Sub Acute Stent Thrombosis: Not an Easy Task to find out the Guilty!

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Abstract

Stent thrombosis is a dramatic event whose correct understanding may help its prevention. We describe the case of a very complex patient experiencing sub acute stent thrombosis of 2 overlapped drug eluting stents, whose mechanisms are incompletely understood. Current drugs (as new antiplatelet agents) and devices available (IVUS or OCT images and drug eluting stent of third generation) in our catheterization laboratories may help to better understanding and treating this sometimes catastrophic event.

Keywords:  DES; Sub-acute Stent Thrombosis; Clopidogrel Resistance; Stent Underexpansion

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Case Presentation

A 67 year old indian male, hypertensive, hypercholesterolemic and with unrecognized diabetes was admitted for a 12-hour persisting chest pain. The ECG showed ST elevation with QS complexes in DII-DIII-aVF, so we decided to give the patient insulin, aspirin and ticagrelor 180mg orally. Coronary angiography performed in urgency manner demonstrated a 2-vessel disease consisting in 3 in sequence stenosis (one of 90% and 2 stenosis of 70%) of a very calcific middle Left Anterior Descending Artery (LAD) and a Right Coronary Artery (RCA) suboccluded in its middle segment with high thrombus burden (Figures 1 and 2). Thus we performed a Percutaneous Coronary Intervention (PCI) with manual thrombus aspiration retrieving big red clots and subsequent implantation of a bare metal stent in the RCA. The echocardiogram showed akinesia of the basal segment and hypokinesia of the middle segment of the inferior
wall, with preserved left ventricular ejection fraction.

Given the high risk profile of the patient, in day IV we brought him to the catheterization laboratory for a Fractional Flow Reserve (FFR)-guided PCI of middle LAD. The procedure consisted in the implantation of 2 overlapping Nobori DES (2.5/28 and 2.25/28 mm) post dilated respectively with a 3.0 mm noncompliant balloon and a 2.5 mm balloon (Figure 3).

The patient was enrolled in the MATRIX study (an ongoing study with double randomization, bivalirudin vs unfractionated heparin, radial approach vs femoral approach), that requires an evaluation of platelet inhibition by the P2Y12 receptor. The Verify Now test performed the day after the staged FFR-guided procedure on LAD stenosis, showed an excessive platelet inhibition by ticagrelor (platelet response unit, PRU = 4) [2], so according to this result and the reduced patient’s compliance therapy in his country of origin (difficulty in obtaining this new antiplatelet agent), thus we switched to clopidogrel 75 mg/day after 300 mg oral loading dose, following the study guidelines.

At day VI, during the patient’s discharge, he experienced chest pain again, at rest, with ST segment elevation in V2-V4. Immediate coronary angiography showed a big white clot and reopening the vessel, then Intravascular Ultrasound Imaging (IVUS) showed a good apposition of the DES, but with an under expansion of distal segment of the second stent in correspondence of small vessel caliber and a minimal area of 1.9 mm² (Figure 5). The procedure finished with further prolonged stent postdilatation with 3.0 mm noncompliant balloons, in order to achieve an adequate minimal stent area (4.7 mm²) (Figures 6 and 7). Contemporarily, the Verify Now test showed clopidogrel resistance (PRU = 380), so we switched to ticagrelor again (90 mg bis in die).

The patient was discharged on day X, asymptomatic and with preserved left ventricular function.

Discussion

This case gives us several insights on the complex pathophysiological milieu involved in stent thrombosis. The event here described occurred in a vessel treated secondarily with FFR-guided PCI. It is questionable if the LAD had to be treated before an ischemia stress test, nevertheless it is our common practice to treat the LAD if the patient is at high risk; in this case we used the FFR guidance, that has been associated to a reduction in adverse events [3].

The use of DES in coronary arteries, after an initial enthusiasm, was hampered by a supposed increased risk of stent thrombosis [4,5], that taught us to correctly prepare the lesion and to post dilate the stents in order to reduce the risk of malapposition and under expansion [6]. Further studies, especially those that involved newer generation DES, showed how these devices did not carry an increased risk of stent thrombosis compared to bare metal stents [7-9].

However, the risk of stent thrombosis may have different causes [10]. Among the others there are possible genetic causes that are incorporated in the term “clopidogrel resistance”: polymorphisms that can modulate the absorption of the drug or metabolic activation (these are the most frequent mutations and involve mainly the CYP2C19 gene) or biological activity, allelic variants that are associated with an increased risk of death, heart attack and stroke [11]. Newer antiplatelet agents like ticagrelor and prasugrel have been shown to be an excellent alternative to clopidogrel and to be superior in terms of antithrombotic efficacy, contemporarily reducing the risk of drug resistance [12,13].

In our case several of these aspects seemed to combine determining sub acute stent thrombosis in this patient, whose cause was probably multi factorial. The patient had a
decompensated and misdiagnosed diabetes, suffered a recent ACS, had resistance to clopidogrel (as demonstrated by the Verify Now test), had 2 long and overlapped DES, and finally the distal portion of the second stent was under expanded despite a correct opposition to the vessel wall (as shown by IVUS imaging).

Clopidogrel resistance may have favored the thrombotic event, that however did not occur in the right coronary artery treated with one big bare metal stent, but involved the small caliber, calcific LAD artery treated with 2 long overlapping DES, with a final minimal area of 1.9 mm². We hypothesize that two factors could have reduce the risk of stent thrombosis event:

1. IVUS-guidance during complex PCI might have lead to a more aggressive post dilation (IVUS not used during the FFR guided procedure on LAD, but only in occasion of stent thrombosis);

2. Avoid the switch of antiplatelet drugs from ticagrelor to clopidogrel, even if the excessive platelet inhibition by ticagrelor (PRU = 4) and the reduced compliance to ticagrelor therapy in his country of origin.

**Conclusion**

This case report provides a number of questions and considerations about the trigger of an episode of sub-acute stent thrombosis in a high risk patient. We believe that the armamentarium available in modern catheterization laboratories, e.g. more potent antiplatelet drugs and IVUS or OCT guidance, may help reducing the risk of thrombotic adverse events, even if sometimes is very difficult to find the guilty.

**References**


