Late Development Localized Aneurysmal Ectasia of Stented Coronary Segments after Sirolimus-Eluting Stent Placement, a Case Series

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Abstract: This case series reviews 3 patients who presented with aneurysmal ectasia, suggestive of pseudoaneurysms, at the site of coronary Cypher drug-eluting stents (DES) with Sirolimus as the eluting agent. We examine risk factors and possible etiologies of DES and Sirolimus related aneurysmal formation, specifically focusing on inhibited vessel healing, increased vascular wall apoptosis, as well as inflammatory and hypersensitivity reactions. We also examine various treatment options, including stenting the lesion with a Jomed covered stent. The clinical value of this report is to foster awareness of aneurysms and pseudoaneurysms as possible complications at stented coronary arteries. The patients described include a 56 year-old male with a Left Anterior Descending (LAD) aneurysmal formation 2 years after a Cypher stent placement, 54 year-old male with multiple areas of LAD ectasia at both Cypher stent sites 1 year after placement, and a 47 year-old female with LAD ectasia at the Cypher stent site 10 months after the intervention.

Keywords: Coronary aneurysm, pseudoaneurysm, ectasia, drug-eluting stent.

INTRODUCTION

This series reviews 3 patients who presented with aneurysmal ectasia at the site of coronary Cypher drug-eluting stents (DES) with Sirolimus as the eluting agent. In the absence of an Intravascular Ultrasound (IVUS) dilatations are referred to as ectasia, however, the angiographic assessment suggested the dilatations to be possible pseudoaneurysms. Upon English-language literature review this is the first case series of aneurysmal ectasia with Sirolimus DES, albeit individual cases have been previously reported [1]. Risk factors and possible etiologies of DES relatedaneurysmal formation are examined, as well as implications and treatment strategies. The clinical value of this report is to foster awareness of aneurysms and pseudoaneurysms as possible complications at stented coronary arteries.

Coronary artery ectasia or dilatation is considered aneurysmal if it measures at least 1.5 to 2 times the diameter of a normal adjacent segment [2]. The incidence of aneurysmal occurrences in the coronary vasculature following percutaneous coronary intervention (PCI) ranges from 0.3 to 6% [3]. Coronary artery pseudoaneurysms are dilatations of a segment of a coronary artery stemming from a hematoma as a result of arterial wall perforation that unlike true aneurysms, do not include all three arterial wall layers and are not formed as a result of arterial wall weakness. Angiographic characteristics suggesting that the lesion may be a pseudoaneurysm are thin-wall, narrow, and saccular appearance. Moreover, pseudoaneurysms are more likely to occur from catheter-based interventions than true aneurysms. Aneurysms and pseudoaneurysms are a serious finding, as they can thrombose and subsequently embolize, or can rupture and may lead to cardiac tamponade [4].

CASE DESCRIPTION

Patient 1

A 56 year-old Caucasian male with history of smoking, hypertension, hyperlipidemia, and prior stenting of proximal Left Anterior Descending (LAD) artery, presented 6 years ago for repeat cardiac catheterization due to unstable angina. An 80% mid-LAD lesionwas revealed and treated with a 3 x 13 mm Cypher stent inflated to 14 atmospheres (atm) of pressure for 60 seconds with excellent angiographic results (Figure **1A**). 2 years later a cardiac catheterization preformed for ischemic heart disease revealed ectasia suggestive of a pseudoaneurysm at the distal area of themid-LAD DES (Figure **1B**). A Jomed covered stent was inserted over the ectasia. He has been free of cardiac complications since that time.

Patient 2

A 54 year-old Caucasian male with history of hypertension, underwent a cardiac catheterization following a positive stress test, 5 years ago. The catheterization revealed 70% proximal and middle sub-total LAD occlusions, and multi-vessel coronary artery

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E-ISSN: 2311-052X/14

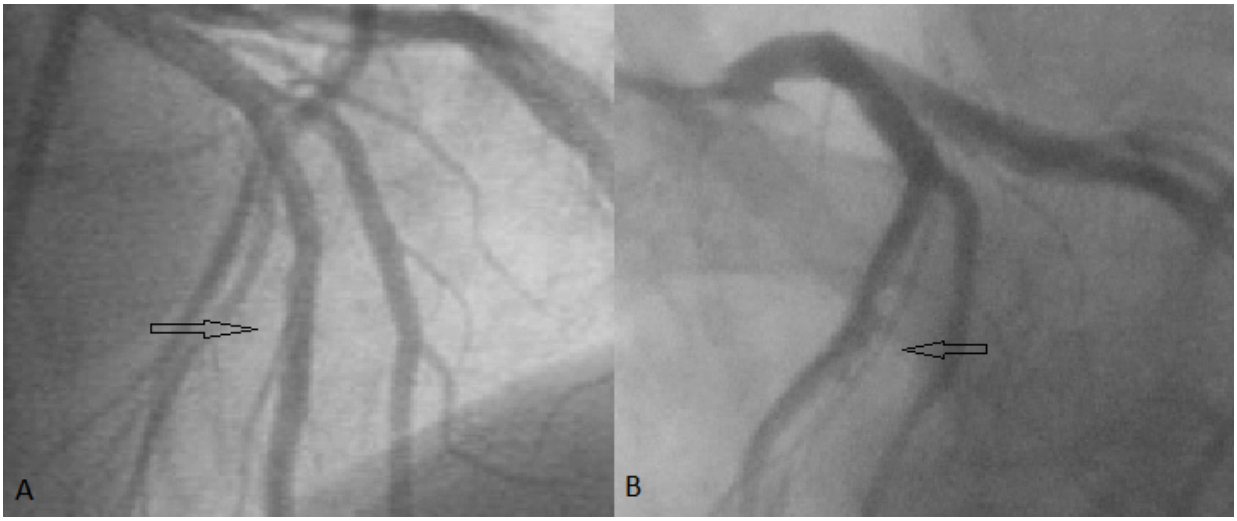

Figure 1: A. Image after placement of the Cypher stent into the mid-LAD. **B**. Follow-up cath showing ectasia at the stent in themid-LAD.

disease (CAD) with moderate stenosis.2.5 x 20mm balloon angioplasty at 12 atm for 35 sec was attempted at the proximal LAD and a focal dissection was induced. The area of dissection and the distal lesion were treated with two Cypher stents, 2.75 x 33mm at 11 atm for 25 sec and 2.75 x 18mm at 20 atm for 25 sec, respectively, with post-dilation of both stents (Figure **2A**). The patient returned in 3 weeks for an additional Cypher stent placement into the Circumflex artery, at which time the treated LAD segment appeared normal. Approximately a year later, due to anterior ischemia on a stress test, a cardiac catheterization was performed and depicted at least two areas of ectasia suggestive of pseudoaneurysms at both LAD stents (Figure **2B**). The ectasia was treated by observation and the patient has been free of cardiac complications since that time.

Patient 3

2 years ago, a 47 year-old African-American female with history of hypertension, hyperlipidemia, morbid obesity and early coronary disease in the family underwent stenting of severe LAD stenosis due to ischemic heart disease. At that time a 2 x 20mm at 12 atm for 9 sec balloon dilatation was performed, followed by a 2.75 x 33 mm at 11 atm for 22 sec Cypher stent deployment (Figure **3A**). 10 months later, the patient underwent a cardiac catheterization for unstable angina pectoris, which revealed mild ectasia suggestive of a pseudoaneurysm at the LAD stented area (Figure **3B**). No intervention was performed. 6 months later she presented with a non-STEMI and the cardiac catheterization showed complete stent occlusion. The stent could not be crossed during the

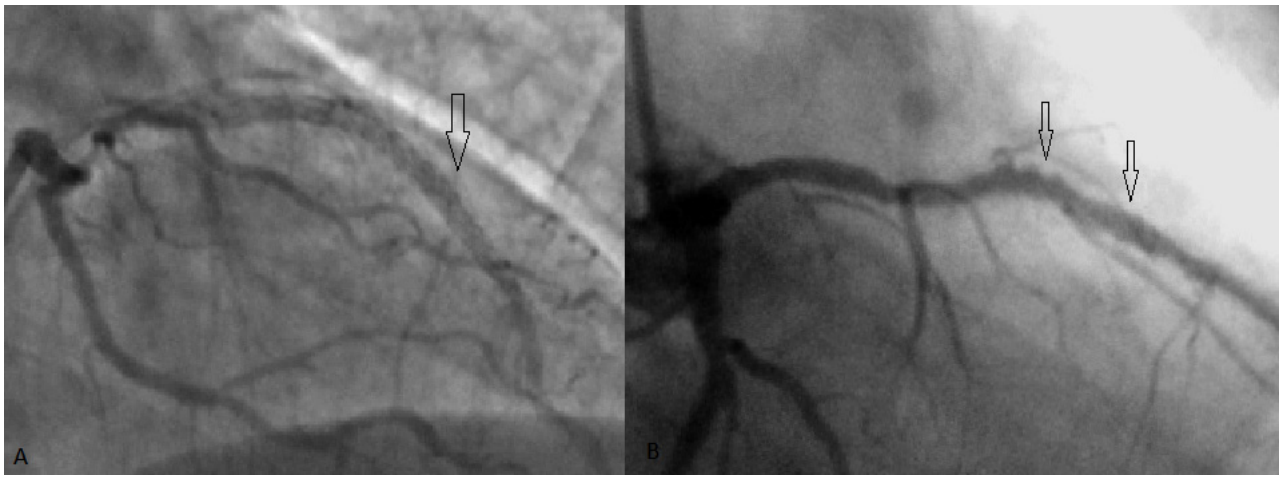

Figure 2: A. Image after placement of two Cypher stents into the proximal and mid LAD. **B**. Follow-up cardiac cath showing two areas of ectasiaat the proximal and distal stents of the LAD.

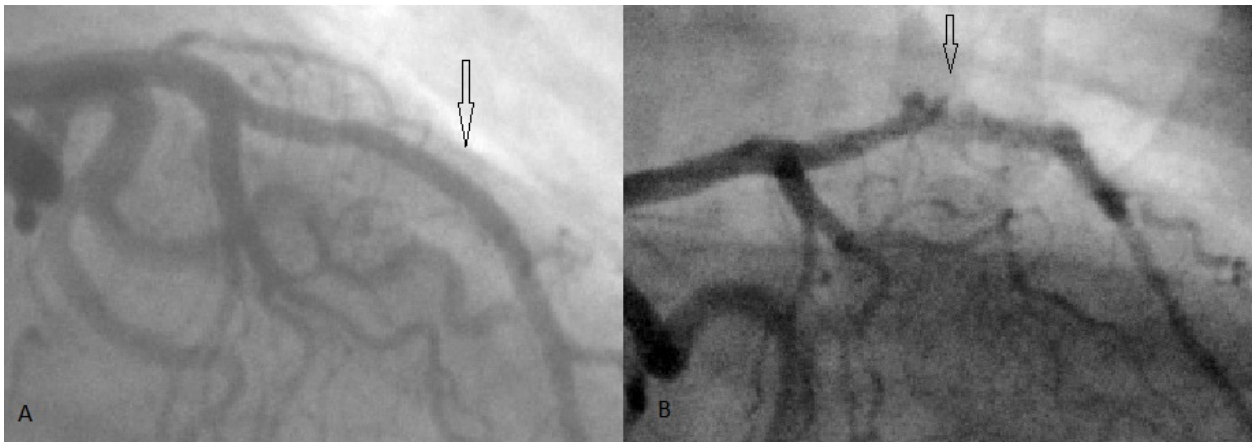

Figure 3: A. Image after placement of theCypher stent into the mid-LAD. **B**. Follow-up cath showing ectasiain the stented area of the mid LAD.

Table 1: Case Summary

	Case 1	Case 2	Case 3
Age	45 years-old	49 years-old	45 years-old
Race	Caucasian	Caucasian	African-American
Sex	Male	Male	Female
Coronary Artery Disease risk factors	Hypertension, hyperlipidemia	Hypertension	Hypertension, hyperlipidemia, morbid obesity, family history of coronary artery disease.
Coronary Lesion	99.9% Left Anterior Descending (LAD). 4 years later 80% LAD stenosis.	70% proximal and middle LAD, 80% Circumflex, 60% First Obtuse Marginal, 60% Right Coronary Artery (RCA).	80% and 60% LAD lesion.
Intervention	Penta stent to LAD, then 4 years later Cypher stent to LAD.	Two Cypher stents to LAD and Cypher stent to Circumflex.	Cypher stent to the LAD
Initial Balloon/Stent data	3 x13 mm at 14 atm x 60 sec	LAD Balloon: 2.5x20 mm at 12 atm x 35 sec, Stents: 2.75x33mm at 11 atm x 22 sec and 2.75x18 mm at 20 atm x 25 sec	Balloon: 2x20mm at 12 atm x 9 sec; Stent: 2.75x33mm at 11 atm x 22 sec
Complications	None	LAD Dissection at balloon dilatation	None
Pseudoaneurysm	2 years later at distal LAD	1 year later at proximal and distal LAD stents	10 months later at LAD.
Treatment	Jomed stent	Conservative	Conservative
Follow-up	50% Jomed instent stenosis. No intervention and no subsequent cardiac events.	No cardiac events.	Complete LAD occlusion 6 months later could not be crossed and underwent a left internal mammary artery bypass to the LAD.

procedure and the patient underwent a left internal mammary artery (LIMA) bypass to the LAD.

DISCUSSION

A potential etiology of coronary ectasiais Drug-Eluting Stents (DES) [5]. All patients underwent Cypher DES placement releasing Sirolimus. A DES consists of 3 components: the stent platform, the polymer, and the anti-proliferative drug. The stent platform may cause a hypersensitivity reaction stemming from a metal allergy, such as to nickel or molybdenum. A similar hypersensitivity can be seen with a bare-metal stent. Additionally, the polymer drug carrier portion of the DES has been shown to cause inflammatory eosinophilic reactions in the arterial wall. Thus, DES

can delay healing if vascular injury occurred, for example, from wall stress or tear during balloon or stent deployment. It is theorized that anti-proliferative drugs eluted from the stent can delay re-endothelialization, cause inflammatory changes in the medial wall, and even cause hypersensitivity reactions. Sirolimus has been found to inhibit vessel healing, by interrupting cellular proliferation, migration and signal transduction, as well as increasing vascular wall apoptosis [6]. Paclitaxel is also a commonly eluted drug that has been linked with similar effects [7]. It is worth noting that there have been reports of spontaneous pseudoaneurysm resolution after Paclitaxel-eluting stents, yet we have not come across similar cases for Sirolimus.

Coronary ectasia etiology can also include coronary wall injury from atherosclerotic plaque rupture or wall dissections resulting in intima-media matrix disruption. Dissection can occur from balloon angioplasty [8], secondary to a large balloon size or high inflation pressure. Patient 2 incurred a focal LAD dissection following a pre-dilation. Medial dissection compromises wall integrity and is a risk factor for aneurysmal formation.

The observed character of the aneurysmal dilatation of the stented segmentsis highly suggestive of pseudoaneurysms. Additionally, the pattern of ulceration is unusual in its distribution in manifesting as multiple adjacent saccular dilations. IVUS allows improved visualization of endothelial wall and subsequent aneurysm classification. The absence of IVUS data is a limitation of this paper.

A specific pattern of patient characteristics placing a patient at a higher risk of coronary ectasia could not be isolated (Table **1**). The lesions were present in Caucasian and African-American patients, of both sexes. In this case series, the notable characteristic was patients' relatively young age of ectasia development. The likely predisposing factor for this phenomenon is the degree of atherosclerosis. No particular pattern was established with respect to balloon and stent pressures.

Aneurysmal dilatation formed within the stented segments can pose a therapeutic challenge. One should be concerned about the possibility of rupture or acute thrombosis of the stent, as well as the decrease in stent adherence to the vessel wall. Several treatment modalities have been attempted in approaching coronary aneurysms. Conservative medical treatment with management of coronary risk factors (diabetes, hypertension, hyperlipidemia, obesity, and smoking), and prolonged anticoagulation can be undertaken, as some coronary ectasia can spontaneously resolve [9, 10]. A pseudoaneurysm can also be resected or repaired during coronary artery bypass grafting [11]. A stent-assisted coil embolization of an aneurysmal sack has also been successfully utilized in lieu of surgery [12]. However, this approach requires considerable expertise and can be quite challenging. Another treatment option includes stenting with a covered stent. In the first case, a Jomed covered stent was placed effectively isolating the ectasia. Covered stents are an attractive option due to stabilizing the arterial segment, thus preventing the potential increase of ectasia and possible rupture. This treatment modality has been successfully used in the past, with one of its major benefits being the prevention of thrombusformation in the aneurysmal area [13].

Coronary artery ectasia associated with stent sites is a troublesome complication of PCIs. Its etiology is multi-faceted and treatment modalities range from conservative to surgical. Large scale studies of adverse effects of drug-eluting stents on coronary vasculature would be beneficial.

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Received on 02-02-2014 Accepted on 14-02-2014 Published on 21-03-2014

DOI: http://dx.doi.org/10.12970/2311-052X.2014.02.01.3