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## Case Report

## Coronary restenosis of in-stent protruding bump with rapid progression: Optical frequency domain imaging and angioscopic observation



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## ABSTRACT

In-stent restenosis (ISR) remains a tough problem after percutaneous coronary intervention (PCI) despite advances in technology of drug-eluting stents (DES). A 63-year-old man undergoing hemodialysis was diagnosed with non-ST elevation acute coronary syndrome (NSTEMI-ACS). An emergency coronary angiography (CAG) revealed severe stenosis in the middle left circumflex artery (LCx). After pre-dilatation with non-compliant balloon, primary PCI was successfully performed with DES implantation. Four months after, CAG was performed again and verified ISR of LCx under diagnosis of recurrent NSTEMI-ACS. Subsequently multimodality intravascular imaging assessment was performed for the ISR lesion. Optical frequency domain imaging showed the eccentric protruding mass with irregular surface with high-backscatter, whereas angioscopy revealed the in-stent bump with yellow color. The ISR lesion was successfully treated by drug-coated balloon angioplasty. However, he suffered recurrent NSTEMI-ACS five months later. CAG revealed de novo stenotic lesions not only in re-restenosis of LCx but also in proximal left anterior descending artery and ostium of right coronary artery. He was scheduled to undergo coronary artery bypass grafting for three-vessel disease. Multimodality assessment is useful to diagnose the recurrent restenosis lesion with calcified nodule.

<Learning objective: In-stent restenosis (ISR) is rarely recurrent even after drug-eluting stent (DES) implantation. In-stent protruding bump is observed in types of ISR morphology by intravascular imaging, and the finding suggests the possibility of recurrent ISR. Diagnosis of the morphology is sometimes difficult, but multimodality imaging assessment is useful to distinguish the ISR tissue.>

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## Introduction

Drug-eluting stents (DES) dramatically reduced in-stent restenosis (ISR) compared with bare-metal stents. Nevertheless, ISR after DES implantation still occurs with a certain probability and there are a few patients who are hard to treat because of recurrent ISR, distal emboli, incomplete dilatation, etc. Although drug-coated balloons (DCB) are effective in treating ISR, the problem of recurrence of ISR is not yet completely resolved. Intravascular imaging is widely used to assess the ISR characteristics after stent implantation, and provide useful information for

the strategy of revascularization. We report a case in which it was difficult to treat the recurrent ISR assessed by multi intravascular imaging after new generation DES implantation.

## Case report

The patient was a 63-year-old man, who had received hemodialysis for 6 years due to diabetic nephropathy. His left lower limb had been amputated due to critical limb ischemia. Four years and two months previously, percutaneous coronary artery intervention (PCI) was performed in the left main coronary artery and right coronary artery (RCA) due to stable angina pectoris. At this time, he was admitted to our hospital for recurrent episodes of chest pain appearing 5 days before. Although the electrocardiogram showed no significant ST-T change, his echocardiography

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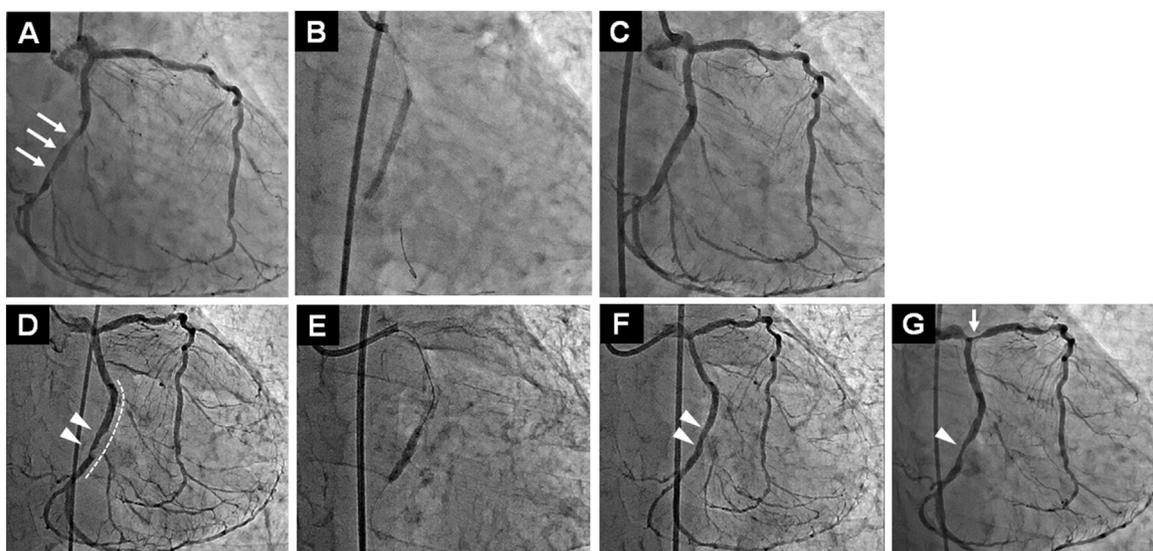


Fig. 1.

Coronary angiography revealed severe stenosis in the middle left circumflex artery (A, arrows). The stenotic lesion was successfully treated by deployment of drug-eluting stent (B, C). Coronary angiography showed recurrent in-stent restenosis (ISR) at the left circumflex artery (D, arrowheads). Balloon angioplasty was performed at the ISR lesion (E), final angiogram revealed residual mild stenosis at the lesion (F, arrowheads). Four months later, angiogram revealed recurrent ISR at the same site (G, arrowhead) and progression of stenosis at the left anterior descending ostium (G, arrow).

showed the new asynergy of the left ventricular lateral wall. Under the diagnosis of non-ST elevation acute coronary syndrome (NSTEMI-ACS), emergency coronary angiography (CAG) was performed and revealed severe stenosis in the middle left circumflex artery (LCx, Fig. 1A, arrows). Intravascular ultrasound revealed eccentric calcification at the LCx lesion. After pre-dilatation with a  $3.0 \times 15$  mm non-compliant balloon (DOBLE<sup>®</sup>, Fukuda Denshi Co., Tokyo, Japan), the stenotic lesion was successfully treated with deployment of a  $3.0 \times 38$  mm drug-eluting stent (Resolute Integrity<sup>®</sup>, Medtronic Co., Minneapolis, MN, USA, Fig. 1B, C). His clinical course was uneventful after the procedure, and he was discharged on the fourth hospital day.

Four months after, he was admitted to our hospital again diagnosed with NSTEMI-ACS. Angiography showed ISR of LCx, which was protruding into the lumen (Fig. 1D, arrowheads). Subsequently,

optical frequent domain imaging (OFDI, Terumo Corp., Tokyo, Japan) and angiography (Inter-Tec, Medicals. Corp., Osaka, Japan) were performed for the ISR lesion. OFDI showed the eccentric protruding structure with irregular surface with high-backscatter (Fig. 2A–C). Angiography revealed an irregular “protruding bump” and the surface color was yellow (grade 1, Fig. 2D, E). Because of incomplete dilatation of the lesion with a  $3.25 \times 15$  mm non-compliant balloon (Hiryu plus, Terumo, Tokyo, Japan) at 24 atm, additional dilatation with a  $3.5 \times 13$  mm scoring balloon (Lacrosse NSE ALPHA, GOOD-MAN Co., Ltd., Aichi, Japan) was performed with residual stenosis <25% (Fig. 1E, F, arrowheads). After balloon angioplasty, OFDI showed the bump with strong attenuation remained but the minimum lumen area improved from 2.0 to 5.2 mm<sup>2</sup> (Fig. 2F–H, distal to proximal). On angiography, the in-stent protruding bump remained, but a part of the bump was compressed by balloon dilation

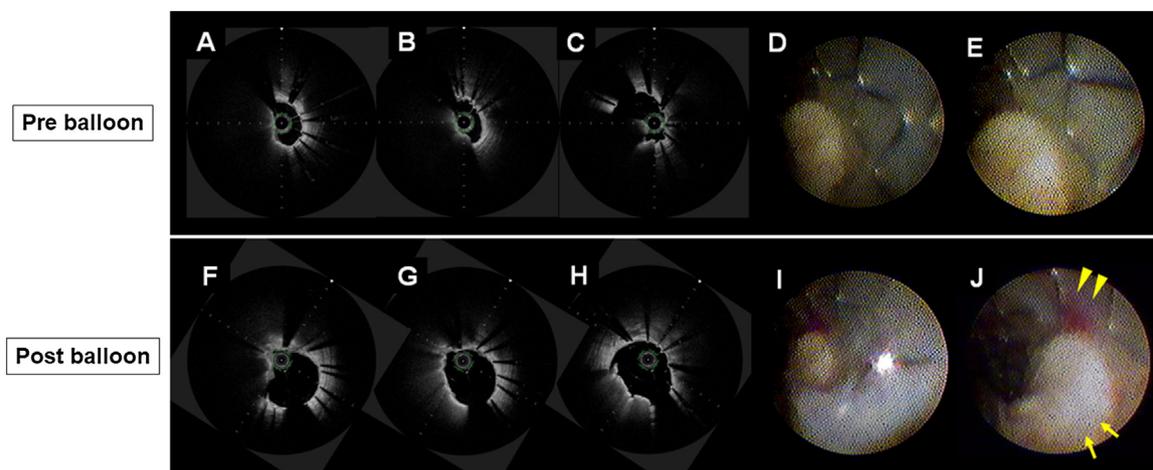


Fig. 2.

Optical frequency domain imaging (OFDI) and angiographic findings before and after angioplasty for in-stent restenosis (ISR). OFDI and angiographic findings before angioplasty for ISR (upper images). OFDI showed in-stent bump with high-backscattering irregular structure before angioplasty (A, B, and C). Angiography showed sharply protruding bump with yellow color surface (D, E). OFDI and angiographic findings after angioplasty for ISR (lower images). OFDI findings of in-stent bump compressed by balloon dilatation (F, G, and H). Angiography showed compressed bump with surface color change light yellow to white (J, arrows), and mural red thrombus adhesion (J, arrowheads).

(Fig. 2I, J, arrows). Furthermore, angiography revealed the surface color change of the bump (light yellow to white) and the appearance of mural thrombus adjacent to the bump (Fig. 2J, arrowhead). Finally, the restenosis lesion was treated with a 2.5 × 20 mm DCB (SeQuent™ Please; B. Braun, Melsungen, Germany). His clinical course was unremarkable after PCI, and he was discharged on the fourth hospital day.

Five months later, he was again admitted to our hospital due to NSTEMI-ACS. CAG revealed recurrent restenosis of LCx lesion (Fig. 1G, arrowhead). Furthermore, lesion progression was detected in the proximal part of the LAD (Fig. 1G, arrow) and the ostium of the RCA. He was scheduled for coronary artery bypass grafting for three-vessel disease.

## Discussion

This case is a hemodialysis patient with ISR due to a protruding bump which progressed rapidly in 4 months after the new-generation DES implantation. We assessed the morphology of the lesion before and after balloon dilatation using OFDI and angiography. Although DCB angioplasty was performed for the restenosis, ISR recurred 5 months after the procedure.

Intravascular imaging modalities are useful to understand the pathogenesis of ISR. In this case, the OFDI finding of ISR tissue showed as high-backscattering protruding mass with strong signal attenuation. ISR may consist of various components, including neointimal proliferation, neoatherosclerosis, and calcification. However, strong signal attenuation assessed by OFDI finding may represent calcified nodule (CN), red thrombus, or vulnerable plaque [1,2]. That is, one imaging modality may have limitations in assessment of the tissue characteristics. To resolve this issue, we performed multiple intravascular imaging for ISR and assessed tissue characteristics. First, angiography before balloon dilation revealed that the surface color of ISR tissue was light-yellow. In a previous study, Shibuya et al. undertook post-mortem ex vivo angiographic examination and reported that the surface of calcification was observed as light-yellow color [3]. This pathological report suggests that “in-stent protruding bump” in this case may be consistent with CN. Second, after balloon dilatation, angiography revealed surface color change of the bump and mural thrombus adjacent to the bump. Another histological report pointed out that CN is associated with old intraplaque hemorrhage and/or healed plaque rupture [4]. Therefore, these angiographic changes may be explained by the deformation and exposure of

content of the CN depending on the mechanical pressure of the balloon dilatation. We consider that combination assessment of OFDI with angiography was useful to understand the morphology of the “in-stent protruding bump”. In addition, retrospective assessment of intravascular ultrasound findings at first PCI may also be useful in understanding the pathogenesis of ISR after stent implantation. Intravascular ultrasound findings revealed that the lesion of “in-stent protruding bump” was composed of eccentric calcification before stent implantation. Progression of underlying calcified plaque may be another possible mechanism for restenosis of in-stent bump.

In dialysis patients, angioplasty for recurrent DES-ISR is often challenging. PCI strategies for CN are mentioned as rotational atherectomy, high-pressure and scoring balloon, etc. [5]. However, the best therapeutics for CN are unclear. Detection of the “in-stent protruding bump” by multimodality intravascular imaging suggests that careful follow up is needed for recurrence of ISR. Further investigation is needed to treat the “in-stent protruding bump”.

## Conclusions

OFDI and angiography are useful to verify the in-stent protruding bump, and the findings suggest paying attention to the risk of recurrent ISR.

## Disclosures

The authors declare that there is no conflict of interest.

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