

[ CASE REPORT ]

## Effectiveness of Bare Metal Stent Implantation for the Treatment of Coronary Artery Aneurysm: A Multimodality Imaging Evaluation

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### Abstract:

Coronary artery aneurysm (CAA) after sirolimus-eluting stent (SES) implantation is one of the most troublesome problems associated with first-generation drug-eluting stents. However, the natural course and standard therapy of CAA has been unknown. A 49-year-old man underwent SES implantation for the left anterior descending artery. Follow-up coronary angiography (CAG) revealed CAA in the SES. We performed bare metal stent (BMS) implantation for treatment of CAA. Ten months after the BMS implantation, the size of the CAA had diminished, and a very thin layer of endothelium on the BMS was observed by optical coherence tomography. CAG assessment revealed that the blood stream of the CAA had been obstructed. We herein report a case of CAA after SES implantation with eight years of follow-up and the findings of a multimodality imaging evaluation.

**Key words:** coronary artery aneurysm, peri-stent contrast staining, sirolimus-eluting stent, intravascular ultrasound, optical coherence tomography, non-obstructive coronary angiography

(Intern Med 56: 3305-3309, 2017)

(DOI: 10.2169/internalmedicine.8532-16)

### Introduction

Coronary artery aneurysm (CAA) is defined as coronary dilatation exceeding the diameter of the normal adjacent segments or the diameter of the patient's largest coronary vessel by 1.5-fold. The incidence of events associated with CAA, such as thrombosis, distal embolization, rupture and vasospasm, varies from 1.5% to 5% (1). Aneurysm formation after sirolimus-eluting stent (SES) implantation is one of the most troublesome problems associated with first-generation drug-eluting stents (DESs). However, the natural course and standard therapy of CAA has been unknown.

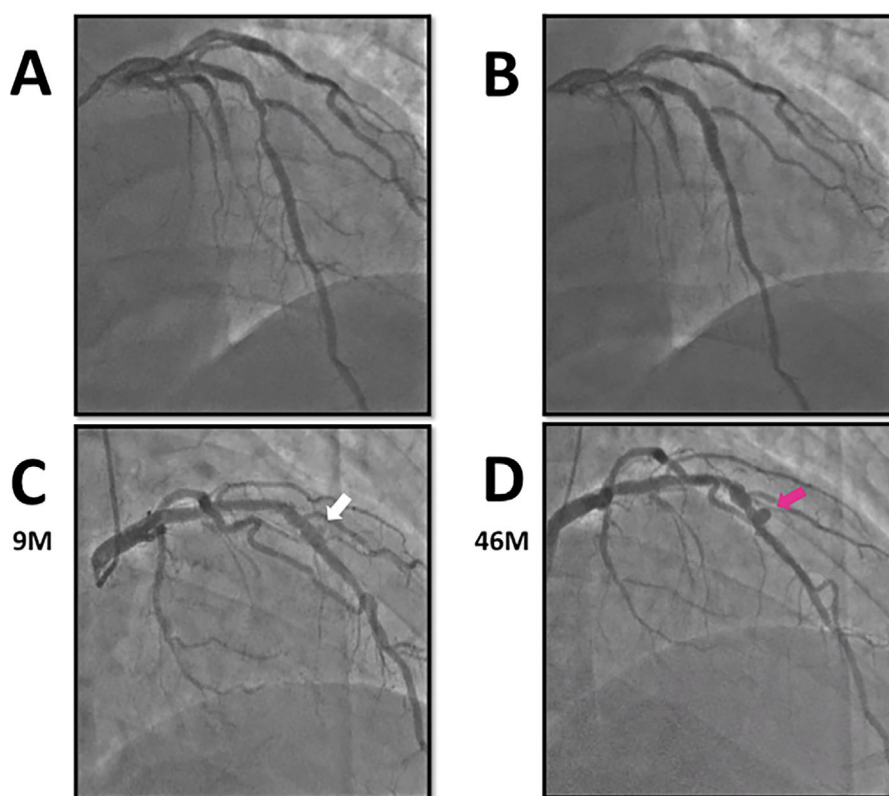
### Case Report

In January 2007, a 49-year-old man was admitted with effort angina. His coronary risk factors were hypertension, dyslipidemia, obesity and smoking. He had undergone bare metal stent (BMS) implantation (BX VELOCITY: 3.5 mm

in diameter, 28 mm in length, Cordis/Johnson and Johnson, Warren, USA) for proximal left anterior descending artery (LAD) 2 years previously. Coronary angiography (CAG) revealed severe stenosis of the mid LAD (Fig. 1A). Intravascular ultrasound (IVUS) revealed severe negative remodeling at the culprit lesion of the mid LAD. He underwent SES implantation (Cypher: 3.5 mm in diameter, 23 mm in length, Cordis/Johnson and Johnson, Warren, USA) for the mid LAD (Fig. 1B). IVUS after SES implantation revealed well-expanded stent struts without incomplete stent apposition.

Follow-up CAG was performed in October 2007 (9 months after SES implantation). Peri-stent contrast staining (PSS) was observed in the SES (Fig. 1C). Control of hypertension was poor, so we reduced his blood pressure more strictly.

When we performed CAG at 46 months after SES implantation, contrast staining outside the stent struts was more marked and met the classic definition of CAA (Fig. 1D). IVUS and optical coherence tomography (OCT) revealed incomplete stent apposition (Fig. 2A, C) and stent fracture at



**Figure 1.** A and B: CAG showed severe stenosis of the mid LAD. An SES was implanted for the mid LAD. C: PSS was observed in the distal portion of the SES at 9M after stenting (white arrow). D: CAA formation was observed in the distal portion of the SES at 46M after stenting (pink arrow). CAG: coronary angiography, SES: sirolimus-eluting stent, LAD: left anterior descending artery, PSS: peri-stent contrast staining, CAA: coronary artery aneurysm, M: month

the CAA (Fig. 2B, D). However, in the BMS, an OCT examination revealed complete stent apposition (Fig. 2E).

Non-obstructive coronary angiography (CAS) revealed the fractured edge of the SES at the CAA (Fig. 3A, B). The fracture had occurred in a joint of the SES. The stent strut was fully visible and not covered by neointima (Grade 0 neointimal coverage). In contrast, complete neointimal coverage was observed in the BMS site and proximal edge of the SES site (Grade 2 neointimal coverage) (Fig. 3A, B and C). No thrombus was detected in the SES.

When we performed CAG at 81 months after SES implantation, the CAA had expanded to more than twice the size of the reference vessel diameter (Fig. 4A). The patient therefore underwent BMS implantation (3.5 mm in diameter, 26 mm in length) to cover the CAA. Fortunately, the flow of the large diagonal branch was maintained after stenting.

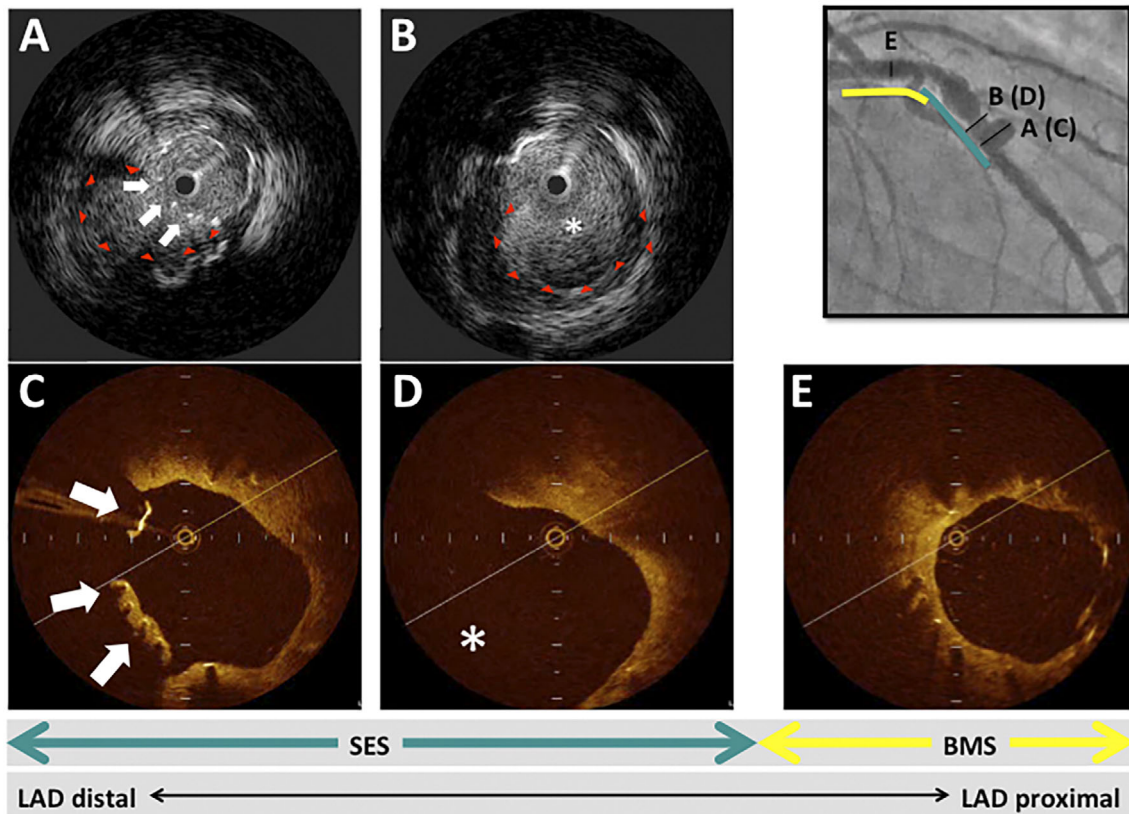
Follow-up CAG was performed at 91 months after SES implantation (10 months after the use of BMS to treat CAA). Regression of the aneurysm was observed (Fig. 4B). OCT revealed vessel wall dilatation and malapposed stent struts (Fig. 5A, C). However, the size of the CAA had diminished, and a very thin layer of endothelium was visible on the struts (Fig. 5B, C). He continued taking 100 mg/day of aspirin and 75 mg/day of clopidogrel. He was free from cardiac events throughout the follow-up period.

## Discussion

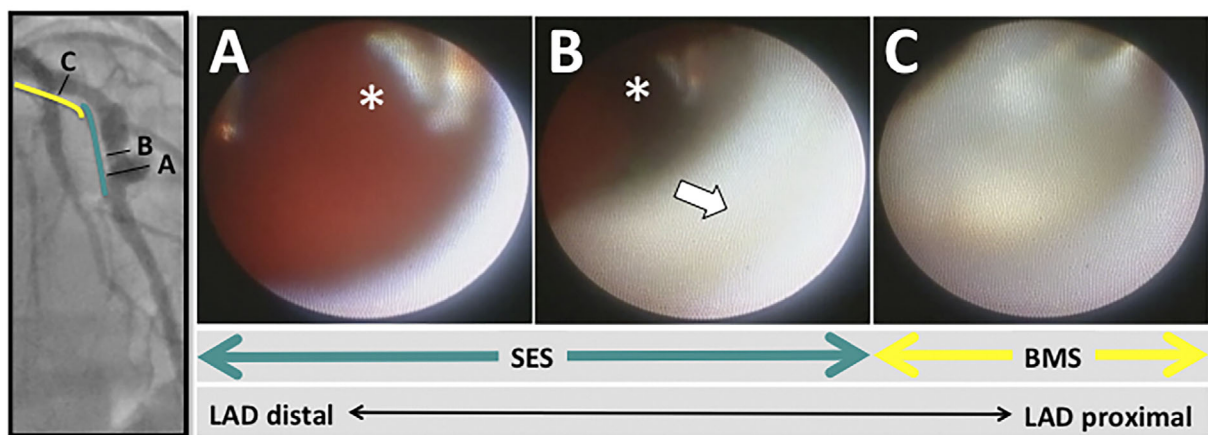
CAA formation after DES implantation is a rare phenomenon, occurring in roughly 1% of cases (2-4). Several mechanisms of CAA formation have been proposed, including deep artery wall injury during the interventional procedure (5), hypersensitivity reactions (6) caused by any of the three components of DESs [stent platform (metal), drug carrier vehicle (polymer) and antirestenotic drug] and infectious processes.

Iatrogenic dissections and deep artery wall injury caused by oversize balloons or stents, high-pressure balloon inflations, atherectomy and laser angioplasty have all been associated with CAAs after coronary intervention. In the present case, IVUS before SES implantation revealed severe negative remodeling at the culprit lesion of the mid LAD. Therefore, excessive stent dilatation might have caused the initial aneurysm.

Hypersensitivity to metals such as molybdenum, nickel and chromium has been reported in 10% of patients undergoing stainless-steel stenting (7). Allergic reactions to such metals is associated with an increased frequency of in-stent restenosis. In the present case, the patient underwent two types of stent implantation for LAD: BX VELOCITY



**Figure 2.** IVUS (A, B) and OCT (C, D, E) assessment at 46M after stenting. A, B, C and D (SES implantation site): Incomplete stent apposition (white arrow) was observed at the aneurysm site (red arrowhead). In addition, stent fracture (\*) was observed in the CAA. E (BMS implantation site): OCT revealed complete stent apposition. IVUS: intravascular ultrasound, OCT: optical coherence tomography, SES: sirolimus-eluting stent, CAA: coronary artery aneurysm, BMS: bare metal stent, M: month



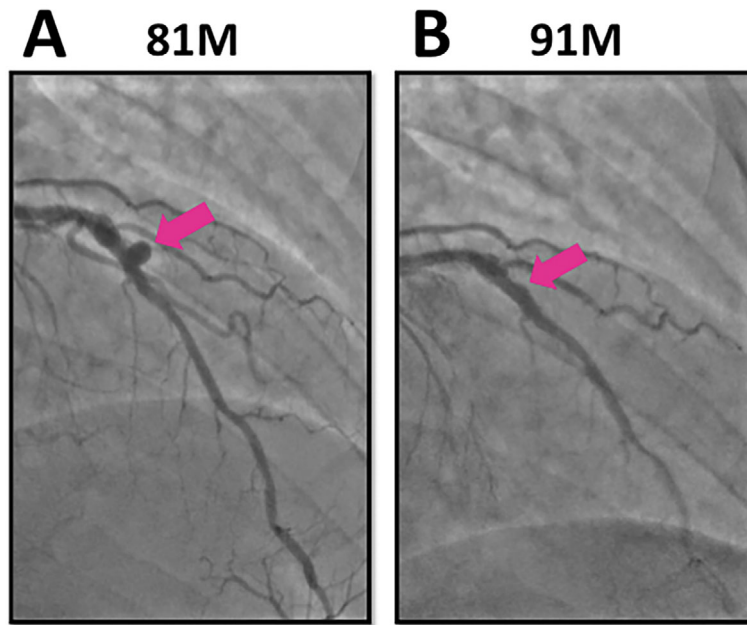
**Figure 3.** CAS examination 58M after SES implantation (70M after initial BMS implantation). A and B (SES site): Complete (white arrow) and incomplete neointimal coverage were both observed. CAA was observed in the area of incomplete neointimal coverage. A fractured edge of SES (\*) was observed in the CAA. C (BMS site): Complete neointimal coverage was observed (Grade 2 neointimal coverage). CAS: non-obstructive coronary angiography, SES: sirolimus-eluting stent, BMS: bare metal stent, CAA: coronary artery aneurysm, M: month

(stainless-steel BMS) and Cypher (sirolimus-eluting BX VELOCITY stent). CAS revealed complete neointimal coverage of the BMS (Grade 2 neointimal coverage) (8). Therefore,

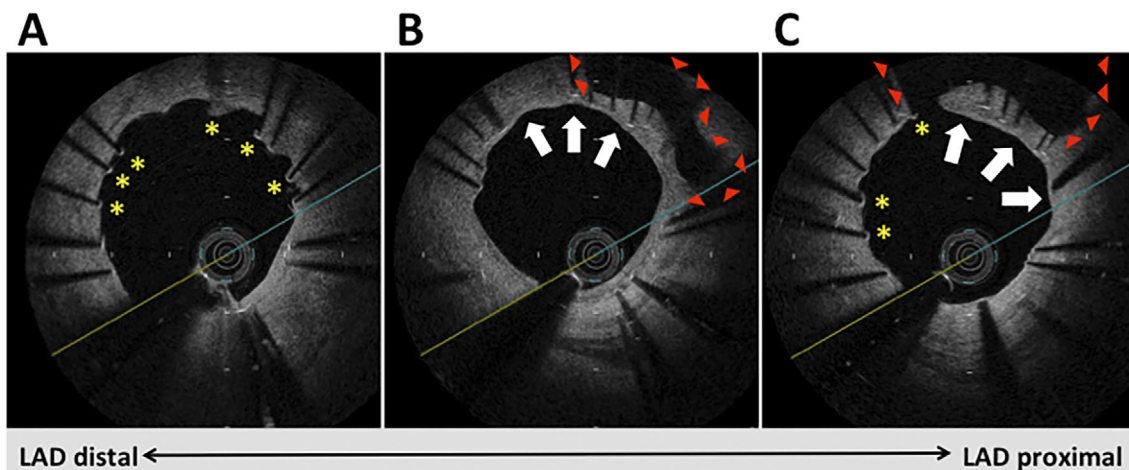
hypersensitivity to the metal was unlikely to have been caused aneurysmal formation in the present patient.

Poly-n-butyl methacrylate and polyethylene-vinyl acetate





**Figure 4.** A: At 81M after stenting, the CAA expanded, and the size of the CAA was more than twice the reference vessel diameter. The patient therefore underwent BMS implantation to cover the CAA. B: At 10M after BMS implantation, regression of the aneurysm was observed. CAA: coronary artery aneurysm, BMS: bare metal stent, M: month



**Figure 5.** OCT at 91M after stenting (10M after the use of BMS to treat CAA). OCT revealed vessel wall dilatation and malapposed stent struts (\*). However, the size of the CAA (red arrowhead) had diminished, and a very thin layer of endothelium (white arrow) was visible on the struts. OCT: optical coherence tomography, BMS: bare metal stent, CAA: coronary artery aneurysm, M: month

components, which are used as an antigen-delivery matrix in SESs, have been shown to induce hypersensitivity reactions (9). In the present case, reactive inflammation to the polymer of the SES was thought to be the cause of the late-phase proximal aneurysm formation.

DESs, which locally elute antiproliferative drugs, can cause CAAs due to delayed re-endothelialization, inflammatory changes of the intima and hypersensitivity reactions. Pharmacokinetic studies performed in dogs and rabbits have shown that sirolimus delivered via a nonerodable polymer matrix is undetectable in the arterial wall by 60 days (9, 10). A case report on the pathology of SES-treated

lesions showed that endothelial coverage was >80% complete after 16 months (11). Serial angiographic findings up to two years after stent implantation revealed that neointimal coverage was completed by three to six months in BMSs; however, healing after SES implantation took well over a year (12). In the present case, CAS at 58 months after SES implantation revealed both complete and incomplete neointimal coverage. CAA was observed in the area of incomplete neointimal coverage. Delayed healing of the endothelium due to the effects of sirolimus may have resulted in CAA formation.

Stent fracture was also observed along with aneurysm in

the present case. Imai et al. reported that stent fracture was observed significantly more frequently in lesions with PSS than in those without PSS (13). When PSS emerged for the first time in the present patient (9 months after stenting), IVUS showed no evidence of any fracture. This stent fracture was formed by hinge motion in part of the PSS site.

The incidence of events associated with CAA, such as thrombosis, distal embolization, rupture and vasospasm, ranges from 1.5% to 5% (1). The indications for treatment (i.e., medical, interventional or surgical treatment) and the best modality have yet to be defined. Medical therapy, such as antiplatelet therapy, anticoagulant therapy and antihypertension agent, is indicated for most patients. Interventional or surgical treatment has been recommended for patients who are symptomatic or develop complications. Interventional treatment consists of polytetrafluoroethylene (PTFE)-covered stent implantation, coil embolization and BMS implantation. Regarding the angiographic and clinical outcomes, a previous investigation using PTFE-covered stents in various clinical settings reported that subacute stent thrombosis occurred in 5.7% of patients (14). BMSs have better flexibility than PTFE-covered stents, making implantation in tortuous vessels easier and permitting access to side branches when a bifurcated lesion is involved (15). Ohtsuka et al. reported a case in which the size of the CAA diminished after stenting of the stenosis just proximal to the aneurysmal site, suggesting two possible mechanisms of CAA reduction: attenuation of hydrodynamic wall stress on the aneurysm, or improvement of the degradation of the extracellular matrix structure through the regulation of MMPs (16). In the present case, OCT revealed good endothelialization of the initial BMS. We therefore implanted another BMS in order to attenuate the blood flow to the CAA. Ten months after treatment of the CAA, its blood flow was found to be obstructed. In addition, OCT revealed a very thin layer of endothelium.

The present patient continued to receive dual antiplatelet and antihypertensive therapy. However, the size of the CAA was more than twice the reference vessel diameter. To avoid occlusion of a large diagonal branch, we performed BMS implantation.

### Conclusion

We herein reported a case of CAA after SES implantation with eight years of follow-up. Vascular injury and the effects of sirolimus are thought to be the cause of CAA in the early phase, while reactive inflammation to the polymer of the SES may cause CAA in the late phase. BMS implantation to treat CAA was performed, and the size of the CAA diminished.

**The authors state that they have no Conflict of Interest (COI).**

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