Case Report

Late Coronary Thrombosis Secondary to Implantation of Paclitaxel-Eluting Stent without Restenosis of Conventional Stents

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A male 39 year-old patient with post-infarction angina. The coronary angiography showed total proximal occlusion of right coronary artery (RCA), obstructive lesions of 95% of the anterior descending artery (ADA), 80% of the second left marginal branch (LM2), and 95% of the circumflex artery (CXA). The patient was successfully implanted with a Taxus 3.0 x 24 mm stent and an Express 2.75 x 24 mm stent in the proximal and distal thirds of the RCA, respectively, and with an Infinnium 3.0 x 24 mm stent in the ADA. After seven months, the patient had an anterior acute myocardial infarct (AMI) due to thrombosis of the Infinnium stent and restenosis of the Taxus stent, with no loss of results in the conventional stents.

Introduction
Randomized multicentric studies comparing drug-eluting stents and conventional stents showed superiority of medicated stents in reducing the rate of restenosis1. Nevertheless, late safety results of these stents have not been completely established. Late in-stent thrombosis (after 30 post-implantation days), which was not observed in the first series of studies, has recently been reported2-4.

This case report of a patient who underwent multiple stent implants in whom late thrombosis occurred in the Infinnium stent associated with the restenosis of the Taxus stent, without restenosis of the conventional stents, raises an interesting discussion on the reasons for this event.

Case Report
The patient is a 39-year-old man admitted with a diagnosis of inferior AMI for two hours. He was medicated with intravenous streptokinase and showed signs of reperfusion. Arterial pressure was 140/90 mmHg and heart rate was 80 bpm. Cardiopulmonary auscultation was normal. Risk factors for coronary artery disease were smoking, obesity, dyslipidemia, and arterial hypertension.

During hospitalization, the patient progressed with post-infarction angina. Coronary angiography showed proximal occlusion of the RCA, obstructive lesions of 95% of the mid third of the ADA, 90% of the proximal third of the CXA, and 80% at the beginning of the second left marginal branch (LM2). Collateral circulation was present from RCA to RCA ++/4+. Left ventriculography showed moderate hypococontractility of the inferior and anterior walls with an ejection fraction of 50%.

The patient was treated with 300 mg oral clopidogrel on the day before the procedure, and was using 200 mg oral aspirin, once a day. An intravenous infusion of tirofiban hydrochloride (Aggastrat™) was initiated 12 hours pre-implant and maintained for an additional 12 hours post-implant. After mechanical recanalization of the RCA with the Shinobi™ 0.014” guidewire, pre-dilation of the proximal and distal lesions was performed with a Wordpass™ 2.0 x 20 mm balloon catheter followed by the successful implantation of an Express™ 2.75 x 24 mm stent at the distal lesion and a Taxus Express™ 3.0 x 24 mm stent at the proximal lesion, both inflated to 12 atmospheres (Figure 1). Next, the ATW™ 0.014” guide-wire, pre-dilation of the proximal and distal lesions was performed with a Wordpass™ 2.75 x 24 mm stent at the distal lesion and a Taxus Express™ 3.0 x 24 mm stent at the proximal lesion, both of them inflated to 12 atmospheres (Figure 1). Next, the ATW™ 0.014” guide-wire was positioned in the ADA, and pre-dilation of the lesion was carried out with the Wordpass™ 2.5 x 20 mm balloon catheter, followed by the Infinnium™ 3.0 x 33 mm stent implantation, inflated to 13 atmospheres (Figure 2). The patient progressed without complications and was discharged from hospital with a prescription for clopidogrel 75 mg a day for 6 months and aspirin 200 mg a day indefinitely.

Two months after the first hospitalization, a BeStent™ 4.0 x 12 mm was implanted at the CXA lesion and an AVE™ 3.5 x 9 mm stent was implanted at the LM2 lesion, both successfully. On pre-implant control coronary angiography it was noted that the Infinnium stent placed in the ADA maintained the initial result (Figure 2).

Seven months after the first hospital stay, the patient was admitted with a diagnosis of anterior AMI for over 12 hours, treated with atenolol, aspirin, simvastatin, enoxaparin, and captopril. The coronary angiography showed a subtotal obstruction of the Infinnium stent with TIMI grade I flow and a 90% focal obstructive lesion on the upper border of the Taxus stent. Conventional stents implanted in the CXA and LM branch showed no loss of results (Figures 1 and 2). Left ventriculography showed accentuated anterior hypocontractility. Patient progressed without complications and was evaluated by the cardiac surgery team, that indicated and scheduled myocardial revascularization surgery for 60 days after hospital discharge.

Key words
Coronary thrombosis; stents; Paclitaxel; coronary reestenosis.

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Fig. 1 - Pre-implant coronary angiography (1), after balloon dilation (2), immediate post-implant period (3), and seven months post-implant of Taxus and Express stents (4).

Fig. 2 - Pre-implant coronary angiography (1), immediate post-implant period (2), two months post-implant (3), and seven months post-implant of Infinnium stent in the ADA (4).
Discussion

This is the first report in medical literature on late post-implant thrombosis of the Infinium stent and it has the unique feature of a restenosis of the Taxus stent with no restenosis of the conventional stents.

Iakovou et al. described the angiographic pattern of post-implant restenosis of the Taxus stent and observed the prevalence of restenosis location in the body portion and borders of the stent (72%), followed by location in the borders (16%) and the body (11%) of the stent. When located in the borders, a proximal predominance was noted that was attributed to a more intense flow in this region of the stent that resulted in “washing” of the drug, leaving the stent more vulnerable to restenosis. The patterns of restenosis observed were focal (50%), diffuse in-stent (4%), proliferative (25%), and total obstruction (21%)\(^3\).

In our case, the Taxus restenosis location was focal in the proximal border, and therefore within the patterns of restenosis reported for this type of stent.

As to the Infinium stent, the clinical and angiographic pictures were typical of late in-stent thrombosis, seven months after implant. The patient received clopidogrel for six months and thrombosis occurred 30 days after interruption of the medication; hence, it does not seem to us that the discontinuation of the drug, per se, was responsible for the thrombotic event. Recent publications have shown that late in-stent thrombosis occurred in 0.35 to 0.72% of the patients who underwent drug-eluting stent implants, most of them after discontinuation of clopidogrel, with a 4-day to 26-month interval between drug interruption and thrombosis, suggesting that an additional mechanism is responsible for this phenomenon, possibly late hypersensitivity to one of the stent components\(^2\).

A recent investigation carried out in the database of the Food & Drug Administration (FDA) and the Research on Adverse Drug/Device Events and Reports (RADAR) found 5,783 reports related to adverse events with drug-eluting stent implantations, and 262 reports of hypersensitivity, 13 of which were classified as probable and 4 of them confirmed by autopsies of patients with deaths associated with late in-stent coronary thrombosis\(^5\).

Post-implant hypersensitivity reactions of drug-eluting stents may occur due to antiplatelet treatments or stent components (polymer, drug, or metal portion).

Hypersensitivity reactions to heavy metals (molybdenum and nickel) were reported in 8% of patients who underwent stainless steel stent implants\(^6\). Hypersensitivity to these metals were associated with restenosis but not with thrombosis, and eosinophilic infiltrate was not observed upon histologic examination of human coronary arteries after implantation of stainless steel stents\(^6\). In our case, it is unlikely that this mechanism was responsible, since three conventional stents were implanted and none of them presented restenosis, and one of them was the Express stent platform for the Taxus stent.

Paclitaxel has been associated with hypersensitivity events, but most of these reactions were attributed to the castor oil vehicle, which is not used in drug-eluting stents\(^5\). The occurrence of a late hypersensitivity reaction to paclitaxel in this case report is unlikely, since the drug used in the Taxus and Infinium stents is completely released within 30 and 48 days post-implant, respectively.

When applied to conventional stents, biodegradable and non-biodegradable polymers trigger local and systemic post-implantation hypersensitivity reactions in coronary arteries of pigs\(^7\). The Taxus Express stent uses the poly (styrene-b-isobutylene-b-styrene) polymer, and the Infinium stent uses three polymers (poly-DL-lactide-co-glycolide, poly vinyl pyrrolidone, and poly lactide-l-co-caprolactone), all of them biodegradable.

In a report on a death by coronary thrombosis 18 months post-implantation of a Cypher\(\text{TM}\) stent, Virmani et al.\(^8\), upon histologic examination, observed giant cells surrounding a polymer fragment that had detached from the stent and numerous eosinophils in the artery wall.

Therefore, we may conclude that this is a case of a late thrombosis of the Infinium stent 30 days after discontinuation of clopidogrel use, probably related to a late hypersensitivity reaction to the stent polymer. As to restenosis of the Taxus stent, it seems to be a local phenomenon not related to allergic reactions.

Potential Conflict of Interest

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

References

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