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Two cases of very late bare-metal stent thrombosis and literature review

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Abstract. – BACKGROUND: Bare metal stents (BMS) are commonly used in the treatment of coronary artery disease. Very late stent thrombosis (VLST) is a quite rare clinical entity. However, it is a serious complication that often results myocardial infarction or death. Since the stent endothelialization is considered to be completed within 4 weeks after the intervention, VLST is not common with BMS.

PATIENTS AND METHODS: The pathogenesis of the VLST is poorly defined. Herein, we report two cases of VLST in which one a 62 year old male patient devoloped VLST of a BMS implanted in the right coronary artery (RCA) and presented inferior myocardial infarction and other a 48 year old male patient devoloped very late thrombosis of a BMS implanted in the RCA and presented inferior myocardial infarction, respectively.

CONCLUSIONS: On the basis of these two cases and our review of the current literature we suggest that what can be done to prevent this rare but offending complication. Moreover, in the light of new imaging modalities such as optical coherence tomography (OCT), the pathophysiology of stent thrombosis will be clearly defined and preventive measures will be taken before it occurs.

Key Words:
Very late stent thrombosis, Bare-metal stent, Atherosclerosis.

Introduction

Very late stent thrombosis (VLST) is quite rare in bare metal stents (BMSs). It refers to any stent thrombosis later than 1 year after stent implantation[1]. Because bare metal stent endothelialization is considered to be complete after four weeks of intervention, VLST is not usual with the use of BMS. In contrast, VLST has been reported following drug-eluting stent (DES) implantation with an incidence of 0.3 to 0.6% per year and has been attributed to delayed strut endothelialization[2].

Case 1

In 2012, a 62 year old hypertensive, non diabetic, hypercholesterolemic male smoker with a history of stable angina was admitted with an acute inferior myocardial infarction. There was a history of percutaneous coronary intervention (PCI) of the right coronary artery (RCA) and left coronary artery (LAD) with BMS 7 years ago. He had a 3.0 × 13 mm BMS (Ephesos, Nemed Ltd., Istanbul, Turkey) deployed in his mid-LAD and a 3.0 × 15 mm BMS (Ephesos, Nemed Ltd., Istanbul, Turkey) in his mid-RCA, respectively. Since 2005, he had undergone follow-up coronary angiography 4 times, and each time the images had shown patent stents in both the LAD and the RCA. His current medications were aspirin 100 mg daily, metoprolol 100 mg daily, ramipril 10 mg daily, atorvastatin 20 mg daily, trimetazidin 20 mg twice daily, amlodipin 5 mg daily and isosorbide mononitrate 40 mg daily. On his last hospital admission, in 2012, echocardiogram showed normal left ventricular function with left ventricular hypertrophy and an ejection fraction of 55%.

Coronary angiography showed a fresh occlusion of the mid-RCA (Figure 1). The mid-RCA lesion was crossed with a guidewire and serially predilated with a 2.5 × 20 mm balloon (Invader, Alvimedica, Copenhagen, Denmark). Due to the patient's questionable compliance and ongoing smoking, we deployed a 3.0 × 12 mm BMS (Driver Sprint, Medtronic, Minneapolis, MN, USA) at 16 atm of pressure for 20 seconds, with good result (Figure 2). An intravenous tirofiban infusion was continued for 36 hours. Testing for hypercoagulation abnormalities and clopidogrel resistance yielded noncontributory results. The patient was discharged from the hospital with advice to follow a lifelong aspirin and clopidogrel regimen and to stop smoking.

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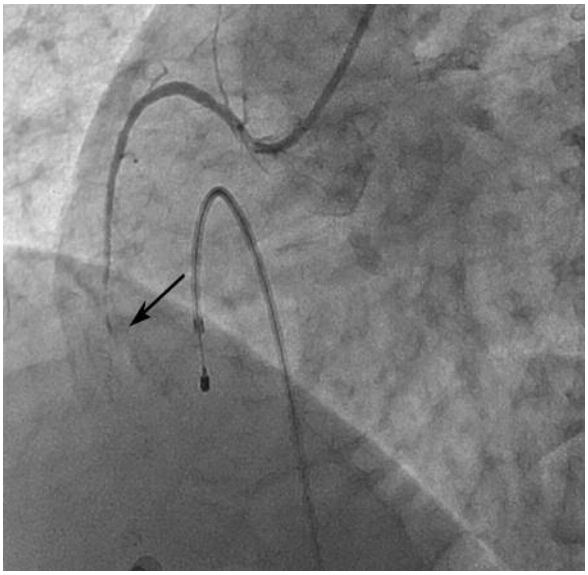

Figure 1. Coronary angiography shows thrombotic occlusion of the stent (*arrow*) in the mid- right coronary artery.

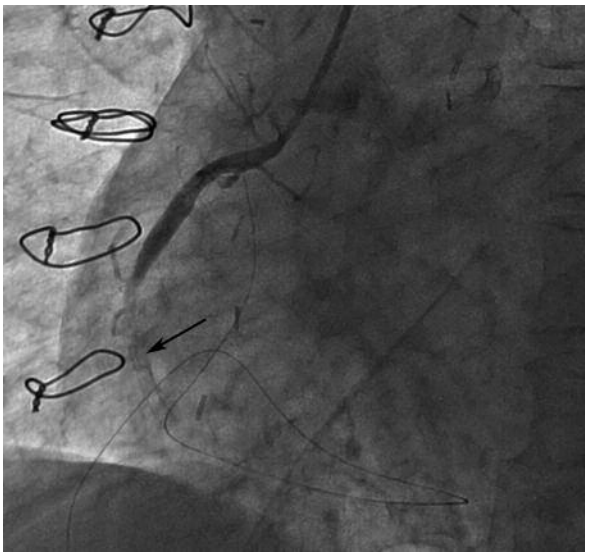

Figure 3. Coronary angiography shows thrombotic occlusion of the stent (*arrow*).

Case 2

In 2013, a 48 year old man was referred to our hospital with an acute inferior myocardial infarction. In 2008, a BMS 2.5 × 13 mm was implated in his proximal LAD. Two years later from the PCI he underwent coronary by pass operation and left internal mammarian artery-LAD, saphen vein-RCA, radial artery-diagonal branch anastomoses were performed. Six months later he was admitted with an inferior myocardial infarction and a 3.0 × 15 mm BMS had implanted in the RCA. There were no treated medical problems except for ongoing smoking. His current medications were aspirin 100 mg daily, metoprolol 25 mg daily, ramipril 2.5 mg daily and atorvastatin 20 mg daily. On the last hospital admission coronary angiography showed occlusion of the proximal RCA compatible with stent thrombosis (Figure 3). The proximal RCA lesion was passed with a guidewire and dilated with 3.5 × 15 mm balloon (Invader, Alvimedica, Copenhagen Denmark) yielding a good angiographic result (Figure 4). We considered stenting, but in light of the episode of stent thrombosis, we thought that adding more metal to a previously stented segment might increase the risk of another thrombotic episode. In addition, there is evidence that stenting in primary PCI increases the chances of coronary slow flow.

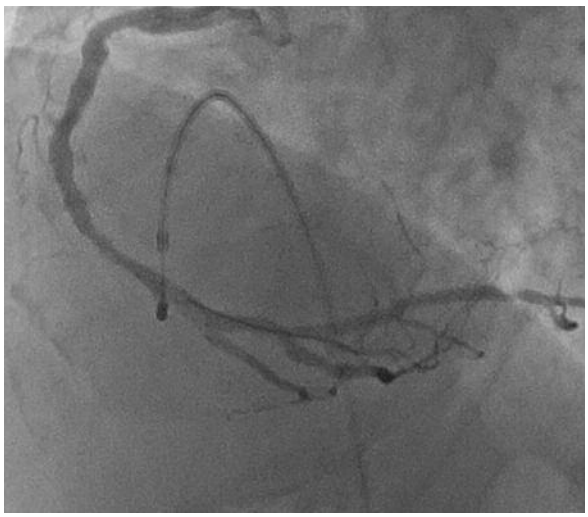

Figure 2. Coronary angiography after stent deployment shows a good angiographic result.

Discussion

VLST is a rare although potentially catastrophic complication occurring after PCI. Stent thrombosis is classified according to time: acute (< 1 day), subacute (1-30 days), late (> 30 days) and very late (after the first year)[3]. About 80% of BMS thromboses occur within the first two days and, to a lesser degree, in the first month of the implantation. The mechanisms involved in VLST in BMSs

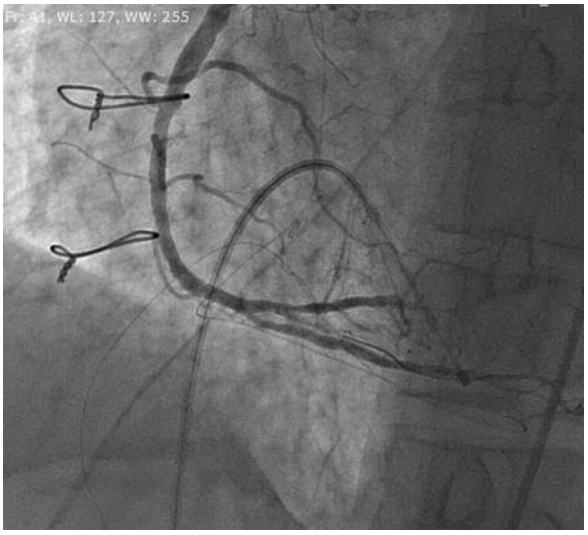

Figure 4. Coronary angiography after balloon inflation shows an excellent angiographic result.

are not clearly defined. However, the mechanism of VLST after DES implantation could be explained by incomplete neointimal coverage, local hypersensitivity reactions and late stent malposition due to excessive positive remodeling[4-5]. BMS does not possess an antiproliferative coating that can cause local hypersensitivity reactions and stent endothelialization is considered to be completed 4 weeks after BMS implantation. Therefore, the pathogenesis of VLST after BMS implantation might be different from that of DES implantation. The most well known risk factor for stent thrombosis still appears to be premature discontinuation of antiplatelet therapy. Assumed causes of BMS thrombosis, both early and late, include noncompliance with antiplatelet agents, exercise-induced procoagulant state, brachytherapy, small stent size and underdeployment of stent[6]. In a recently published trial[7], the investigators examined the histopathology of 14 BMS thrombosis lesions using tissue obtained by directional coronary atherectomy in 10 patients and they suggested that new atherosclerotic progression occurs inside the implanted stent without peristrut inflammation. Therefore, VLST after BMS implantation may be a consequence of *de novo* atherosclerotic progression and plaque rupture on the neointimal layer inside the stent. In an another study[8], pathological analysis of the stented human coronary arteries demonstrated heavy infiltration of lipid-laden macrophages around the struts beyond 5 years after coronary stenting, which indicates chronic inflammatory reactions. This chronic inflammation might induce late atherosclerotic progression of the treated lesions. Also, in a case of very late BMS thrombosis[9], ruptured neointima and thrombus at a previously stented segment were identified by intravascular ultrasound (IVUS) examination. In a study[10], the investigators retrospectively reviewed 4503 patients treated with at least one BMS. They showed that the occurrence of BMS thrombosis was 0.8% at 1 year of follow-up and 2.0% at 10 years of follow-up. This finding indicates that 60% of stent thrombosis occurs after 1 year following BMS implantation. According to a meta-analysis of four randomized, controlled trials involving 878 patients treated with a sirolimus-eluting stent, 1400 patients with a paclitaxel-eluting stent and 2267 patients with BMS, there was no difference between DES and BMS in terms of stent thrombosis during 4-year follow-up.This means that VLST occurs not only in patients receiving DES but also in those who had undergone BMS implantation[11]. A recent relevant study[12] demonstrated that stent fracture was a common finding in stent thrombosis after DES and BMS implantation. Re-PCI is the commonly accepted approach to restore blood flow in the occluded stent. It is unclear whether balloon inflation alone, if associated with a good result, is preferable to redeploying a further stent. However, there is insufficient data to support stenting within a stent. In the pathogenesis of very late BMS thrombosis various imaging techniques such as optical coherence tomography (OCT), IVUS, Coronary angioscopy should be considered when assessing patients who present with VLST. According to a recently published case[13], in the light of OCT findings, atheromatous neointimal degeneration, complicated by plaque rupture, plays an important role in VLST in BMSs. In our cases we could not perform any of these imaging methods.

Conclusions

VLST is not only a problem of DES, it also occurs after BMS implantation. Because BMS thrombosis often presents as acute coronary syndrome, it seems that every measure should be taken to suppress atherosclerotic progression after BMS implantation. The pathogenesis of very late BMS thrombosis might be different from that of DES, that is to say plaque rupture on the newly formed neointimal layer within the stent. Further investigations are needed to clarify the mechanism of very late BMSt thrombosis.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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