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Covered-Stent Treatment of Coronary Aneurysm after Drug-Eluting Stent Placement

Case Report and Literature Review

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Most commonly, coronary artery aneurysms are secondary to atherosclerosis, but cases have been reported in patients who have vasculitis or tissue disorders, and in patients who have undergone interventional procedures. However, over the past few years, an increasing number of cases of coronary artery aneurysms after drug-eluting stent implantation have been reported. The exact mechanism is unknown. Experimental animal studies have shown that both the active drug and the polymer coating, under certain circumstances, might cause progressive luminal dilation, positive vascular remodeling, and aneurysmal formation. Complications like rupture, thrombosis, embolization, myocardial infarction, and even sudden death have been reported. Treatment options vary from aggressive surgical ligation of the aneurysm, in union with distal bypass surgery, to percutaneous implantation of a covered stent or conservative medical management with continued antiplatelet therapy. Currently, there is no consensus on an ideal approach to treating coronary artery aneurysm after drug-eluting stent implantation. Polytetrafluoroethylene-covered stents, easy and rapid to deploy, have emerged as a newer option. We report a case of coronary artery aneurysm at the site of a previous drug-eluting stent. The lesion was successfully treated with a polytetrafluoroethylene-covered stent. (*Tex Heart Inst J* 2010;37(4):449-54)

Key words: Blood vessel prosthesis; coronary aneurysm/etiology/therapy; coronary disease/therapy; covered stents; dilatation, pathologic; drug delivery systems/adverse effects; drug-eluting stents/adverse effects; polytetrafluoroethylene; postoperative complications; sirolimus/administration & dosage; stents/adverse effects

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Aneurysmal dilation of the coronary arteries was first described by Bougon in 1812.¹ Most commonly, coronary artery aneurysms are secondary to atherosclerosis,² but cases have been reported in patients who have vasculitis (Kawasaki syndrome,³ for example) or tissue disorders (Ehlers-Danlos⁴ or Marfan syndrome,⁵ for example), and in patients who have undergone interventional procedures.^{6,7} Over the past few years, an increasing number of case reports have described a growing incidence of coronary artery aneurysms after drug-eluting stent (DES) implantation.⁸⁻¹¹ Since 2003, when the U.S. Food and Drug Administration approved the 1st such stent, DESs have unequivocally demonstrated their superiority to bare-metal stents in regard to in-stent restenosis.⁹⁻¹² Nevertheless, safety concerns brought up from time to time—especially regarding the increased risk of late stent thrombosis¹³—have raised questions about the long-term safety of DES implantations.

The exact mechanism of coronary artery aneurysmal formation after DES placement is unknown. Complications such as rupture,¹⁴ thrombosis,¹⁵ distal embolization,¹⁶ myocardial infarction,¹⁷ and even sudden death¹⁸ have been reported. Here we report a case of coronary artery aneurysm at the site of DES implantation, which we successfully treated with a polytetrafluoroethylene (PTFE)-covered stent. In addition, we present a review of the literature on the use of PTFE-covered stents in the repair of coronary artery aneurysms that have formed at the site of DES implantation.

Case Report

In May 2006, a 47-year-old man with a history of hypertension, dyslipidemia, and smoking—and a family history positive for coronary artery disease—was referred to our institution for emergent cardiac catheterization due to a diagnosis of ST-elevation myocardial infarction. Cardiac catheterization revealed 90% stenosis of the posterior descending coronary artery (PDCA) (Fig. 1A). The lesion was treated success-

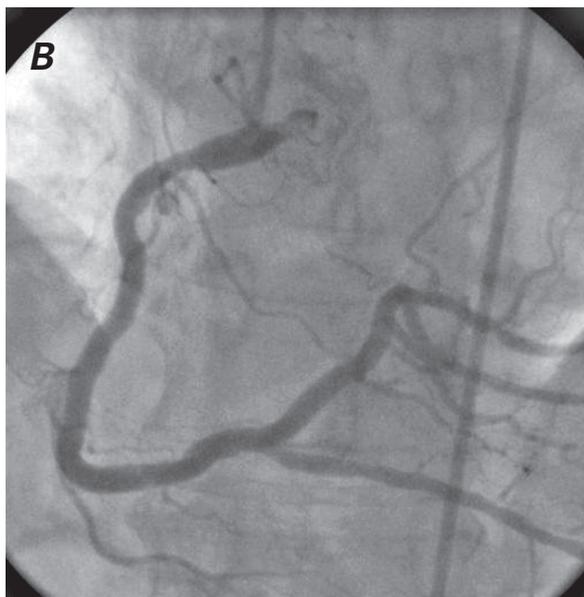
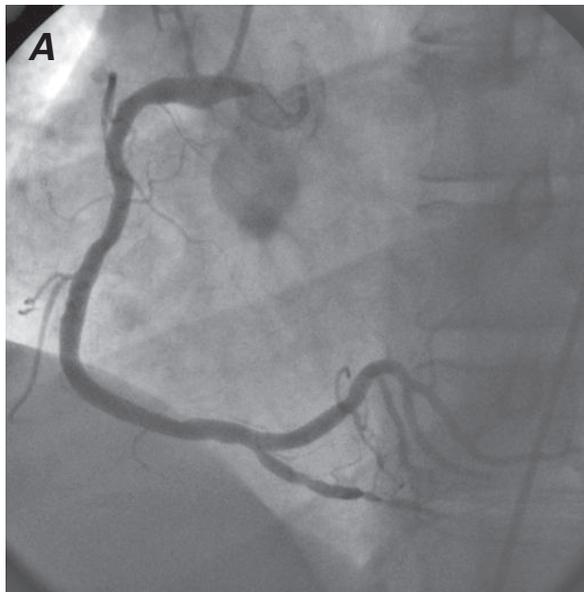


Fig. 1 Coronary angiograms (both left anterior oblique view) show **A)** posterior descending coronary artery stenosis and **B)** resolution of posterior descending coronary artery stenosis after the implantation of a drug-eluting stent.

fully with a sirolimus-eluting stent (Fig. 1B). After 1 year, the patient presented again at the hospital with exertional chest tightness of 1 month's duration, which had gotten worse over that time. An electrocardiogram showed sinus rhythm with no ST-T changes and with Q waves in leads III and aVF. Cardiac catheterization revealed 80% stenosis in the proximal right coronary artery (RCA) and a large PDCA aneurysm at the previous stent site, with 70% to 80% stenosis distal to the stent (Fig. 2A). In consideration of the aneurysm's size, we decided to repair it with a covered stent.

Eptifibatide was given during the procedure. An 8F JR4 guiding catheter was used. A 0.014-in Hi-Torque

Balance Middle Weight guidewire (Abbott Vascular, part of Abbott Laboratories; Abbott Park, Ill) was advanced across the lesions in the RCA and the PDCA. A 2.5 × 15-mm VOYAGER™ balloon (Abbott Vascular) was used to dilate the PDCA lesion at 6 atm. A 3 × 19-mm PTFE-covered stent, the JOSTENT® GraftMaster (Abbott Vascular), was deployed at 12 atm across the mid-PDCA lesion. The post-stent angiogram revealed a well-deployed stent in the PDCA with no residual stenosis, no residual aneurysm, and good distal flow (Fig. 2B). A 4 × 15-mm VISION™ stent (Abbott Vascular) was deployed at 14 atm across the proximal RCA

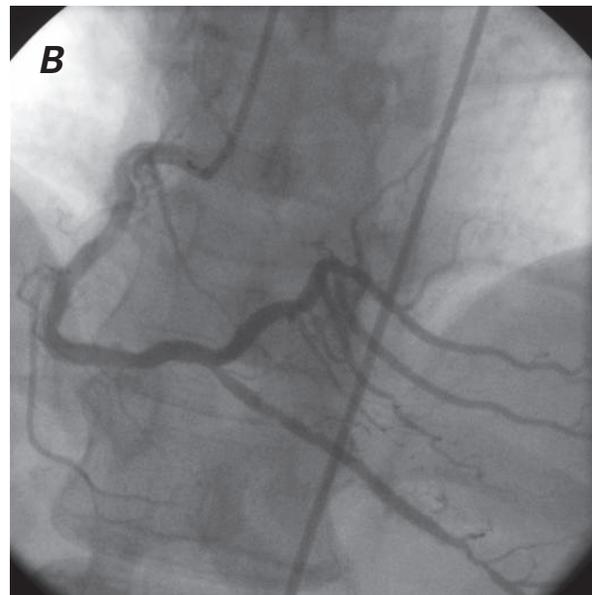
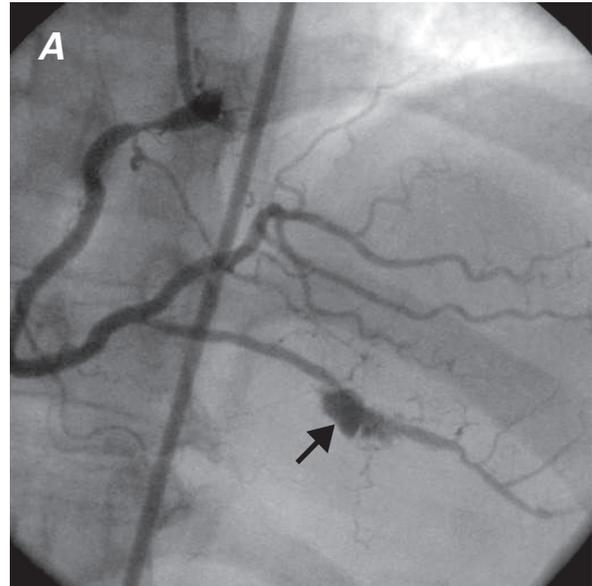


Fig. 2 Coronary angiography **A)** in right anterior oblique view shows proximal right coronary artery stenosis and aneurysmal formation after 1 year, at the site of the drug-eluting stent (arrow); and **B)** in anteroposterior view shows resolution of the coronary artery aneurysm after implantation of a covered stent.

lesion. The postoperative period was uneventful, and the patient was discharged from the hospital on aspirin, clopidogrel, metoprolol, atorvastatin, and enalapril. After 2 years of follow-up, the patient underwent an exercise Cardiolute® stress test (Lantheus Medical Imaging, Inc.; N. Billerica, Mass), which revealed an ejection fraction of greater than 0.70 and no evidence of reversible ischemia. The patient has been regularly monitored in our cardiology clinic and has been doing well.

Discussion

Coronary artery aneurysms have been defined as localized coronary dilations with diameters at least 1.5 times the diameters of adjacent normal coronary segments. Coronary artery aneurysms are relatively uncommon and are usually identified incidentally during angiography. The incidence ranges widely, from 0.3% to 4.5%.^{3,19} A close review of the available literature makes it apparent that coronary artery aneurysms, increasingly, are being found at DES implantation sites.^{8,11}

In our patient, a sirolimus-eluting stent had been placed. Sirolimus-eluting stents are balloon-expandable, intracoronary, 316L stainless-steel stents that are composed of iron, nickel, chromium, and molybdenum, coated with polymethacrylates and polyolefin copolymers. These polymers elute sirolimus gradually at the local site, causing a sustained suppression of vascular smooth muscle and neointimal proliferation. Sirolimus—the immunosuppressive ingredient—elutes completely over a period of a few months, whereas the other stent components persist in the vascular wall.

The exact mechanism of coronary aneurysmal formation is unknown, but several hypotheses have been proposed. In biopsied aneurysmal segments, hypersensitivity vasculitis—characterized by an extensive inflammatory infiltration of lymphocytes, plasma cells, macrophages, and eosinophils—has been found to involve the intima, media, and adventitia.¹³ Although the stainless-steel stents and the non-erodible polymers used for drug delivery are considered to be highly biocompatible, these have been known to interact adversely with the anti-proliferative drugs that they carry. Experimental animal studies have shown that the active drug,^{20,21} as well as the polymer coating,^{22,23} can under certain circumstances damage the vessel through progressive luminal dilation, positive vascular remodeling, aneurysmal formation, and even, at times, rupture.

Treatment options vary: aggressive surgical ligation of the aneurysm accompanied by distal bypass surgery,¹⁰ percutaneous covered stenting,⁹ and conservative medical management with continued antiplatelet therapy.⁸ Yet there is no consensus on an ideal approach to use in patients who develop coronary artery aneurysm after DES implantation. Percutaneous treatment is a newer option that involves the placement of a covered stent to

obstruct blood flow into the aneurysmal sac. The synthetic membrane of the stent-graft effectively prevents plaque protrusion, successfully sealing the aneurysm—a safer and less invasive alternative in the treatment of coronary aneurysms. These PTFE-covered stents, easy and rapid to deploy, have emerged as a new tool for the treatment of coronary artery aneurysms,^{24,25} coronary perforations or ruptures,^{26,27} coronary artery fistulae,²⁸ saphenous vein graft disease,²⁹ carotid artery aneurysms,³⁰ and aortic and peripheral vascular disease.^{31,32}

Polytetrafluoroethylene has ideal characteristics as a single layer, and it can be rolled to form a thin multilayer covering that can be expanded 4 to 5 times its original diameter (when the stent expands) without laceration or shrinkage. Furthermore, the negative charge of the polymer prevents blood-protein coagulation on the tissue surface and limits platelet activation and thrombus formation.³³ Chemically composed of carbon chains saturated with fluorine, PTFE for vascular prosthetic applications is known as expanded polytetrafluoroethylene (ePTFE). Expansion is part of the manufacturing process, in which the solid material is modified into a porous lattice. When ePTFE is used to cover a balloon-expandable metal stent, the material dilates simultaneously with the stent, with a resulting decrease in the thickness of the material wall. To avoid disruption of the ePTFE during deployment, the total balloon length, including the tapered ends, should match the length of the ePTFE membrane.³⁴ Polytetrafluoroethylene-covered stents for coronary and saphenous vein graft use have been developed by Boston Scientific Corporation (the Symbiot® stent, consisting of a double layer of ePTFE surrounding a modified self-expanding RADIOUS-like nitinol stent), by Abbott Vascular (the JOSTENT Coronary Stent Graft, consisting of a single ePTFE layer sandwiched between 2 stents), and by CardioVasc Inc. (now Nfocus Neuromedical, Inc., Palo Alto, Calif, maker of the NuVasc® Stent-Graft, a stainless-steel stent surrounded by ePTFE coated with the synthetic peptide P-15, a cell adhesion protein to promote endothelialization).³⁵ However, some multicenter randomized trials, in comparing ePTFE stent-grafts with bare-metal stents, have shown that these stents do not improve clinical outcomes and may be associated with a higher incidence of restenosis and early thrombosis.³⁶

On reviewing the available data in the English-language literature (Table I),^{8-11,13,37-61} we encountered only 2 previously reported cases in which PTFE-covered stents were used exclusively in the repair of coronary artery aneurysms at the DES site. Vik-Mo and colleagues⁹ described the case of a 43-year-old man who developed an RCA aneurysm 6 months after receiving a paclitaxel-eluting stent. Angiography and intracoronary ultrasonography revealed a lack of contact between the stent and the vascular wall in a 15-mm-long segment with a maximal aneurysmal diameter of 6 mm. The patient

TABLE I. Review of Reported Cases of Coronary Artery Aneurysms at the Drug-Eluting Stent Site with Pertinent Data in the English-Language Literature

Author	No. Pts.	Age, yr	Sex	Type of Stent	Location of Stent	Time to Treatment	Maximum Diameter of Aneurysm, mm	Treatment
Vik-mo H, et al. ⁹	1	43	M	Paclitaxel	RCA	6 mo	6	Covered stent
Okamura T, et al. ³⁷	1	73	F	Sirolimus	RCA	8 mo	17	Covered stent
Subramaniam KG and Akhunji Z ³⁸	1	65	F	Sirolimus	LAD	36 mo	6	Surgery
Lee KH, et al. ³⁹	1	67	F	Sirolimus	LAD, LCx	40 mo	—	Conservative
Sharma J, et al. ⁴⁰	1	79	F	Heparin	LAD	36 mo	19	Conservative
Latchumanadhas K, et al. ⁴¹	1	—	M	Paclitaxel	LAD	1 mo	—	—
Levisay JP, et al. ⁴²	1	56	M	Sirolimus	LAD, RCA	3 mo	7	Conservative
Chen D, et al. ⁴³	1	49	M	Paclitaxel	LAD	1 mo	3	Conservative
Lee SE, et al. ⁴⁴	1	64	M	Sirolimus	LAD	35 mo	—	Conservative
Zbinden R, et al. ¹¹	1	—	—	Evorolimus	OM	3 mo	—	Conservative
Lee SH, et al. ⁴⁵	1	63	F	Paclitaxel Sirolimus	LCx LAD	6 mo 32 mo	13	Conservative
Yamen E, et al. ⁴⁶	1	43	F	Paclitaxel	LAD	2 mo	—	—
Gurvitch R, et al. ¹⁰	1	50	M	Paclitaxel	LAD, RCA	1 mo	19.7	Surgery
Jindal RK, et al. ⁴⁷	1	66	M	Sirolimus	LCx	2 mo	—	Surgery
Kishida K, et al. ⁴⁸	1	70	M	Sirolimus	RCA	2 mo	30	Surgery
Ruiz-Nodar JM, et al. ⁸	1	60	M	Paclitaxel	LAD	5 mo	—	Conservative
Zhang F, et al. ⁴⁹	1	44	M	Paclitaxel	LAD	1 mo	—	Conservative
Wang D and Gunalingam B ⁵⁰	1	71	F	Paclitaxel	RCA	9 mo	—	Conservative
Aziz S, et al. ⁵¹	1	70	F	Sirolimus	LAD	26 mo	4.77	Conservative
Luthra S, et al. ⁵²	1	50	M	Sirolimus	LAD	48 mo	15	Surgery
Bavry AA, et al. ⁵³	4	44–49	F, M	Sirolimus, paclitaxel	—	6–21 mo	5–14	Surgery, conservative
Le MQ and Narins CR ⁵⁴	1	73	M	Sirolimus	LCx	7 mo	5	Surgery
Virmani R, et al. ¹³	1	58	M	Sirolimus	LCx	18 mo	—	—
Kim JW, et al. ⁵⁵	1	56	F	Paclitaxel	LAD	6 mo	4.97	Conservative
Gupta RK, et al. ⁵⁶	2	32, 55	M	Sirolimus	LAD	5–14 d	—	Surgery
Anandaraja S, et al. ⁵⁷	1	45	F	Paclitaxel	LAD	6 mo	8	—
Li SS, et al. ⁵⁸	1	12	F	Sirolimus	RCA	12 mo	10.1	Conservative
Singh H, et al. ⁵⁹	1	56	M	Sirolimus	LAD	1 mo	28	Surgery
Stabile E, et al. ⁶⁰	1	53	F	Sirolimus	LAD, RCA	7 mo	20	Conservative
Alfonso F, et al. ⁶¹	15	32–75	F, M	Paclitaxel, sirolimus	LAD, LCx, and RCA	1–24 mo	3.43–8.1	Conservative, angioplasty

F = female; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; M = male; OM = obtuse marginal branch; Pts = patients; RCA = right coronary artery

was successfully treated with implantation of a covered stent (JOMED Implantate, Abbott Vascular). Okamura and associates³⁷ described the case of a 73-year-old woman who was found to have a large, eccentric sacular RCA aneurysm (17 × 9 mm) at the site of a siro-

limus-eluting stent that had been implanted 8 months before the presentation. The aneurysmal opening was sealed with a PTFE-covered stent.

In conclusion, we have presented the case of a 47-year-old man who developed a large aneurysm at the stent

site 1 year after receiving a sirolimus-eluting stent in the PDCA branch of the RCA. The aneurysm was successfully treated with a PTFE-covered stent deployed via the percutaneous approach. Although intravascular ultrasonography was not performed in this particular patient, the aneurysm was large enough to prompt our decision to repair it with a covered stent. Had the coronary artery aneurysm been small (with lower risk of rupture), conservative management with dual antiplatelet therapy might have been appropriate. Similarly, if we had encountered a large aneurysm with risk of impending rupture, surgical repair might have been more appropriate. One of the limitations of our case study is that no repeat angiography was done after stent placement, because the patient was doing well clinically and because a noninvasive follow-up, in the form of an exercise Cardiolute stress test, had shown no reversible ischemia and a good ejection fraction.

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