CJC Open 5 (2023) 802–804

Case Report

Late Neointimal Regression 5 Years After Polymer-Free Biolimus A9-Coated Stent Implantation: A Case Report

Masaya Kusuda, MD, Takayuki Ishihara, MD, Osamu Iida, MD, PhD, Takuya Tsujimura, MD, Yosuke Hata, MD, Taku Toyoshima, MD, Naoko Higashino, MD, Sho Nakao, MD, and Toshiaki Mano, MD, PhD

Kansai Rosai Hospital Cardiovascular Center, Amagasaki, Japan

A polymer-free biolimus A9-coated stent (PF-BCS; BioFreedom, Biosensors Interventional Technologies, Singapore) can elute the drug even without a polymer by retaining the drug on the rough surface of the stent wall.[1] Here, we present a case of late neointimal regression 1-5 years after percutaneous coronary intervention (PCI). We performed PCI for severe stenosis of the proximal right coronary artery and implanted a PF-BCS. The neointimal thickness in the stent evaluated by optical coherence tomography was 0.30 ± 0.24 mm at 1 year after PCI but decreased to 0.17 ± 0.09 mm at 5 years after PCI, indicating late neointimal regression.

Case Report

A 75-year-old man with dyslipidemia and a history of smoking was referred to our hospital with chest pain on exertion. Effort angina pectoris was suspected, and coronary angiography (CAG) revealed severe stenosis of the obtuse marginal branch, the high lateral branch, and the proximal part of the right coronary artery (RCA; Fig. 1A). We initially performed PCI in the left coronary artery. We implanted 2 PF-BCSs (2.5 × 18 mm and 2.5 × 28 mm) in the stenoses of the obtuse marginal branch and the high lateral branch, respectively. One month later, we performed PCI on the proximal part of the RCA. A Hyperion 6-Fr JR4.0 guiding catheter (Asahi Intecc, Nagoya, Japan) was inserted into the RCA via the left radial artery. Subsequently, we successfully crossed the lesion with a SION blue 0.014-inch guidewire (Asahi Intecc) and observed it, using optical coherence tomography (OCT; Dragonfly OpStar, Abbott, Abbott Park, IL). We dilated the lesion in the proximal part of the RCA using an NSE Alpha 2.75-mm scoring balloon (2.75 × 9 mm; Nipro, Osaka, Japan). Subsequently, we implanted a BioFreedom PF-BCS (3.5 × 18 mm; Biosensors Interventional Technologies) in the stenotic lesion of the RCA. Finally, an NC TREK noncompliant balloon (4.0 × 12 mm; Abbott) was fully dilated to the stented site without under-expansion. The final angiographic results showed no evidence of other complications (Fig. 1B).

Follow-up CAG was performed 1 year after PCI, according to the protocol of our clinical study (Collaboration-1 study, a multicentre prospective observational study[2]). This procedure showed no new stenotic lesions or in-stent restenosis in the RCA (Fig. 1C). OCT revealed a relatively thick neointima proximal to the drug-coated stent (Fig. 2A; Video 1, view video online). However, the lumen area was sufficiently preserved, and follow-up observations were continued without additional PCI. Dual-antiplatelet therapy with aspirin 100 mg/d and prasugrel 3.75 mg/d was continued until 1-year follow-up, after which only aspirin was prescribed. CAG was performed 5 years after stent implantation, because the patient had chest symptoms, and myocardial scintigraphy indicated possible myocardial ischemia. However, the CAG showed no new stenotic lesions or in-stent restenosis (Fig. 1D). OCT showed a thinner stent neointima than that at 1 year after treatment (Fig. 2B; Video 2, view video online). Using the intravascular imaging analysis system "QIvus," we analyzed the stent at 0.2-mm intervals and calculated the neointimal thickness for each stent strut. Given that the 2-mm segment from the proximal end of the stent cannot be evaluated adequately, due to the influence of neointimal coverage at 1 year and the presence of the guiding catheter at 5 years after PCI, we have excluded this segment from the analysis in both phases. The mean neointimal thickness decreased from 0.30 ± 0.24 mm (after 1 year) to 0.17 ± 0.09 mm (after 5 years). In addition, we evaluated the neointimal thickness of the PF-BCSs that were implanted in the left coronary artery. The mean neointimal thicknesses of the PF-BCS in the obtuse marginal branch at 1 year and 5 years were 0.12 ± 0.06 mm and 0.11 ± 0.06 mm,

Received for publication May 8, 2023. Accepted July 25, 2023.

Corresponding author: Dr Takayuki Ishihara, Kansai Rosai Hospital Cardiovascular Center, 3-1-69 Amagasaki, Hyogo 660-8511, Japan. Tel.: +81-6-6416-1221; fax: +81-6-6419-1870.

E-mail: t.ishihara31@gmail.com

See page 804 for disclosure information.

https://doi.org/10.1016/j.cjco.2023.07.011

Novel Teaching Points

- We experienced a case of late neointimal regression after PF-BCS implantation.
- The polymer-free characteristics of PF-BCS may contribute to late neointimal regression, which has potential to reduce adverse events during the chronic period.

respectively, and those in the high lateral branch were 0.29 ± 0.08 mm and 0.26 ± 0.05 mm, respectively.

Discussion

We performed PCI for severe stenosis of the proximal RCA and implanted a PF-BCS. The neointimal thickness in the stent evaluated by OCT was 0.30 ± 0.24 mm at 1 year after PCI, but it decreased to 0.17 ± 0.09 mm at 5 years after PCI, indicating late neointimal regression.

Kimura et al. previously reported that plaque regression occurs, and the minimal luminal diameter increases during the chronic phase from 6 months to 3 years after bare-metal stent (BMS) implantation.[3] The pathology of the neointima showed that proliferating smooth muscle cells were of predominantly the synthetic type, and an abundance of extracellular matrix substance was present, composed chiefly of proteoglycans, within 6 months after BMS implantation.[4] In contrast, contractile smooth muscle cells are dominant, and the extracellular matrix is composed chiefly of collagen from 6 months to 3 years after BMS implantation.[4] These temporal changes in the pathologic pattern are thought to tighten the neointima, reduce its thickness, and increase the luminal diameter.

The cumulative target lesion revascularization rate increased progressively 1 year after durable-polymer drug-eluting stent (DES) implantation.[5] Therefore, unlike with a BMS, the luminal diameter may gradually decrease, even in the late phase. This phenomenon may be caused by the difference in vessel response after stenting with a BMS vs a durable-polymer DES. In contrast, late neointimal regression was reported in a biodegradable polymer DES with Combo anti-CD34 antibodies (OrbusNeich Medical, Fort Lauderdale, FL).[6] Based on previous data, residual polymers may prevent plaque regression in the chronic phase.

A PF-BCS is a polymer-free stent that releases drugs within 30 days and becomes a BMS after 1 month.[1] In the current case, we used a PF-BCS and observed novel late neointimal regression, which has not been reported previously with a PF-BCS. The polymer-free characteristics of the PF-BCS may contribute to the occurrence of late neointimal regression, reducing adverse events during the chronic period after stent implantation.

This case report has several limitations. First, the location of the OCT images in Figure 2 (the panels a-d and a'-d') was based on the distance from the distal stent edge. The 2-mm segment from the proximal end is excluded from evaluation and analysis in both phases, owing to the influence of neointimal coverage at 1 year and the presence of the guiding catheter at 5 years after PCI. The lack of evaluation could influence the calculation of the neointimal thickness. However, the neointimal regression was obvious judging from the OCT, as shown in Videos 1 and 2 (view videos online). Second, the medications and lifestyle habits could influence the neointimal proliferation. Regarding the medication, at the time of 1-year follow-up CAG, the patient was on dual-antiplatelet therapy consisting of aspirin and prasugrel. However, after that therapy, we switched to single-antiplatelet therapy with only aspirin. Rosuvastatin 2.5 mg/d was continuously prescribed from the baseline to 5 years after PCI and the low-density lipoprotein cholesterol level remained generally unchanged, staying in the range 82-94 mg/dL over the 5 years after PCI. The medication regimen included antiplatelet agents, proton pump inhibitors, and statins, and no other medications were administered from before PCI to 5 years post-PCI. In terms of lifestyle habits, the patient had already quit smoking before the PCI, and no significant changes were made in lifestyle habits. Third, this result and hypothesis are difficult to generalize, due to their being based on a single case report. We need to conduct further analysis and additional research in a large-scale study to validate this issue.

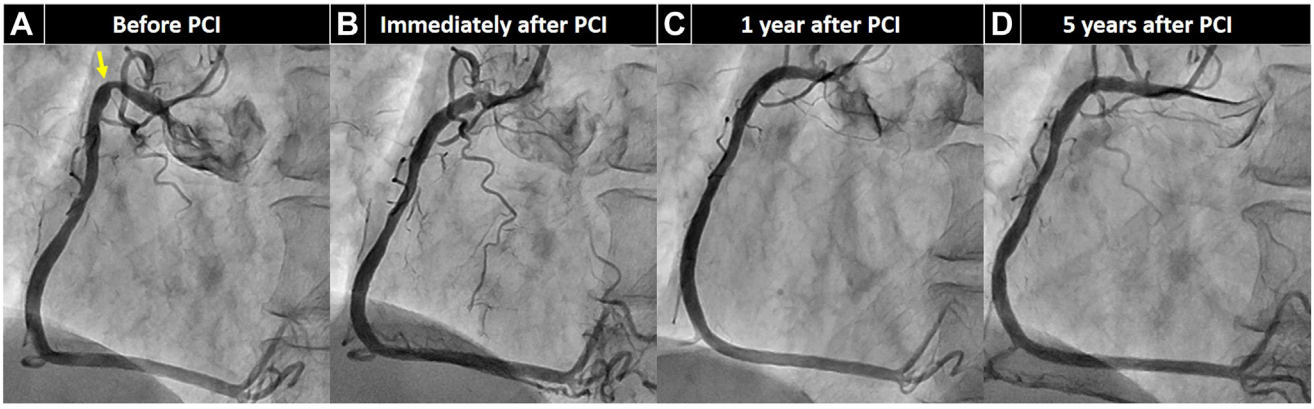

Figure 1. Coronary angiography (CAG). (**A**) Initial CAG. Severe stenosis was detected in the proximal right coronary artery (**yellow arrow**). (**B**) Final CAG. A polymer-free biolimus A9-coated stent (PF-BCS, 3.5 × 18 mm) was implanted, which resulted in excellent angiographic results. (**C**) CAG 1 year after PF-BCS implantation. CAG showed no in-stent restenosis. (**D**) CAG 5 years after PF-BCS implantation. CAG demonstrated that the PF-BCS implantation site was still patent. PCI, percutaneous coronary intervention.

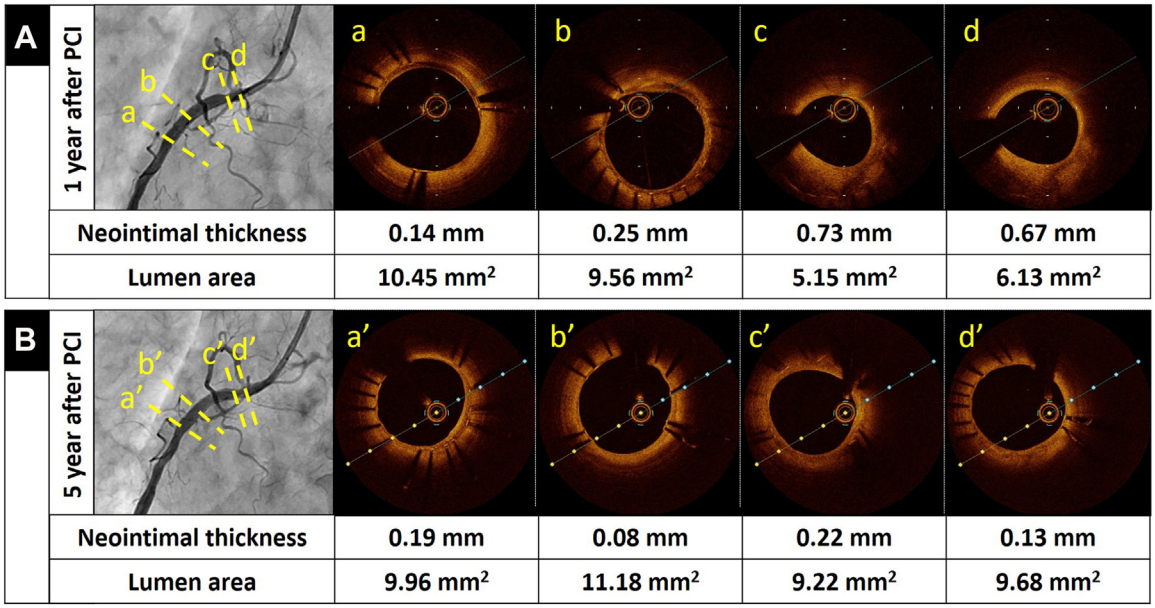

Figure 2. Optical coherence tomography (OCT) images after implantation of a polymer-free biolimus A9-coated stent (PF-BCS). (**A**) OCT 1 year after percutaneous coronary intervention (PCI). (**B**) OCT 5 years after PCI. (**a**, **a'**) Distal stent edge. (**b, b'**) 6.4 mm proximal from the distal stent edge. (**c, c'**) 14.4 mm proximal from distal stent edge. (**d, d'**) 16 mm proximal from distal stent edge, which are the proximal ends within the analyzed range. The thickness of the neointima decreased from 1 to 5 years after PCI, especially at the proximal portion of the stent (from **c** and **d** to **c'** and **d'**). Neointima thickness: (**a**) 0.14 mm; (**b**) 0.25 mm; (**c**) 0.73 mm; (**d**) 0.67 mm. (**a'**) 0.19 mm; (**b'**) 0.08 mm; (**c'**) 0.22 mm; (**d'**) 0.13 mm. Lumen area: (**a**) 10.45 mm^2; (**b**) 9.56 mm^2; (**c**) 5.15 mm^2; (**d**) 6.13 mm^2. (**a'**) 9.96 mm^2; (**b'**) 11.18 mm^2; (**c'**) 9.22 mm^2; (**d'**) 9.68 mm^2. Diameters of the lumen (average, minimum, and maximum): (**a**) 3.65 mm, 3.57 mm, 3.78 mm; (**b**) 3.49 mm, 3.39 mm, 3.60 mm; (**c**) 2.56 mm, 2.39 mm, 2.72 mm; (**d**) 2.79 mm, 2.56 mm, 2.98 mm; (**a'**) 3.56 mm, 3.45 mm, 3.70 mm; (**b'**) 3.77 mm, 3.60 mm, 3.91 mm; (**c'**) 3.43 mm, 3.32 mm, 3.54 mm; (**d'**) 3.51 mm, 3.32 mm, 3.76 mm.

Conclusion

Here, we described a case of late neointimal regression at 5 years after PF-BCS implantation.

Ethics Statement

This case report has adhered to the relevant ethical guidelines.

Patient Consent

The authors confirm that patient consent is not applicable to this article. This is a retrospective case report using de-identified data; therefore, the IRB did not require consent from the patient.

Funding Sources

The authors have no funding sources to declare.

Disclosures

T.M. received a research grant from Abbott Vascular Japan. The other authors have no conflicts of interest to disclose.

References

1. Tada N, Virmani R, Grant G, et al. Polymer-free biolimus A9-coated stent demonstrates more sustained intimal inhibition, improved healing, and reduced inflammation compared with a polymer-coated sirolimus-eluting cypher stent in a porcine model. Circ Cardiovasc Interv 2010;3:174-83.
2. Ishihara T, Mizote I, Nakamura D, et al. Comparison of 1-month and 12-month vessel responses between the polymer-free biolimus A9-coated stent and the durable polymer everolimus-eluting stent. Circ J 2022;86:1397-408.
3. Kimura T, Abe K, Shizuta S, et al. Long-term clinical and angiographic follow-up after coronary stent placement in native coronary arteries. Circulation 2002;105:2986-91.
4. Nobuyoshi M, Kimura T, Ohishi H, et al. Restenosis after percutaneous transluminal coronary angioplasty: pathologic observations in 20 patients. J Am Coll Cardiol 1991;17:433-9.
5. Ueda Y. Intracoronary imaging of in-stent atherosclerosis by coronary angioscopy and optical coherence tomography. Circ J 2014;78:61-2.
6. Lee SW, Lam SC, Tam FC, et al. Evaluation of early healing profile and neointimal transformation over 24 months using longitudinal sequential optical coherence tomography assessments and 3-year clinical results of the new dual-therapy endothelial progenitor cell capturing sirolimus-eluting Combo stent. Circ Cardiovasc Interv 2016;9:e003469.

Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2023.07.011.