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CASE REPORT
Coronary intervention

Effectiveness of directional coronary atherectomy in treating recurrent in-stent restenosis: a case report

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Background In-stent restenosis (ISR) remains a significant clinical problem. It is estimated that 10–20% of patients who develop a first event of ISR will develop recurrent ISR (R-ISR). However, the pathology of R-ISR remains largely unknown, and recommendations for its optimal management are lacking. In this case report, we discuss the effectiveness of directional coronary atherectomy (DCA) as an atherectomy device and the mechanism of R-ISR based on pathological findings obtained from DCA.

Case summary We report the case of a 62-year-old man with a history of ST-segment elevation myocardial infarction treated with percutaneous coronary intervention (PCI) to the mid left circumflex artery using a bare metal stent. Even after the introduction of adequate secondary prevention therapy for ISR, the patient underwent a total of six PCI sessions over 10 years following primary PCI for R-ISR. Eventually, the decision was made to institute treatment with DCA and a drug-coated balloon. No symptoms of restenosis were observed over the following 4 years.

Discussion In this case report, we demonstrate the effectiveness of DCA treatment for debulking a wide range of collagen-rich plaques and show that DCA treatment should be considered for the treatment of R-ISR.

Keywords Coronary atherectomy • Directional coronary atherectomy • Drug-coated balloon treatment • Recurrent in-stent lesion • Intracoronary imaging • Case report

ESC curriculum 3.1 Coronary artery disease • 3.2 Acute coronary syndrome • 3.3 Chronic coronary syndrome

Learning points

- Directional coronary atherectomy (DCA) should be considered in treating recurrent in-stent restenosis lesions.
- The pathological findings obtained by DCA revealed a collagen-rich plaque with fibrin deposition caused by stent or balloon compression.

Introduction

The treatment of patients with in-stent restenosis (ISR) remains a significant clinical challenge.[1–4] Previous studies showed that achieving acute lumen gain is an important principle in the treatment of ISR; atherectomy devices, such as excimer laser coronary atherectomy (ELCA) or rotational atherectomy (RA), may be useful for ISR treatment[1] and drug-eluting stents (DES) and drug-coated balloons (DCBs) provide the best clinical and angiographic results in patients with the first episode of ISR.[5–7] However, data and understanding of whether these strategies would work equally well for subsequent recurrent ISR (R-ISR) remain limited.

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In this case report, we describe a case of R-ISR after bare metal stent (BMS) implantation and discuss the effectiveness of directional coronary atherectomy (DCA) and the mechanism of R-ISR based on the pathological findings of plaques obtained after DCA.

Summary figure

then performed using a scoring balloon and an everolimus-eluting stent. Nine months later, follow-up CAG was performed because we assumed that this case was a high-risk patient for ISR, which revealed a fourth episode of ISR [fractional flow reserve (FFR), 0.72; *Figure 1D*]. The plaque was identified as having a layered pattern using optical coherence tomography (OCT); we successfully treated the lesion using a scoring balloon and a paclitaxel-coated balloon (PCB).

Time	Event
May 2006	ST-segment elevation posterior myocardial infarction (STEMI) was diagnosed. Percutaneous coronary intervention (PCI) was performed for the left circumflex artery with a bare-metal stent (BMS).
August 2006	Follow-up coronary CT revealed ISR. Percutaneous coronary intervention for the in-stent restenotic lesion of the BMS was performed with a sirolimus-eluting stent (SES).
December 2013	Unstable angina pectoris (UAP) occurred as a result of the second episode of ISR in the BMS and SES. Percutaneous coronary intervention was performed with a cutting balloon.
February 2014	Unstable angina pectoris developed because of the third episode of ISR in the same lesion. Percutaneous coronary intervention was performed with a scoring balloon and everolimus-eluting stent.
November 2014	Follow-up coronary angiography (CAG) showed a fourth episode of ISR (fractional flow reserve: 0.72). PCI was performed with a scoring balloon and paclitaxel-coated balloon.
November 2015	Unstable angina pectoris occurred because of the fifth episode of ISR. Percutaneous coronary intervention was performed with rotational atherectomy, a scoring balloon, and a paclitaxel-coated balloon.
November 2016	Stable AP developed because of the sixth episode of ISR. Percutaneous coronary intervention was performed with a cutting balloon and paclitaxel-coated balloon.
November 2017	Unstable angina pectoris occurred because of the seventh episode of ISR. Percutaneous coronary intervention was performed with a directional coronary atherectomy and paclitaxel-coated balloon.

Case presentation

A 62-year-old male patient was initially referred to the emergency department with chest pain as the chief complaint in May 2006. A 12-lead electrocardiogram was performed, showing ST elevation at V1–V4 leads, leading to a diagnosis of an ST-segment elevation myocardial infarction. The patient had a medical history of dyslipidaemia. Emergent coronary angiography (CAG) revealed occlusion in the middle of the left circumflex artery; therefore, we performed primary percutaneous coronary intervention (PCI) using a BMS. Optimal medical therapy, including potent statin and dual antiplatelet therapy (DAPT) using ticlopidine (200 mg/day) and aspirin (100 mg/day), was initiated. The patient was discharged without complications.

Three months later, the patient complained of mild chest pain on exertion. Coronary computed tomography angiography (CTA) was performed, and ISR was suspected. Therefore, CAG was performed and a diffuse ISR lesion on the BMS was confirmed (*Figure 1A*). We successfully treated ISR using a first-generation sirolimus-eluting stent (SES) implantation. After the second procedure, the patient had no symptoms for 7 years. In July 2013, CTA showed no ISR, and we decided to discontinue ticlopidine according to the guidelines. However, 6 months later, the patient developed unstable angina pectoris (UAP) caused by a second episode of ISR in the SES in BMS (*Figure 1B*). Percutaneous coronary intervention was performed with a cutting balloon. Thereafter, DAPT was resumed with clopidogrel (75 mg/day).

In February 2014, UAP recurred as a result of a third episode of ISR in the same lesion (*Figure 1C*). Percutaneous coronary intervention was

In November 2015, UAP occurred as a result of a fifth episode of ISR (*Figure 1E*). Percutaneous coronary intervention was performed using RA, scoring balloon, and PCB. Post-procedural OCT revealed minimal stent area (MSA; 4.3 mm^2). Prasugrel (3.75 mg/day) was administered as a substitute for clopidogrel. Patch tests for Co, Cr, and Ni showed no significant findings. One year later, the patient experienced frequent chest pain. Coronary angiography was performed, which revealed a sixth episode of ISR (*Figure 1F*). We then performed a PCI for the lesion with a cutting balloon and a PCB.

In November 2017, the angina pectoris of the patient was observed to be worsening. His vital signs were stable and physical examination revealed no specific abnormalities. His medication compliance was not an issue, and the only other risk factor was dyslipidaemia, which was well controlled, as the LDL-cholesterol level was around 60 mg/dL owing to the administration of a potent statin (rosuvastatin 10 mg/day). Coronary angiography revealed a seventh ISR (*Figure 1G*); PCI was performed using DCA followed by PCB (*Figure 1H*) (*Supplementary material*). Post-procedural intravascular ultrasonography indicated MSA (5.4 mm^2). Pathological findings of the plaque obtained using DCA showed an extracellular matrix in the superficial layer, fibrin deposition, and dense collagen-rich fibres in the deep layer (*Figure 2*). After the procedures, the patient had no chest pain or ISR for 5 years (*Table 1*).

Discussion

Treatment in patients with ISR remains an important clinical problem.[1–4] Obtaining objective evidence of myocardial ischaemia is recommended

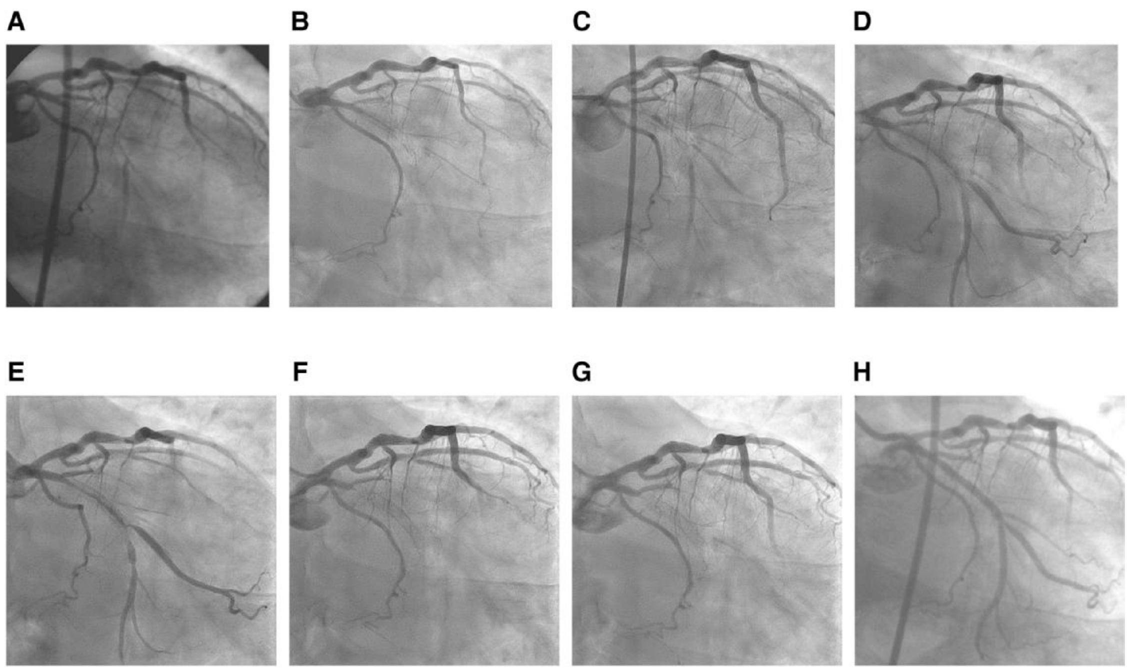

Figure 1 Coronary angiography demonstrating occlusion of the proximal circumflex coronary artery and revascularization. Occlusion of the proximal circumflex coronary artery and revascularization after percutaneous coronary intervention with a bare metal stent was performed. There were a total of six occurrences of in-stent restenosis. (*A–F*) Coronary angiography showing the seventh in-stent occlusion of the same lesion (*G*) and revascularization after performed percutaneous coronary intervention with directional coronary atherectomy and a drug-coated balloon (*H*).

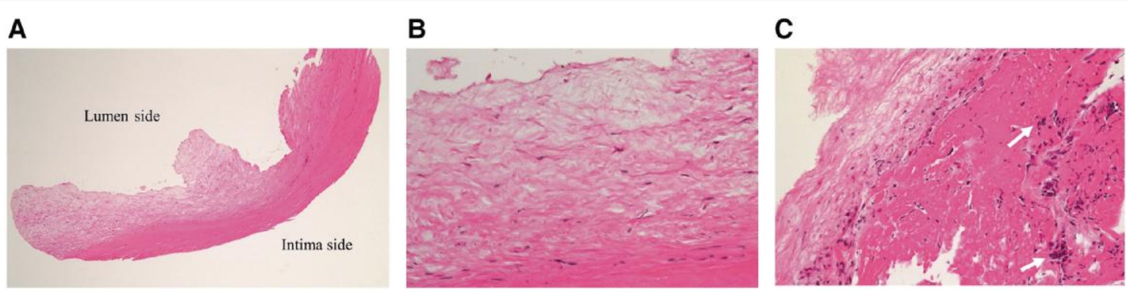

Figure 2 Pathological findings. Low-power (*A*; 40×) and high-power [*B*; superficial layer (lumen side) and *C*; deep layer (intima side), 200×] magnification images obtained by directional coronary atherectomy. In the superficial layer, rich collagen fibre and layered sparse cellular components consisting of smooth muscle cells, indicate a new stenotic lesion (*B*). In the deep layer, there are fibrin depositions (Arrows) in smooth muscle cells (*C*).

before repeat intervention, with deferral of revascularization in patients with ISR with FFR > 0.80, showing equivalent outcomes to *de novo* native coronary artery stenosis.[8] According to recent guidelines, intracoronary imaging devices should be used as an essential component in the revascularization of ISR to select the appropriate treatment and avoid persistent errors,[9] and PCI with DES or DCB is recommended (Class 1, Level of Evidence A).[5–7]

However, optimal management of R-ISR lacks clear recommendations.[10,11] Previous studies demonstrated that the possible mechanisms underlying R-ISR include stent under-expansion, loss of mechanical integrity, neointimal hyperplasia, or neoatherosclerosis; therefore, understanding the point of failure during the previous stent implantations and enlisting the aid of intracoronary imaging devices may facilitate an individualized approach for each patient.[9–12] Pathological evaluation is also critical for understanding the pathophysiology of R-ISR and may provide useful information for treatment; however, there are few reports on the pathology of R-ISR.

In this case report, we describe the characteristics of plaques obtained using DCA after BMS and DES implantation. The pathological findings revealed different characteristics in the superficial and deep layers. Extracellular matrix was predominant in the superficial layer, indicating a new stenotic lesion. In the deeper layers, fibrin deposits, layered sparse cellular components, and dense collagen-rich fibres were seen, all of which were thought to have been formed by compression from repeated balloon angioplasty procedures. One possible cause of R-ISR was that the presence of these thick collagen-rich and dense fibres caused neointima's recoil, which prevented the achievement of

Table 1 Schedule of treatments for the proximal circumflex artery

Date	Event	PCI procedure
March 2006	STEMI	BMS 3.0 × 23 mm
October 2006	1st ISR	SES 3.0 × 33 mm
December 2013	2nd ISR	Cutting balloon 3.0 mm
February 2014	3rd ISR	EES 3.0 × 38 mm
November 2014	4th ISR	PCB 3.0 mm
November 2015	5th ISR	RA 2.15 mm burr + PCB 3.0 mm
November 2016	6th ISR	PCB 3.0 mm

This table illustrates how to treat the proximal circumflex artery.
BMS, bare -metal stent; EES, everolimus-eluting stent; ISR, in-stent restenosis; PCB, paclitaxel-coated balloon; PCI, percutaneous coronary intervention; RA, rotational atherectomy; SES, sirolimus-eluting stent; STEMI, ST-segment elevation myocardial infarction.

lumen enlargement. Therefore, achievement of acute lumen gain as much as possible by compressed plaque removal with atherectomy procedures such as DCA, ELCA, or RA, which are reportedly useful for lesion preparation for first ISR, may be a useful strategy for the treatment of R-ISR. In the present case, we consider that the use of DCA to obtain a larger lumen led to good patency. Since the pathological examination did not show any predominantly calcified lesions, intravascular lithotripsy was not utilized in this case. However, the potential efficacy of intravascular lithotripsy in R-ISR treatment remains uncertain. Further research is warranted, especially in patients with a high burden of calcification, to determine its utility in this context.

In this case, the selection of antiplatelet agents was influenced by the prevailing standards during the study period, considering factors such as drug availability, and adherence to guidelines. Moreover, the current guidelines do not recommend routine follow-up CAG for asymptomatic patients based on the results of the Re-ACT trial published in 2017.[13] However, in this case, follow-up CAG was performed twice in 2006 and 2014, even though the patient was asymptomatic, in accordance with the governing guidelines at that time.

Conclusion

This case report described a patient with seven episodes of ISR, in whom DCA was successful in the management of R-ISR.

Lead author biography

Shota Naniwa graduated from Osaka City University in 2015. He completed his residency programme at the Japanese Red Cross Kobe Hospital and worked as a fellow in cardiology at the Kita-Harima Medical Center. Currently, he continues his fellowship at the Division of Cardiovascular Medicine, Department of Internal Medicine, Kobe University Graduate School of Medicine. His areas of interest are coronary intervention and structural heart disease.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

Consent: The authors confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

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Data availability

The data underlying this article are available in the article.

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