

Nightmare: Simultaneous Subacute Stent Thrombosis of Different New-Generation Drug-Eluting Stents in Multiple Coronary Arteries

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Simultaneous stent thrombosis (ST) of first-generation drug-eluting stents (DES) has been rarely reported and could lead to high morbidity and mortality. However, to date there was no literature discussing simultaneous ST of different new-generation DESs in multiple coronary arteries. Herein, we report a 60-year-old male suffering from acute myocardial infarction complicated with cardiogenic shock. He had percutaneous coronary intervention (PCI) performed approximately 7 days prior to admission at a local teaching hospital, with different DES devices implanted over the left anterior descending and the left circumflex artery. Emergency coronary angiography revealed simultaneous subacute ST over both vessels. After PCI, there was a gradual improvement in both cardiogenic shock and acute pulmonary edema. High dose clopidogrel (150 mg) was used initially, which was later shifted to ticagrelor. Genetic testing of CYP2C19*2 G681A polymorphism revealed heterozygous genotype and platelet function testing showed substantial inhibition after a medication change. This rare case should remind physicians that new-generation DES thrombosis in multiple vessels is still a possible complication of PCI, and checking genetic and/or platelet function testing might be indicated in these high risk patients. The use of a new antiplatelet drug was also strongly suggested to avoid possible clopidogrel resistance.

Key Words: Clopidogrel resistance • Drug-eluting stents • Genetic testing • Platelet function • Stent thrombosis

INTRODUCTION

Though rarely reported, simultaneous stent thrombosis (ST) of first-generation drug-eluting stents (DES) can lead to high morbidity and mortality.^{1,2} However, there is scant literature discussing simultaneous ST of

different new-generation DES in multiple coronary arteries. Herein we reported a case with simultaneous subacute DES thrombosis involving two different coronary arteries where the patient survived after emergent percutaneous coronary intervention (PCI). Platelet function and genetic testing were both checked in this case to investigate the possible mechanism of ST.

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CASE REPORT

A 60-year-old male suffering from acute chest pain while swimming in the morning was brought to our emergency department (ED). A review of his medical history indicated hypertension and dyslipidemia. A week earlier, the patient had undergone coronary angiography at a local teaching hospital and was diagnosed with

coronary artery disease with three-vessel diseases. At that time, a PROMUS Element 3.0×20 mm stent was deployed over the proximal left anterior descending artery (LAD) and post-dilatation with a Maverick 3.0×8 mm balloon at maximal 20 atm. In addition, a Nobori 3.0×28 mm stent was deployed over the middle left circumflex artery (LCX) and further post-dilatation with Maverick 3.0×8 mm balloon at maximal 20 atm. The patient's right coronary artery was not treated due to the presence of a distal lesion. The patient was then discharged with a recommended course of treatment of dual-antiplatelet therapy (Aspirin 100 mg and clopidogrel 75 mg daily); further information suggested that he complied well with the therapy.

Upon arrival at our ED this time, his blood pressure was 71/55 mmHg. His electrocardiogram (ECG) showed ST elevation over leads I, aVL, and V2-V6 (Figure 1) and chest X-ray showed acute pulmonary edema. A preliminary diagnosis of ST elevation myocardial infarction (STEMI) complicated with cardiogenic shock was made, and vasopressor was used and emergency coronary angiography was performed. Surprisingly, simultaneous subacute stent thrombosis were noted over both the LAD and LCX (Figure 2A & B). The patient first underwent intraaortic balloon pumping (IABP) for hemodynamic support and glycoprotein IIb/IIIa inhibitor (Eptifibatid) was also given for high thrombus burden. Primary PCI with balloon angioplasty over LAD and LCX was subsequently performed. TIMI 2-3 flow was finally restored in the two vessels (Figure 2C & D). The patient

was then transferred to our cardiac care unit (CCU) for intensive care.

During the CCU stay, the patient's hemodynamics became more stable and we gradually removed the vasopressor and IABP. Dual-antiplatelet medication with aspirin 100 mg and clopidogrel 150 mg was given under the impression of possible drug resistance. After high dose clopidogrel was used for one week, we checked

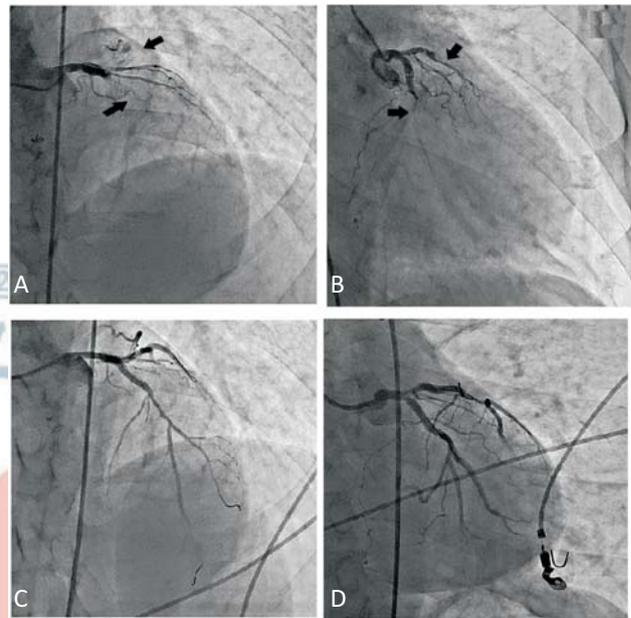


Figure 2. Simultaneous subacute stent thrombosis were noted over both of left anterior descending (LAD) and left circumflex artery (LCX). (A & B, see black arrows). Primary percutaneous coronary intervention with balloon angioplasty over LAD and LCX was performed and TIMI 2-3 flow was restored finally (C & D).

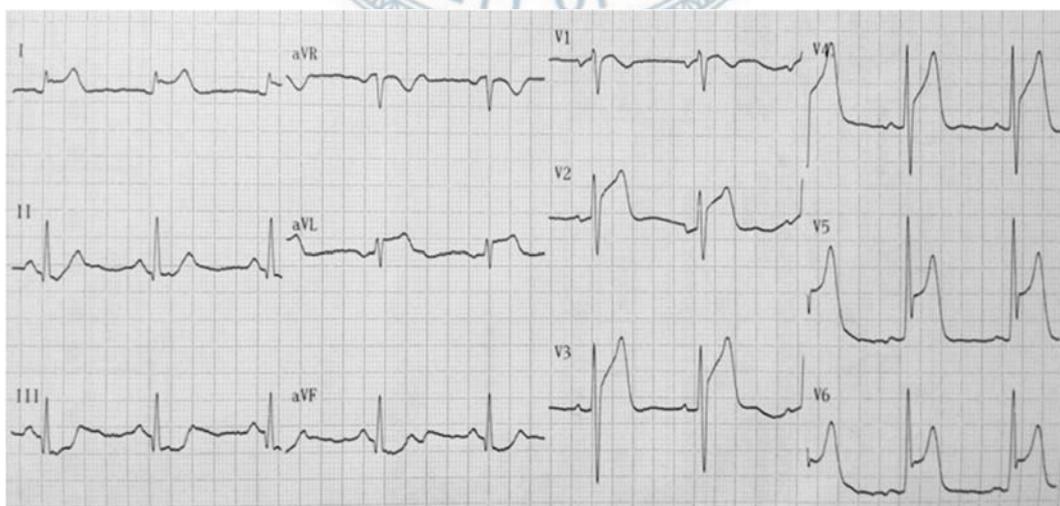


Figure 1. Electrocardiogram showed ST elevation over leads I, aVL, and V2-V6.

the patient's platelet function by VerifyNow P2Y12 assay and found that P2Y12 reaction unit (PRU) was 213 with only 13% P2Y12 inhibition even under high dose clopidogrel use. Genetic testing of CYP2C19 was also evaluated and the results showed heterozygous polymorphism of CYP2C19*2 (G681A). With his condition now relatively stable, the patient was discharged with aspirin and high dose clopidogrel use. At 1st outpatient visit, we changed his medication of clopidogrel to Ticagrelor 90 mg for a twice daily dosage and we further rechecked platelet function about 2 weeks later. The results showed PRU was 66 with 78% P2Y12 inhibition. Therefore, we continued aspirin and ticagrelor use in this patient to avoid the possible recurrent ST episode.

DISCUSSION

ST is an uncommon but troubling complication, and the most frequent clinical manifestation is STEMI associated with high mortality. ST can present as acute (within 24 h), subacute (within 30 days), late (31 days to one year) or very late (more than one year) after stent implantation. Bare metal stent (BMS) thrombosis usually occurs within the first 24 to 48 hours, or much less often within the first month after stent implantation. Similar to BMS, most episodes of DES thrombosis occur in the first year and many of these within the first 30 days. ST related to DES continues after one year for at least five years, and very late ST is more commonly seen with DES than BMS because of the consequence of delayed endothelialization. Nevertheless, DES is safe and efficacious in both on-label and off-label use compared to BMS, and the cumulative rate of ST is similar for BMS and the first-generation DES such as Sirolimus-eluting stent (SES) and Paclitaxel-eluting stent (PES). In addition, in the recent literature, new-generation DES has been reported to be associated with significant lower risk of restenosis and ST.³

Most of the cases of ST in the literature had occurred in single coronary vessel, but there were still some rare cases reporting that simultaneous ST in multiple coronary vessels.^{1-2,4} In these reports, Kang et al. presented a case of simultaneous subacute ST after implantation of SES and BMS.⁴ Other reports showed simultaneous multi-vessel DES thrombosis using first-

generation SES or PES.¹⁻² However, there was no literature discussing about the similar condition in the new-generation DES. To our knowledge, our case was the first report of simultaneous subacute ST of different new-generation DES in multiple coronary arteries. Both the platelet function and genetic testing were checked in this case to investigate the mechanism. According to the literature, the most important cause of ST for DES is premature cessation of dual antiplatelet therapy, but our case did not withdraw the dual antiplatelet medication. In addition, the possibility of stent fracture, stent underexpansion, or thrombosis in one stent with retrograde extension into another stent was not likely in our case because thrombosis did not occur in the left main artery and proximal LAD and LCX but simultaneously in both in-stent territories. Because genetic cause is another important issue of antiplatelet resistance, we also checked platelet function by measuring VerifyNow assay and the results showed partial clopidogrel resistance (PRU: 213 under 150 mg clopidogrel use) which might be related to heterozygous CYP2C19*2 polymorphism. CYP2C19*2 polymorphism is associated with reduced responsiveness to clopidogrel and poor clinical outcome after stent implantation.⁵ Furthermore, in the previous GRAVITAS study, achievement of treatment reactivity < 208 PRU after PCI or during follow-up was associated with a lower risk for cardiovascular events.⁶ Hence, we changed high dose clopidogrel to ticagrelor use later and PRU level revealed significant improvement which implied better platelet inhibition under new-generation antiplatelet use. In the current guideline of use of PCI, despite the evidence being insufficient to recommend either routine genetic or platelet function testing, genetic and/or platelet function testing still may be useful in high risk patients with left main stenosis, diffuse atherosclerotic disease with complex coronary lesions undergoing PCI, or patients with stent thrombosis such as in our case.⁷

CONCLUSIONS

Simultaneous ST of different new-generation DESs in multiple coronary vessels was extremely rare but still a possible complication of PCI and could lead to catastrophic clinical outcome. This rare case reminds physi-

cians that in an era of new-generation DES, we should still keep multiple ST in mind and consider checking platelet function and/or genetic testing in the high risk patients with poor clinical outcomes. Furthermore, new-generation antiplatelet drugs such as ticagrelor or prasugrel were also suggested to avoid possible clopidogrel resistance in these patients.

CONFLICT OF INTERESTS

None to be declared.

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