Stent Thrombosis Eight Years Past Drug-Eluting Stent Placement – A Case Report

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Introduction

Stent thrombosis (ST) is a major concern in the drug-eluting stents (DES) era. There are several reports of stent thrombosis occurring up to five years after stent implantation. We report the case of a sixty eight-year-old woman with very late ST presenting as acute ST-elevation myocardial infarction (STEMI) after stopping antiplatelet therapy eight years past DES placement. The long time-to-event of this case brings new questions to the controversial aspects of optimal follow-up time and the safety of antiplatelet therapy cessation after recommended times are met in patients with DES.

Case Report

We present the case of a sixty eight-year-old woman with a history of multiple cardiovascular risk factors (diabetes, hypertension and hyperlipidemia) and a previous acute coronary syndrome (ACS) in 2003. At that time the coronary angiogram revealed total occlusion of the left anterior descending artery (LAD), long sub-occlusive stenosis of the left circumflex artery (LCX) and irregularities of the right coronary artery. Two sirolimus-eluting stents (2,5*28mm and 2,25*28mm) were implanted in the LAD and another two (2,25*28mm and 2,25*13mm) in the LCX, with a final Thrombolysis in Myocardial Infarction (TIMI) flow grade of III. The echocardiogram showed akinetic apical segment and preserved left ventricle function.

During the follow-up (2008) aspirin was changed to clopidogrel due to gastrointestinal side effects. She was on clopidogrel in addition to rosuvastatin, lisinopril, carvedilol and oral antidiabetics since then and remained asymptomatic until December 2010 when she described effort-related chest pain. A treadmill exercise stress test was performed and no ST-segment changes were observed but the patient referred chest pain at the peak of stress test. A myocardial perfusion scintigraphy showed normal left ventricle function (ejection fraction of 57%) and an extensive anterior, septal and apical defect, without reversibility.

Keywords

Myocardial Infarction; Drug-Eluting Stents; Thrombosis.

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In July 2011 she was admitted to the emergency department with chest pain associated with nausea. Five days earlier, she had voluntary stopped clopidogrel after analgesic prescription for arthralgias. Physical examination was unremarkable except for diaphoresis. The electrocardiogram showed sinus rhythm, Q waves from V2-V4 and ST segment elevation in leads V2 through V5, DII, DIII and AVF (figure 1). The diagnosis of anterior acute STEMI was made and four hours after symptom onset she was referred for primary percutaneous coronary intervention (PCI). The coronary angiogram revealed thrombotic occlusion of the medium LAD at the site of previous stent placement (figure 2, left panel), patency of LCX stents and irregularities of the other coronary segments. Aspiration thrombectomy was performed, which achieved a good result with TIMI 3 flow (figure 2, right panel). Eptifibatide infusion was started and she underwent new coronary angiography forty eight hours later showing LAD irregularities, maintaining TIMI 3 flow. She had no adverse events during hospitalization and was discharged five days later on dual antiplatelet therapy.

Discussion

Coronary artery stents are widely used in patients undergoing PCI. DES dramatically reduce restenosis rates with a significant reduction of repeat revascularizations, when compared to bare-metal stents (BMS)[1]. However, ST is a major concern, as the clinical consequences of ST are generally catastrophic, almost always presenting as death or large non-fatal myocardial infarction, usually with ST-segment elevation[2]. Most cases of ST occur within the first thirty days after stent placement, but the risk is continuous at a rate of 0,6% per year for at least four years after stenting[3]. The longest time-to-ST case reports the authors found happened four to five years after stent deployment[4,5]. Recently the results of the DESERT registry were presented. It included 922 patients from more than 40 clinical centers who implanted first-generation DES, mainly Cypher and Taxus stents and experienced definite late or very late ST. The majority of the late ST occurred after 1 year (75%) and continued to occur up to 7.3 years[6], extending the risk period even further. Our case report has twice the time-to-event of the other cases, and presented even later than the 7.3 years of the largest registry of DES thrombosis (DESERT), making the optimal follow-up duration of patients with DES stents even more uncertain.

The main pathologic mechanism of ST is delayed arterial healing characterized by incomplete endothelialization as showed by analysis of 40 consecutive autopsies of patients

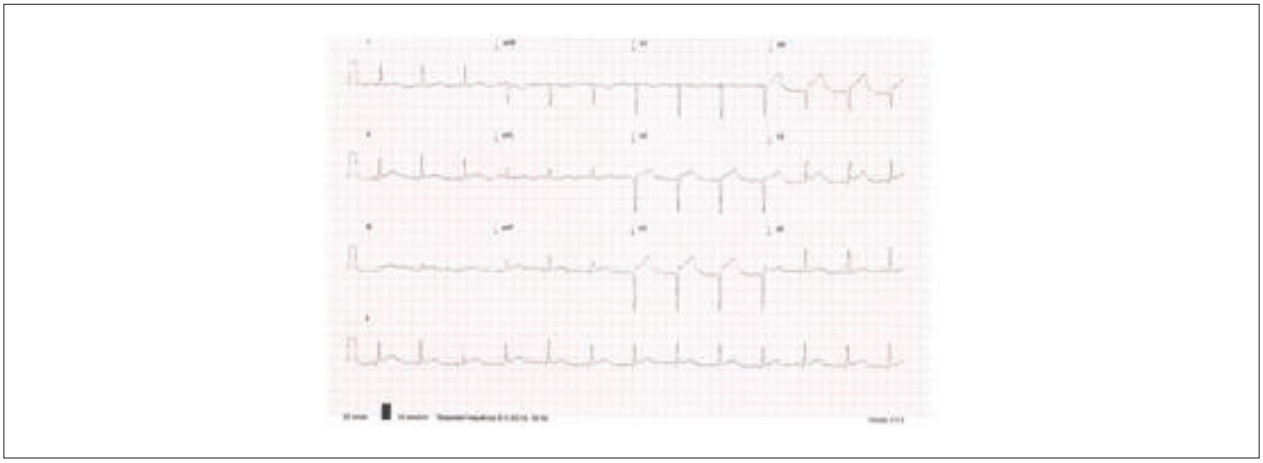

Figure 1 - *Electrocardiogram at the time of presentation showing Q waves from V2-V4 and ST segment elevation in leads V2 through V5, DII, DIII and AVF.*

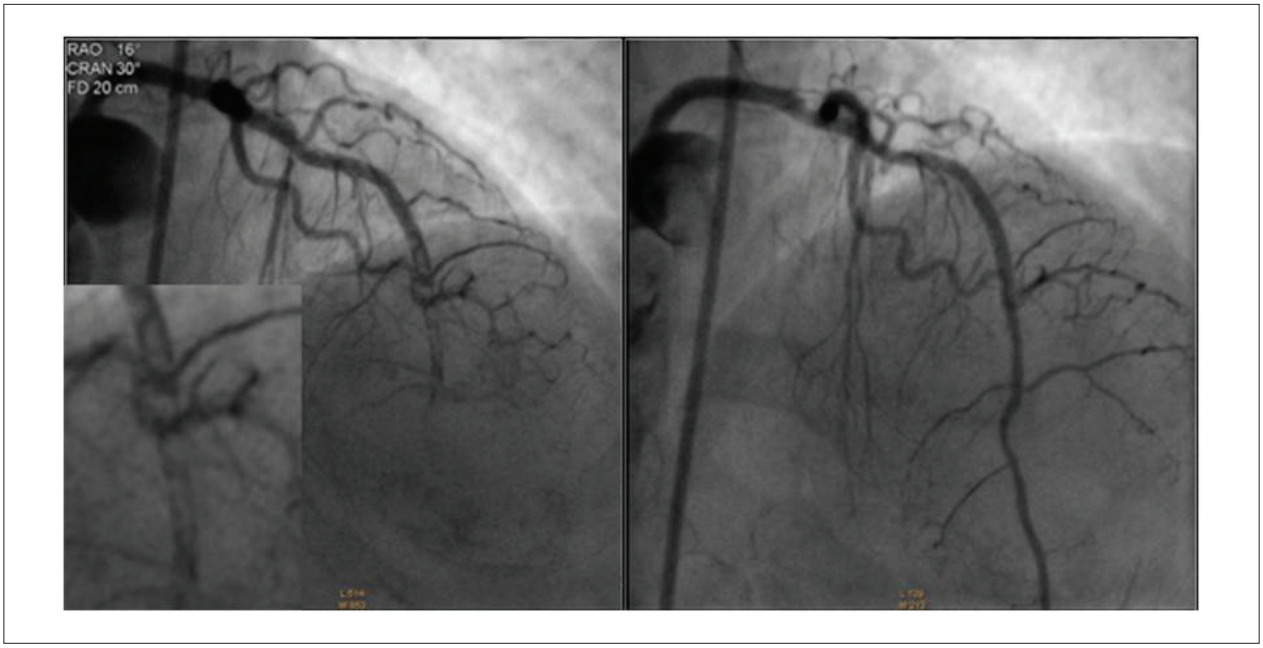

Figure 2 - *View of the LAD showing thrombotic occlusion of the medium LAD at the site of previous stent placement (left panel) and complete reperfusion following aspiration thrombectomy (right panel). LAD (left anterior descending artery).*

with stents – complete endothelialization of BMS occurred by six to seven months, whereas incomplete endothelialization persisted in the DES group beyond forty months[7]. Emerging evidence suggests in-stent neoatherosclerosis as another important substrate for late ST[8]. Although the precise mechanisms of neoatherosclerotic development remain unknown, the incidence of neoatherosclerosis is greater in DES lesions (31% vs 16% in BMS) and occurs earlier (420 days [361 to 683 days] vs. 2,160 days [1,800 to 2,880 days])[8]. Neoatherosclerosis is a probable explanation for ST during the first years after DES placement, but probably a less important mechanism for this case report with a much longer time-to-event. There are other risk factors concurring to ST including procedural aspects such as bifurcation stenting and incomplete stent apposition (ISA). ISA is defined as the absence of stent strut contact with the underlying vessel wall (not overlying a side branch). Late acquired ISA has been observed in 7% to 21% of DES[9] and positive arterial remodeling with an increase of the external elastic membrane out of proportion to changes in plaque and media appears to be its most likely mechanism[9]. This patient had two 2,25*28mm stents in the LAD which may correspond to undersized stents. DES implantation occurred in context of ACS following a thrombotic occlusion of the LAD, the decrease of plaque with dissolution of jailed thrombus may have limited the stent size choice, with later influence in the occurrence of ISA. Also, withdrawal of antiplatelet therapy seems to be an important risk factor for ST. The median

time from dual antiplatelet therapy cessation to a thrombosis-related clinical event is seven days (with a range of 3 to 150 days)[4]. In clinical practice it isn't unusual to have to consider antiplatelet therapy cessation due to, for example, surgery or gastrointestinal bleeding. In this case report the patient was on single antiplatelet therapy until the event occurred five days after she voluntarily stopped medication even eight years after stent implantation. This raises questions about the safety of discontinuation of therapy even after the recommended times are met.

Conclusion

Our case report draws the attention to the serious clinical implications of ST, highlighting the need to consider its possibility many years after stent implantation. As one of the longest reported time-to-event case it shows how the potential risk of ST should always be considered when antiplatelet therapy cessation is contemplated in patients with DES.

Author contributions

Acquisition of data: Baptista A, Ferreira C; Analysis and interpretation of the data and Critical revision of the manuscript for intellectual content: Baptista A, Ferreira C, Mateus P; Obtaining funding: Carvalho H; Writing of the manuscript: Baptista A.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any post-graduation program.

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