed that the stent was fully expanded to 4 mm, and intimal thickening was a major factor associated with the development of the stenosis.

3.5×13-mm Lacrosse NSEα balloon (Goodman Medical Ireland, Galway, Ireland) and dilated it to 14 atm. A 4.0×8.0-mm Xience Sierra™ drug-eluting stent (Abbott Vascular, Chicago, IL, USA) was placed at 14 atm at the LMT ostium without crossing over the left circumflex artery (LCX). Post-balloon dilation proceeded using a 4.0×10-mm NC Kamui balloon at 20 atm in the LMT stent. IVUS showed good expansion of the stent.

The patient's hemodynamics gradually stabilized, and the IABP was withdrawn on hospital day 4. The levels of creatine kinase (CK) and CK-MB peaked at 1,733 and 191 IU/L, respectively. However, the patient's consciousness level did not improve, and a tracheostomy proceeded on hospital day 8. His respiratory condition worsened due to exacerbated pulmonary fibrosis, and he died of respiratory failure on hospital day 23.

Discussion

Several randomized control trials of PCI and CABG for LMT lesions have been conducted in recent years [1]. The EXCEL trial showed that PCI for LMT is comparable to CABG if the Syntax score is not high (≤32) [2]. In the European Society of Cardiology (ESC) 2018 guidelines, PCI for LMT with intermediate SYNTAX score (23-32) is a class IIa indication for PCI [3]. The reported incidence of target lesion revascularization after LMT stent deployment has varied from 2% to 16% [4]. However, in our patient new stenosis occurred at the LMT ostium 25 months after the stent deployment even though no stenotic lesion was evident 21 months later, and this resulted in a CPA. It seemed rather unusual that the ISR developed so rapidly when the ostium of the LMT was plaque-free only 4 months earlier, and we searched the PubMed database for similar situations or cases, with no success. The results of the 10-year-long PRECOMBAT trial indicate that myocardial infarction occurred in about 3% of patients who underwent PCI for left main coronary disease, but it is not clear whether the myocardial infarction is due to a rapid restenosis [5]. It can be argued that the cause of the myocardial infarction was stent thrombosis rather

Table 1 Laboratory data

	at 21 months	at the time of emergency
Laboratory Parameters		
White blood cell, /mm^3	9,000	24,100
Red blood cell, $\times 10^4$/mm^3	471	415
Hemoglobin, g/dL	15.3	13.4
Hematocrit, %	46.2	43.1
Platelet, $\times 10^4$/mm^3	25.5	22.9
Prothrombin time international normalized ratio		1.76
Activated partial thromboplastin time, sec		52.9
D-dimer, μg/mL		105.6
Asparate aminotransferase, IU/L	22	159
Alanine aminotransferase, IU/L	11	44
Lactate dehydrogenase, IU/L	181	536
Total bilirubin, mg/dL	0.4	0.4
Albumin, mg/dL	3.7	2.7
Blood urea nitrogen, mg/dL	12	12.7
Creatinine, mg/dL	0.73	1.24
Estimated glomerular filtration rate, mL/min/1.73m^2	83.4	46
C-reactive protein, mg/dL	0.16	0.69
Creatine kinase, IU/L		190
Creatine kinase MB, IU/L		58
Triglyceride, mg/dL	81	58
Low-density lipoprotein cholesterol, mg/dL	95	68
High-density lipoprotein cholesterol, mg/dL	52	37
Glucose	111	557
Hemoglobin A1c, %	5.9	6.0
Brain natriuretic peptide, pg/mL	103	257
High-sensitivity Troponin I, pg/mL		34.5

than ISR. However, the IVUS findings in the present case still suggested intimal hyperplasia, and dilation with a non-slipping balloon was possible although a non-compliant balloon slipped.

Neoatherosclerosis is a novel arteriosclerosis in a stent, and it has been reported to cause restenosis in a stent [6]. Histologically, neoatherosclerosis is neointima with calcification and a necrotic core, and it is composed of macrophages that are rich in lipid components [6]. Although we did not use optical coherence tomography (OCT) in the present case (only IVUS), we observed that the patient's neointima was homogeneous and consisted of fibrous plaques without calcification or a necrotic core (Fig. 3D).

Poor lipid control, poor glycemic control, smoking, and drug neglect are usually considered risk factors for ISR. In our patient's case, the lipid control and diabetes control were good (LDL cholesterol, 68 mg/dL and HbA1c, 6.0%; Table 1). The patient was not a smoker and was taking his medications correctly; the medications were thus unlikely to pose a risk for restenosis.

Antiplatelet therapy was required to prevent stent occlusion in this case, and the patient was properly taking aspirin, an antiplatelet drug. The possibility of a link between allergies to metal (*e.g.*, nickel) and stent restenosis has been described [7]. It is necessary to consider this possibility in our patient as well, but the following three points were confirmed. (1) The patient had no allergies and was taking steroids. (2) There was no problem 21 months after the stent deployment, and it was unlikely that allergies would appear in the next 4 months. (3) Restenosis was observed in the LMT ostium but at no other sites.

A possible factor peculiar to this patient's case was the presence of scleroderma, but the disease state of scleroderma was stable under treatment with steroids and immunosuppressive drugs. Although long-term oral steroids may promote atherosclerosis, there are no reports that they cause in-stent restenosis [8]. We had not tested for antiphospholipid syndrome in this patient. A case of coronary artery disease with antiphospholipid syndrome that showed repeated stent

thrombosis was reported [9], and we should thus have examined our patient for antiphospholipid antibody syndrome.

Another possible cause of restenosis is that the intima in the stent was damaged during the follow-up CAG, but this is unlikely because the intimal proliferation in the stent was on the minor curvature side of the LMT. Usually, a catheter contacts the major curvature side of the LMT. There is a report of a case in which CAG was performed while the patient was taking steroids and a dissection was formed at the entrance of the coronary artery with a catheter [10], but to the best of our knowledge there has been no report of restenosis occurring in the chronic phase. In addition, the dose of prednisolone was high in that case at 12.5 mg/day, whereas our patient's prednisolone dose was 5 mg/day. It is possible that the placement of a stent put a burden at the proximal stent edge in our patient's case, but it was confirmed by angiography that there was no problem 21 months later. Although there were no IVUS records of the proximal edge of the LMT stent at the first PCI, it is unlikely that an excessive physical force was applied during the next 4 months.

The cause of rapid restenosis in the chronic stage in this case is thus not clear. A careful follow-up is required for patients with collagen disease who have a stent placed in the LMT, because ISR of an LMT stent can be fatal.

In conclusion, even if a patient's status has remained stable for a long time after stent placement in the LMT, the status could change in some patients, and continued long-term careful monitoring such as repeated exercise tests soon after procedures are conducted within a short period may be essential for the early detection of restenosis.

Limitations. There are several limitations in this report. It is difficult to explain the process of restenosis only with angiographic observation. It could have been informative to use OCT to clarify the pathological condition, but only IVUS was used at the PCI. In addition, pathological findings are needed to thoroughly investigate what happened during the 4-month period described above for this patient.

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