Coronary artery aneurysm (CAA) formation is a rare complication after percutaneous coronary intervention (PCI) with stent implantation. Why CAA occurs in these unusual instances is not well understood. Though cases with drug-eluting stent (DES) induced CAA have been reported before, none was reported to be associated with a titanium nitric oxide-coated bioactive stent. Herein, we describe the first case where CAA developed after titanium nitric oxide-coated bioactive stent implantation. Several mechanisms may account for stent-related CAA formation, including mechanical trauma, vessel remodeling, acute myocardial infarction, long or multiple DES stent implantation, DES malapposition and hypersensitivity reaction to polymers.

A 53-year-old man presented initially with recent MI and ongoing chest pains. Coronary angiography revealed a 90% occlusion of the middle left anterior descending coronary artery (LAD). PCI was performed on the patient, and a titanium nitric oxide-coated bioactive stent was implanted. Due to a positive thallium scan 28 months later, a follow-up coronary angiography scan revealed a true CAA, which was then further confirmed by intravascular ultrasound. Thereafter, the patient remained asymptomatic at subsequent follow-ups, and continued medical treatment without further intervention. Herein, we discuss the possible etiologies, mechanisms and further treatments of CAA formation after titanium nitric oxide-coated bioactive stent implantation.

Key Words: Coronary artery aneurysm • Intravascular ultrasound • Titanium nitric oxide-coated stent

CASE REPORT

In June 2007, a 53-year-old man visited our cardiovascular outpatient clinic with intermittent chest tightness which had persisted for 10 days. The patient was an ex-smoker, and taking medication for hypertension. An initial thallium scan revealed reversible myocardial ischemia at the left ventricle (LV) anterior wall. Laboratory data showed mildly elevated cardiac enzymes (troponin I: 1.42 ng/mL), and recent myocardial infarct was diagnosed. Coronary angiography revealed a high degree of stenosis with irregular surface at the middle portion of the left anterior descending coronary artery (LAD), with nearly 90 percent stenosis (Figure 1, panel A). A Sprinter balloon (2.25*20 mm semi-compliant balloon, Medtronic, U.S.A) was initially utilized to predilate the lesion (pressure: 10 atm), with subsequent successful Titan 2 stent implantation (3.0*28 mm, titanium nitric oxide-coated bioactive stent, Hexacath, France). A final coronary angiography showed no residual stenosis (Figure 1, panel B). After discharge, the patient remained asymptomatic, and was prescribed dual anti-platelet agents at regular follow-ups with our outpatient clinic. However, the patient suffered angina symptoms almost two years later, and a follow-up thallium scan showed a small region myocardial ischemia at the LV anterior wall. Further diagnostic coronary angiography incidentally revealed aneurysm formation (at
middle-LAD) within the previous stent implantation segment (Figure 1, panels C&D). Intravascular ultrasound confirmed that the aneurysm was in-stent true, with the size estimated to be 7.0 mm in diameter (Figure 2). Instead of using a surgical approach, we implemented a regimen of close observation and conservative medical treatment, prescribing atrovastatin 40 mg once daily, aspirin 100 mg once daily, clopidogrel 75 mg once daily, ramipril 5 mg once daily and carvedilol 3.125 mg twice daily. Eight months later, the patient remained asymptomatic under conservative medication treatment.

**DISCUSSION**

The most common etiology of coronary artery aneurysm (CAA) could be atherosclerosis, which presents itself in 50-80% of all CAA cases.\(^1\) It may also occur secondary to mechanical trauma, such as blunt trauma or iatrogenic injury related to coronary intervention. The incidence of CAA after DES implantation is low, occurring in 0.2% to 2.3% of the reported cases. This may partly be explained by the coated anti-proliferative drugs on the stents which inhibit neointimal growth and proliferation.\(^2\) From our literature review, CAA after bioactive stent implantation has never been reported before.

In our reported case, CAA was found 2 years post titanium nitric oxide-coated bioactive stent implantation. Several possible mechanisms may be involved in the formation.

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**Figure 1.** (A) Post myocardial infarction, coronary angiography showed 90% stenosis (white arrow) at middle portion of left anterior descending coronary artery. (B) Immediately after deployment of titanium nitric oxide-coated bioactive stent (white arrow), there was no significant residual stenosis with TIMI 3 flow observed. (C&D) angiography illustrating coronary artery aneurysm formation at left anterior descending coronary artery after titanium nitric oxide-coated bioactive stent deployment about 28 months later (white arrows).

**Figure 2.** Intravascular ultrasound-guided imaging for coronary structural assessment and lumen size quantification relating to the CAA (B) and the distal (C) and proximal (A) segments by pull-back loops recording. Continuous recording of the coronary structure and morphology was also shown (From A to L in the lower panel: From distal to proximal segment). Outer large white arrows indicated border of aneurysm while the inner white or yellow small arrows indicated stent struts. The size of aneurysm was estimated to be 7 mm in the maximum diameter.
mation of a CAA in this case. Previous study suggests that DES-related CAA may be induced by mechanical trauma from a coronary intervention, including oversized balloon angioplasty or high-pressure inflation leading to coronary artery dissection. There is no doubt that a hypersensitive reaction to polymer of the stent could be one of the mechanisms in this case. Aneurysmal dilation has even been reported at the stented segment in a case with severe hypersensitivity. In addition, weakening of the medial layer of the vascular wall, which may be in part be due to chronic overstimulation of endothelium-derived relaxation factor such as endogenous nitric oxide, has also been postulated to be the cause of aneurysm formation. Nitric oxide released from the titanium nitric oxide-coated bioactive stent may theoretically induce coronary artery ectasia and contribute to CAA formation as well.

Coronary angiography as a diagnostic tool of CAA helps portray the silhouette of the lumen, but may fail to distinguish true from false aneurysms. In this regard, intravascular ultrasound (IVUS) is a useful tool which directly images the vessel inside, allowing measurement, distribution and the determination of exact vessel composition. Therefore, IVUS can now provide more accurate measurement of tissue properties than traditional gray-scale images by different methods of tissue characterization, and it was performed in patients with possible CAA with coronary angiography in order to differentiate the exact type aneurysm (true or false), and the size of the aneurysms. Unlike true aneurysms, pseudoaneurysms may lack the normal 3 layers (intima, media, and adventitia) because of the loss of vessel wall integrity and damage to the adventitia or perivascular tissue. In this case, intravascular ultrasound was used to depict the ectasia of the middle portion of LAD which measured up to 7 mm, with a true aneurysm identified to be the main pathology.

The appropriate treatment for patients with CAA remains controversial. So far, there is no statistically significant association between aneurysm size and long-term survival rate; instead, the type of the aneurysm found seems to be the major determinant. A true aneurysm is associated with low morbidity and mortality, while a pseudo aneurysm has the potential to progressively enlarge, or eventually rupture. Possible treatment options include percutaneous treatment, surgical intervention, and conservative medical management with continued dual antiplatelet agent therapy. Percutaneous treatment is a newer option that involves the placement of a covered stent (ex: a polytetrafluoroethylene-covered stent) to obstruct blood flow into the aneurysmal sac. The synthetic membrane of the stent-graft may effectively seal the inlet of the aneurysm – a safer and less invasive alternative in the treatment of coronary aneurysms. Surgical treatment may be a choice in patients who have giant saccular-form aneurysms, where the potential incidence of future adverse events is elevated and concerning, such as rupture, thrombosis and fistula formation. The surgical procedures for dealing with CAA include total resection or plication of the aneurysm, ligation, aneurismal thrombectomy, aneurysmorrhrectomy and isolation of blood flow to the aneurysm. Earlier studies indicate that prolonged dual antiplatelet agent therapy can be effective in DES-related CAA to reduce stent thrombosis. Regarding whether and how often CAA developed after implantation of a bioactive stent, however, the published data is limited. In our reported patient, a 7.0 mm true aneurysm was identified in the middle portion of the left anterior descending coronary artery. The patient was kept on medical treatment and remained asymptomatic during subsequent follow-up.

REFERENCES


