CASE REPORT

Coronary vasomotion dysfunction after everolimus-eluting stent implantation

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(Received: January 8, 2014; Revised manuscript received: June 26, 2014; Accepted: October 7, 2014)

Abstract: First generation drug-eluting stent can cause a paradoxical “in-segment” coronary vasoconstriction. This phenomenon was seen with sirolimus, paclitaxel, and, more recently, also with zotarolimus-eluting stent. For the first time, we describe a case of coronary-induced vasoconstriction by everolimus-eluting stents (EES).

Keywords: coronary artery disease, coronary spasm, everolimus-eluting stent, DES, coronary flow reserve

Introduction

First generation sirolimus and paclitaxel-eluting stents can cause “in-segment” paradoxical coronary vasoconstriction (PCV) [1, 2]. This phenomenon has been specifically drug-eluting stent (DES) related, and, more recently, it has been also reported with zotarolimus (ZES) [3]. We describe a case of coronary-induced vasoconstriction by everolimus-eluting stents (EES).

Case Description

A 54-year-old male, active marathon runner, with a clinical history of hypertension, was hospitalized after the onset of stable effort angina. He underwent dipyridamole stress test that showed a preserved left ventricular ejection fraction and no alterations of kinesis at rest but lateral wall hypokinesia at high dose. Thus, the patient was referred for coronary angiography that showed a long severe stenosis of a well-developed obtuse marginal branch (OM) and two focal intermediate stenosis at mid and distal anterior descending artery (LAD) (Fig. 1A and 1B). Based on stress test result, only the OM had been treated at that time, by implanting two overlapping EES (2.5 × 38 mm and 2.75 × 16 mm; Promus™, Boston Scientific, Natick, MA, USA) (Fig. 1C). Due to the recurrence of stress angina, 5 days after the discharge, the patient had been readmitted to the same hospital. The patient underwent to stress 2D echocardiogram with the assessment of LAD coronary flow reserve (CFR) that showed a CFR of 2.1 which was considered cogent with LAD ischemia; coronary angiography was repeated, documenting the OM stents patency and confirming the angiographic intermediate stenosis of LAD. Two other EES were, at the time, implanted at the mid (2.75 × 18 mm, Xience V™, Abbott Vascular, Santa Clara, CA) and distal (2.5 × 16 mm, Promus™) LAD (Fig. 1D).
Two weeks later, the patient, still symptomatic, was hospitalized at our institution. Angina occurred now mainly at rest and overnight, accompanied by spontaneous transient anterior upper concavity ST-elevation (Fig. 2). The angiographic control showed diffused spasms along the non-stented LAD segments, promptly

![Fig. 1. Basal left coronary angiography in right oblique cranial view (A), showing two separated lesions, located in mid and distal LAD artery; proximal LAD is only mildly diseased, as better evident in right oblique caudal view (B, arrow), which reveals also a long critical stenosis of the most developed proximal OM branch. In C, this last stenosis has been treated with two overlapped EES implantation. In D, two other EES (arrows) have been implanted in LAD (see text for abbreviations and interventions timing)](image)

![Fig. 2. Upper concavity ST-elevation during rest angina, extended to all the anterior ECG leads)](image)
dissolved by i.c. nitroglycerin (TNG) boluses (Fig. 3A and 3B). Intravascular ultrasound (IVUS) showed a short, eccentric, fibro-lipid composed plaque in proximal LAD, which was left untreated because of a minimal lumen area well above 4 mm² (Fig. 4).

Symptoms continued unmodified despite optimal medical therapy, and, therefore, a new percutaneous coronary intervention (PCI) was performed by direct stenting of proximal LAD with XIENCE V EES (3.0 × 18 mm) (Fig. 5).
After this last intervention, the patient was asymptomatic, no adverse events happened at 9-month follow-up and he started to run again.

**Discussion**

Alterations in autonomic tone, mediated by impairment of coronary $\beta_2$-adrenergic receptor response during sympathetic activation, may cause vasoconstriction [4]. Moreover, smooth muscle hyper-contractility and inflammation, as well as allergic responses, are supposed to be possible but not clearly demonstrated vasoconstriction mechanisms. The mechanism of DES-induced vessel spasm has not yet been fully elucidated [5]. In the case described, spontaneous clinical, instrumental, and imaging coronary variations have been observed and recorded. Dynamic changes of the non-stented LAD segments caliber are plotted in Fig. 6. The observed variations in LAD CRF findings suggest a vasomotion impairment, since the IVUS excluded the presence of any other significant untreated stenosis or ruptured plaque. The regional involvement should lead to exclude any systemic inflammatory process but rather suggests a local hypersensitive reaction, possibly related to each of the DES components (metallic platform, polymer coating, or eluted drug). At this regard, we hypothesize that the metallic platform is the less probable responsible element, given the large number of BMS implanted worldwide in absence of recurrent coronary spasms [2]. We are, rather, hypothesizing an important role of the eluted drug, which is the same in all the implanted DES. In fact, the continuous drug exposure could have induced local toxicity and/or inflammatory response at the level of a not severe coronary plaque, thus impairing vascular relaxation, reducing vascular NO formation, and increasing transmural reactive oxygen species (ROS) production [4]. The absence of atherosclerosis nearby the two EES implanted in the OM branch does probably explain why the same phenomenon did not affect this latter vessel.

At our best knowledge, this is the first case of coronary vasomotion impairment induced by EES. In the same way that in the case reported after ZES implantation, it was elicited by close, moderate, and untreated coronary atherosclerotic disease and seems to confirm that even second generation DES may affect vasomotoricity. Further studies are needed in order to confirm our hypothesis and give a better understanding of such a complex phenomenon.
**Funding sources:** No financial support was received for this study.

**Authors’ contribution:** PG wrote the manuscript and made revisions; TA proposed the case report, made the angiographies, contributed to write the manuscript; MDM contributed to write and revise the manuscript; EMB, MVP, CB, FV, MRDM contributed to review the literature and to write the manuscript; SDT, ARG, FP revised the manuscript improving its quality. All authors had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Conflict of interest:** The authors declare no conflict of interest.

**References**


