Early Neoatherosclerosis as a Cause of Second-Generation Drug-Eluting Stent Restenosis

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ABSTRACT
A case of everolimus-eluting stent restenosis caused by neoatherogenesis is reported. Optical coherence tomography indicated the presence of a superficial arch with high optical intensity in the in-stent mid-segment, followed by significant signal attenuation with poorly defined borders, indicating the presence of lipid infiltration and/or a necrotic core, similar to that observed in de novo coronary lesions. Signs suggesting macrophage/foam cell infiltration were observed inside the fibrous cap, indicating the presence of local inflammatory activity. The development of new in-stent atherosclerosis at the site of pre-existing neointimal tissue (neoatherosclerosis) was recently identified as an additional cause of coronary stent failure. The present report is one of the first to demonstrate the finding of neoatherosclerosis as a second-generation drug-eluting stent failure.


Case Report

The case of a 58-year-old male patient is reported, an ex-smoker, with hypertension and prior coronary artery bypass grafting surgery, who presented with acute myocardial infarction without ST-segment elevation on January 1, 2012, and was submitted to percutaneous coronary intervention on January 18, 2012, with implantation of an everolimus-eluting stent in the middle third of the left circumflex artery.

Six months after the procedure, the patient returned complaining of stable angina class II according to the classification of the Canadian Cardiovascular Society (CCS).

A new angiography showed focal in-stent restenosis (Figure 1). An optical coherence tomography was performed (Figures 2 and 3) and demonstrated a heterogeneous vascular response pattern throughout the previously treated segment. The distal segment of the stent had a satisfactory vascular healing pattern, with a thin layer of neointimal hyperplasia with circumferential distribution and regular borders, in which the tissue had a homogeneous pattern of high optical intensity (Figure 2, panel 1). In contrast, the proximal intrastent segment showed more pronounced neointimal suppression, with the heterogeneous distribution of a fine layer...
Figure 1 – Coronary angiography of the procedure and at 6 months. In A, angiography shows an eccentric lesion in the middle third of the left circumflex artery. The arrow points to the stenosis. In B, the final angiographic result after implantation of an everolimus-eluting stent of 3.5 x 23 mm, post-dilated with a non-compliant balloon of 4 x 12 mm up to 16 atm. A satisfactory angiographic result without residual stenosis in the in-stent segment, no signs of injury at the borders and preserved distal epicardial flow (Thrombolysis In Myocardial Infarction – TIMI 3) were observed. Yellow arrows delimit the stent borders. In C, coronary angiography six months after the procedure with binary angiographic restenosis (stenosis diameter of 62%), focal, restricted to the in-stent segment is shown. Yellow arrows delimit the stent borders, and the green arrow points to the site of restenosis.

Figure 2 – Optical coherence tomography. In the top panel, longitudinal reconstruction of the left circumflex artery. The stent limits are identified by the yellow vertical bars. The white dotted vertical bars identify three representative images of the intrastent distal segment, site of restenosis and intrastent proximal segment corresponding to images of cross-sections of the vessel shown in the lower panel. Bottom Panel 1: distal segment of the stent showing a region with normal neointimal hyperplasia characterised by homogeneous circumferential distribution, a regular outline and high optical intensity. Bottom Panel 2: site of restenosis with eccentric distribution of neointimal tissue that has characteristics similar to those of a lipid plaque in de novo lesions. The white dots indicate the position of the stent struts that were not visualised due to important attenuation of the optical signal. The yellow arrows indicate areas of increased superficial brightness within the fibrous cap, suggesting the infiltration of macrophages/foam cells. Bottom Panel 3: proximal stent segment showing heterogeneous vascular healing with the presence of struts not covered by neointimal tissue (arrows).
A series of 299 autopsy cases demonstrated that the incidence of neoatherosclerosis is greater in lesions treated with first-generation drug-eluting stents (DES; 31%) compared with bare-metal stents (BMS; 16%), and the time to its onset is shorter after implantation of a DES (420 days – 361 days to 683 days) when compared to BMS (2,160 days – 1,800 days to 2,880 days). To date, descriptions of encountering neoatherosclerosis in second-generation DES are scarce. The present report is one of the first to report the finding of neoatherosclerosis as a second-generation stent failure.

The prematurity of this phenomenon is noteworthy and deserves further investigation.

**CONFLICTS OF INTEREST**

The authors declare no conflicts of interest.

**REFERENCES**


