Acute and Subacute Stent Thrombosis in a Patient With Clopidogrel Resistance: A Case Report

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ABSTRACT

Drug-eluting stents (DES) are considered the treatment of choice for most patients with obstructive coronary artery disease when percutaneous intervention (PCI) is feasible. However, stent thrombosis seems to occur more frequently with DES and occasionally is associated with resistance to anti-platelet drugs. We have experienced a case of recurrent stent thrombosis in a patient with clopidogrel resistance. A 63-year-old female patient suffered from acute myocardial infarction and underwent successful PCI of the left anterior descending coronary artery (LAD) with two DESs. She was found to be hyporesponsive to clopidogrel and was treated with triple anti-platelet therapy (aspirin 100 mg, clopidogrel 75 mg, and cilostazol 200 mg daily). Three days after discharge, she developed chest pain and was again taken to the cardiac catheterization laboratory, where coronary angiography (CAG) showed total occlusion of the mid-LAD where the stent had been placed. After intravenous administration of a glycoprotein IIb/IIIa inhibitor, balloon angioplasty was performed, resulting in Thrombolysis In Myocardial Infarction (TIMI) III antegrade flow. The next day, however, she complained of severe chest pain, and the electrocardiogram showed marked ST-segment elevation in V1-V6, I, and aVL with complete right bundle branch block. Emergent CAG revealed total occlusion of the proximal LAD due to stent thrombosis. She was successfully treated with balloon angioplasty and was discharged with triple anti-platelet therapy.

KEY WORDS: Thrombosis; Stents; Clopidogrel.

Introduction

In recent years, drug-eluting stents (DES) have been demonstrated to dramatically reduce the rate of restenosis and the need for repeat revascularization.1-3 Despite these promising results, stent thrombosis seems to occur more frequently with DES and often seems to be associated with clopidogrel resistance.4 We report a case of recurrent stent thrombosis associated with clopidogrel resistance in a patient with acute myocardial infarction.

A 63-year-old female was transferred to the Emergency Department complaining of squeezing chest pain that had increased over the past twelve hours. The electrocardiogram (ECG) showed ST-segment elevation in V1-V3 (Fig. 1). She underwent emergent coronary angiography (CAG), which revealed critical stenosis in the proximal and middle left anterior descending coronary artery (LAD). She was successfully treated with two paclitaxel-eluting stents (3.0 × 12 mm and 2.5 × 28 mm Taxus stents, Boston Scientific, Reading, PA, USA) in the proximal and middle LAD (Fig. 2). She was treated with triple antiplatelet therapy (aspirin 100 mg, clopidogrel 75 mg, and cilostazol 200 mg daily) because she was found to be hyporesponsive to clopidogrel when tested for adenosine diphosphase (ADP)-induced platelet aggregation utilizing the VerifyNow P2Y12 point-of-care assay (181/0...
Three days after discharge, she again developed chest pain and presented to the emergency department with mental confusion associated with acute pulmonary edema. The ECG showed ST-segment elevation in V1-V5 (Fig. 3) and the cardiac enzymes were elevated (creatine kinase-MB 34.0 U/L, Troponin-I 67.01 ng/mL, Troponin-T 5.5 ng/mL). Emergency CAG, after intubation due to hypoxemia, showed total occlusion of the mid-LAD due to stent thrombosis (Fig. 4). After intravenous administration of a glycoprotein IIb/IIIa receptor blocker (ReoPro®), balloon angioplasty was carried out multiple times using a 3.0 mm balloon at 10-12 atm because of recurrent, immediate thrombus formation and coronary occlusion. The next day, however, she complained of severe chest pain again, and the ECG showed marked ST-segment elevation in V1-V6, I, and aVL; and new-onset complete right bundle branch block with left anterior fascicular block (Fig. 5). Emergent CAG revealed thrombotic total occlusion of the proximal LAD (Fig. 6). She was successfully treated with balloon angioplasty and a final angiogram revealed improved flow over stented LAD without intraluminal filling defect. Despite the cilostazol medication, ADP-induced platelet aggregation

![Fig. 1. The electrocardiogram showed ST-segment elevation in V1-V3.](image1)

![Fig. 2. A: coronary angiogram revealed critical stenosis in the proximal and middle left anterior descending coronary artery (LAD) (arrows). B: two paclitaxel-eluting stents (3.0 × 12 mm and 2.5 × 28 mm Taxus stents, Boston Scientific, Reading, PA, USA) were successfully placed in the occluded LAD.](image2)
showed that she was still hyporesponsive to clopidogrel (171/0 P2Y12 reaction unit/%). She was discharged after uneventful recovery with triple anti-platelet therapy using an increased dose of aspirin (aspirin 200 mg, clopidogrel 75 mg, cilostazol 200 mg daily). The patient has been followed up at the outpatient department without further symptoms.

**Discussion**

We report this case to draw more attention to stent thrombosis associated with clopidogrel resistance after DES implantation. This case shows that a DES patient with clopidogrel resistance can be vulnerable to stent thrombosis even if treated with triple anti-platelet therapy, which in recent studies has been shown to be more effective in preventing stent thrombosis than conventional dual anti-platelet therapy. Recently, there have been safety concerns with DES due to late stent thrombosis. Stent thrombosis is an uncommon but serious complication of coronary artery stents that often presents as myocardial infarction (MI) or death. Over several trials, the incidence of stent thrombosis was 0.58-1.3% in DES. Several factors have been associated with stent thrombosis, including older age, black race, diabetes mellitus, bifurcation lesion, in-stent restenosis lesion, procedure-related factors such as stent malposition, greater stent length, postprocedure acute renal failure, non-compliance to anti-platelet agent and anti-platelet resistance. Anti-platelet resistance as an independent predictor of stent thrombosis, even several years after implantation of DES, increases the risk of stent thrombosis. In this

**Fig. 3.** The electrocardiogram showed newly developed ST-segment elevation in V1-V5.

**Fig. 4.** A: emergent coronary angiogram showed near-total occlusion of the mid-left anterior descending coronary artery (LAD) due to stent thrombosis (arrow). Balloon angioplasty was carried out multiple times using a 3.0 mm balloon at 10-12 atm with the aid of platelet glycoprotein IIb/IIIa inhibitor. B: a final coronary angiogram showed Thrombolysis In Myocardial Infarction (TIMI) III antegrade flow with some remaining filling defects in the LAD.
patient, stent thrombosis may have been caused by several risk factors, especially anti-platelet resistance.

The treatment of anti-platelet resistance is as yet undefined. Several therapeutic approaches (the addition of cilostazol or a glycoprotein IIb/IIIa inhibitor, increased dosage of clopidogrel and aspirin) might be taken for a patient with anti-platelet resistance. In our patient, although cilostazol (200 mg daily) was added to conventional dual anti-platelet therapy, recurrent stent thrombosis occurred. Subsequently, the daily dose of aspirin was increased from 100 mg to 200 mg.

In the DES era, stent thrombosis is a fatal complication and anti-platelet therapy has been shown to be very important in preventing stent thrombosis. Thus, assessment of the patient’s responsiveness to anti-platelet agents may be a crucial factor in monitoring these drugs’ therapeutic efficacy and improving clinical outcomes after implantation of DES. Recent studies have shown that adequate anti-platelet effects are not achieved in 5% to 45% of the patients taking aspirin and in 4% to 30% of patients taking clopidogrel and therefore suggest that many patients are resistant or only partially responsive to the anti-platelet agents. Currently, however, routine screening for anti-platelet resistance remains a persistent, unresolved issue and further evidence is necessary before it will be possible to recommend this testing as part of standard assessment of PCI candidates. In addition, further prospective studies are needed to set guidelines for optimal treatment of patients with antiplatelet resistance who are at increased risk of stent thrombosis, a catastrophic complication of DES implantation.

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Fig. 5. The next day, she complained of chest pain, and the electrocardiogram showed ST-segment elevation in V1-V6, I, and aVL; and new-onset complete right bundle branch block with left anterior fascicular block.

Fig. 6. A: emergent coronary angiogram revealed thrombotic total occlusion of the proximal left anterior descending coronary artery (LAD) (arrow). Balloon angioplasty was performed several times using a 2.5 mm balloon. B: a final coronary angiogram showed Thrombolysis In Myocardial Infarction (TIMI) III antegrade flow with resolution of the thrombus burden.
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