

## Coronary Artery Aneurysm One Year and Five Months After Sirolimus-Eluting Stent Placement

Luciano Abreu, George César Ximenes Meireles, Antonio Artur Forte,  
Marcos Sumita, Jorge Hayashi, José Solano  
*Departamento de Cardiologia do Hospital Stella Maris - São Paulo, SP - Brazil*

A 52-year-old man with diagnosis of post-infarction unstable angina. Coronary angiography revealed 90% luminal obstruction in the middle third of the right coronary artery and 90% in the marginal branch of the circumflex artery. After the administration of clopidogrel 300 mg associated with acetylsalicylic acid, the patient underwent the implantation of a sirolimus-eluting stent

(CYPHER; Johnson & Johnson – Cordis) 2.5 x 1.8 mm in the lesion located at the left marginal branch. One year and five months after the CYPHER stent implantation, a new angiography showed intrastent coronary aneurysm at the left marginal branch. This case report suggests that the implantation of a sirolimus-coated coronary stent may cause late formation of coronary artery aneurysm.

Randomized studies with the use of drug-eluting stents have demonstrated an inhibition of neointimal hyperplasia in the majority of patients<sup>1,2</sup>. With the increasing use of these stents, information on their long-term effect is extremely important. The presence of a coronary aneurysm one year and five months after the implantation of a sirolimus-eluting stent is of utmost interest due to the lack of previously reported case reports.

### CASE REPORT

The patient was a 52-year-old male admitted with a history of very intense oppressive precordial pain at rest. He presented risk factors for coronary disease, systemic arterial hypertension and was a smoker; he also used captopril 12.5 mg twice a day. An electrocardiogram and enzyme measurements were carried out and an acute myocardial infarction was diagnosed, with no upper unleveling of the ST segment. During hospital stay, he presented precordial pain and post-infarction angina was diagnosed. At the physical examination he presented arterial pressure of 120/70 mmHg and cardiac frequency of 80 bpm. Cardiopulmonary auscultation was normal.

The electrocardiogram showed a sinus rhythm, with no abnormalities. Thorax X-ray showed a cardiothoracic index of 0.5, elongated aorta and normal pleuropulmonary fields.

The patient underwent a coronary angiography by the Sones technique, which disclosed a luminal obstruction of 90% in the middle third of the right coronary artery (RCA) and 90% in the first marginal branch (MG) (fig. 1) of the circumflex artery (CA). The ventriculography showed a slight lower lateral hypocontractility.

The patient was medicated with clopidogrel 300 mg and acetylsalicylic acid (AAS) 200 mg on the same day the angiography was carried out, and on the following day, after a pre-dilation with a Wordpress balloon-catheter (Johnson&Johnson-Cordis) 2.0 x 20 mm, he underwent the implantation of a sirolimus-eluting stent (CYPHER; Johnson&Johnson-Cordis) 2.5 x 18 mm in the lesion at the MG branch with success (fig. 2). The stent was released with a 12 ATM pressure and the right femoral artery (RFA) was the access via used.

The use of the Philips System for the quantitative angiographic analysis of the measurements of the left marginal branch disclosed, at the pre-implantation assessment, a reference diameter of 2.50 mm, a percent

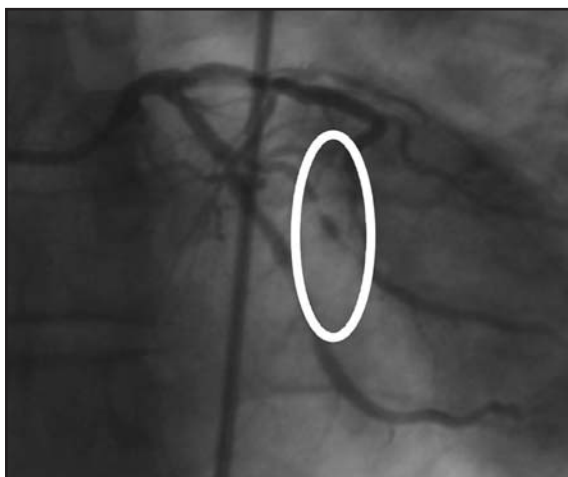
of stenosis in diameter of 81.01%, minimal luminal diameter of 0.47 mm and lesion extension of 8.21 mm. After the implant, the reference diameter was 2.50 mm and the minimal luminal diameter was 2.54 mm (fig. 3).

Post-procedure laboratory assessment showed levels of creatine phosphokinase of 60 U/L with a 5U/L MB fraction and 227 U/mL lactate dehydrogenase. The RFA introductory device was removed 4 hours after procedure completion and a manual compression was performed for 15 minutes. There was no post-compression bleeding or hematoma.

During hospital stay, the patient evolved with no precordial pain and no electrocardiographic or enzymatic alterations were observed. Two days after stent implantation, he was released from the hospital with a clopidogrel prescription of 75 mg/day for 60 days and AAS 200 mg from the release date on, indefinitely.

Thirty-six days after the first stent placement, a Bx Velocity stent (Johnson&Johnson-Cordis) 4.0 x 23 mm was successfully implanted at the RCA lesion.

The patient presented a new episode of precordial pain



**Fig. 1** - Obstructive lesion of 90% at the marginal branch of the circumflex artery



**Fig. 2** - Sirolimus-eluting stent placement (CYPHER; Johnson & Johnson/ Cordis) 2.5 x 18 mm in the lesion site at the left marginal branch

one year and five months after the implantation of the sirolimus-eluting stent. He then underwent a new coronary angiography, which disclosed the presence of a coronary aneurysm in the marginal branch, in the intra-stent proximal portion, with no luminal obstruction in both stents (fig. 4).

## DISCUSSION

The formation of a coronary artery aneurysm, defined as a dilation of the coronary artery that exceeds 1.5 times the reference diameter of the adjacent coronary segments that are angiographically normal<sup>3</sup>, has been reported after coronary angioplasty, directed coronary atherectomy, and laser angioplasty at a frequency that varies from 2 to 10%<sup>4</sup>. At the STRESS<sup>3</sup> study, the presence of a coronary artery aneurysm was observed in 3.9% of the patients submitted to Palmaz-Schatz stent implant.

Stent placement associated to anti-inflammatory agents has been correlated to an increased frequency of coronary aneurysms. Rab et al<sup>5</sup> have reported the occurrence of coronary artery aneurysms in 32% of patients submitted to stent placement, when corticoid drugs and colchicine were administered after the implant. These investigators concluded that the aneurysm formation was probably increased due to the concomitant use of anti-inflammatory agents.

The new drug-eluting stents approved for medical practice, such as paclitaxel<sup>6</sup> and sirolimus<sup>1,2</sup>, are capable of inhibiting neointimal hyperplasia. Sirolimus acts specifically at the G1 phase of the cell cycle. Due to its early action on the cell cycle, sirolimus can block cell proliferation with late vascular sequelae potential<sup>2</sup>. Additionally, sirolimus stimulates apoptosis and reduces inflammation<sup>7</sup>. Thus, drug-eluting stents can lead to the formation of coronary aneurysms and among the late post-implantation findings, the incomplete apposition of the stent filaments could be the responsible mechanism.

The late incomplete apposition of the stent filaments, observed during the follow-up with intracoronary ultrasound, is defined as a separation of one or more stent filaments from the *intima*, with no overlap on the lateral branch and evidence of blood flow behind the filament. It occurs in 4 to 5% of non-eluting stents and at an unknown frequency in drug-eluting ones. Many hypothesis have been formulated to explain its origin, such as positive regional vascular remodeling, plaque regression, late dissolution of the thrombotic material captured by the stent filaments, cell necrosis, apoptosis, and allergic reaction to sirolimus<sup>8</sup>.

At the RAVEL<sup>1</sup>, SIRIUS<sup>2</sup>, E-SIRIUS<sup>3</sup> and C-SIRIUS<sup>4</sup> studies, the presence of aneurysms was not reported, in patients evaluated by angiography and intra-coronary ultrasound six to eight months after sirolimus-eluting stent placement.

Recently, 13 patients with incomplete apposition were evaluated by intra-coronary ultrasound, six to twelve



Fig. 3 - Immediate post-stent placement outcome

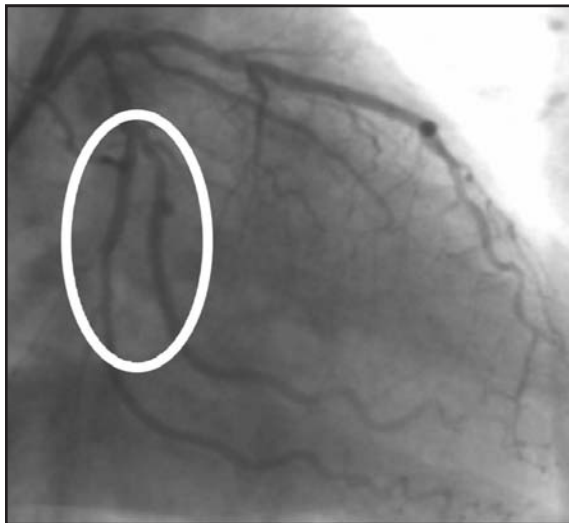


Fig. 4 - One year and five months after CYPHER stent placement, a new coronariography disclosed an intra-stent coronary aneurysm in the left marginal branch

months after sirolimus-eluting stent placement and it was observed that the area of incomplete apposition did not show alterations during this period, except in one patient in whom the presence of a coronary aneurysm was observed during the follow-up period of twelve months; the condition was probably pre-existing at the time of the stent placement and failed to be detected due to the fact that it was filled with a thrombus. Based on the fact that sirolimus elution of the stent filaments remains for only six weeks, with a half-life of sirolimus in tissue for 60 hours, it is unlikely that sirolimus itself can induce long-term alterations of the vessel wall. The possibility that this aneurysm was probably present since the first evaluation, having been masked by a thrombus, was then raised<sup>9</sup>.

Regarding the present case, a possible explanation for the aneurysm formation, which is unrelated to use of a sirolimus-eluting stent, is that, being an acute myocardial infarction with no upper unleveling of the ST segment, there was a spontaneous dissection that was not visible through the angiography, which triggered the acute coronary syndrome. The presence of a dissection has been observed by intra-coronary ultrasound prior to Palmaz-Schatz stent placement, and the image did not disappear entirely immediately after the implant. The angiography was repeated six months later and the presence of an intra-stent aneurysm was observed. The coronary ultrasound disclosed that the same dissection presented continuity with the coronary aneurysm, suggesting that the dissection was responsible for the aneurysm formation<sup>10</sup>.

A limitation observed in the present study was the lack of an intra-coronary ultrasound, which is the only way to detect the incomplete stent apposition.

No other therapeutic measures were applied in this case, as patients with coronary artery aneurysm post-percutaneous coronary intervention have shown a benign clinical course, with no association with an increase in mortality, acute myocardial infarction or artery rupture<sup>3</sup>.

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