Two cases of acute coronary syndrome that occurred by preoperative discontinuation of antiplatelet therapy in the chronic phase after stent implantation

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Summary
After stent implantation in the coronary arteries, patients sometimes have to undergo invasive examination or treatments that mandate discontinuation of antiplatelet therapy for several days. We encountered two cases of acute coronary syndrome that occurred after preoperative discontinuation of antiplatelet agents in the chronic phase after stent implantation. In the first case, antiplatelet agents were temporarily stopped 5 months after the implantation of a bare metal stent (BMS) in preparation for a kidney transplant. In the second case, antiplatelet agents were stopped 1.5 months after BMS implantation in preparation for esophageal bypass surgery. In both cases, acute myocardial infarction occurred just after the invasive operation, despite the fact that they had continued dual antiplatelet therapy for the period recommended by the American Heart Association/American College of Cardiology guideline. This report provides a warning about the temporary discontinuation of antiplatelet agents even in the chronic stage of coronary stent implantation.

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that patients should be treated with clopidogrel and aspirin for 1 month after BMS implantation, 3 months after sirolimus-eluting stent implantation, 6 months after paclitaxel-eluting stent implantation, and ideally, up to 12 months if possible, in order to provide continued protection for in-stent thrombosis [3]. The U.S. Food Drug and Administration recommends adherence to the labeling for use of stents to avoid in-stent thrombosis. However, it is unclear how long dual antiplatelet therapy should be continued before the patients safely stop antiplatelet agents. Here we report two cases of acute coronary syndrome that occurred after preoperative discontinuation of antiplatelet therapy following stent implantation. In both of the cases reported here, the patients had been administered dual antiplatelet agents for at least as long as recommended by the AHA/ACC guideline, but stent thrombosis occurred during the discontinuation of antiplatelet therapy in the perioperative period. This report will alert physicians that preoperative discontinuation of antiplatelet therapy may be a risk for acute coronary syndrome even in the chronic stage after stent implantation.

Case reports

Case 1

A 51-year-old man was admitted to our hospital to undergo kidney transplantation in October 2007. He had a past history of diabetic nephropathy, and had started to undergo hemodialysis in September 2006. He was admitted to our hospital to undergo kidney transplantation on April 24, 2007. Stress thallium scintigraphy performed on April 27 revealed stress-induced ischemia in the anteroseptal area of the heart. Coronary angiography revealed severe stenosis in the mid-portion of the left anterior descending artery (Fig. 1A). He underwent percutaneous coronary intervention (PCI) on May 25, 2007. A bare metal stent (Liberte stent, 2.75 mm × 24 mm) was implanted in the stenotic lesion (Fig. 1B and C). Dual antiplatelet therapy using 100 mg of aspirin and 200 mg of ticlopidine per day was started and he was discharged from the hospital on May 30. The patient was subsequently readmitted to the hospital for kidney transplantation on October 10. Aspirin and ticlopidine were discontinued and intravenous administration of
Figure 2. Angiographic findings of Case 2. (A) Coronary angiography (CAG) was performed in June 2008. There was a severe stenosis in the mid-portion of the right coronary artery (RCA). (B) A Driver stent (3.5 mm × 18 mm) was implanted in the RCA on July 2. (C) Final angiogram at percutaneous coronary intervention showed adequate dilatation of the stent. (D) Acute myocardial infarction occurred on September 3. CAG showed thrombosis at the proximal portion of the Driver stent. (E) After thrombectomy and balloon dilatation (Marverick, 3.75 mm × 20 mm, 12 atm), another Driver stent (3.5 mm × 15 mm) was successfully implanted in the thrombosed lesion. (F) Final angiogram of the target lesion revascularization.

Heparin at a dose of 400—600 units/h was started on October 11, keeping the activated partial thromboplastin time (APTT) between 40 and 60 s. On October 23, oral administration of beta-blocker (5 mg of bisoprolol per day) was stopped. On October 24, he underwent kidney transplantation. In the morning of the next day, he complained of chest compression. The time from discontinuation of heparin to the onset of chest compression was 18 h. An electrocardiogram (ECG) showed ST elevation in leads V1–V5. He underwent emergent coronary angiography, which showed definite thrombosis according to the Academic Research Consortium (ARC) definitions in the existing Liberte stent (Fig. 1D). Red thrombus was collected by thrombectomy followed by successful balloon angioplasty (Voyager, 2.75 mm × 20 mm, max. 10 atm, Fig. 1E). Peak serum creatine kinase was 1200 IU/ml (16 h after the onset). There were no other major complications and the patient was discharged from the hospital on December 9.

Case 2

A 66-year-old man was admitted to our hospital with the diagnosis of carcinoma of the esophagus on June 15, 2007. Stress scintigraphy revealed stress-induced ischemia in the inferior wall. He underwent coronary angiography (CAG) on June 30. CAG showed severe stenosis in the mid-portion of the right coronary artery (RCA). He started dual antiplatelet therapy (100 mg of aspirin and 200 mg of ticlopidine per day), and underwent PCI on July 2. A bare metal stent (Driver stent, 3.5 mm × 18 mm) was successfully implanted (Fig. 2A–C). Aspirin and ticlopidine were discontinued and intravenous administration of heparin at a dose of 500–700 units/h was started on August 12, 2007, keeping APTT between 40 and 60 s. Oral administration of beta-blocker (60 mg of metoprolol) was stopped on August 18. He underwent esophageal bypass surgery on August 19, 2007. Heparin was restarted on August 22. However, before restarting the antiplatelet and beta-blocker therapy, on September 2, he complained of chest pain and an ECG revealed ST elevation in leads II, III, and aVF. He underwent emergent CAG on suspicion of acute myocardial infarction. CAG showed definite thrombosis in the stent according to the ARC definitions (Fig. 2D). Red thrombus was collected by thrombectomy followed by balloon dilatation and the implantation of another Driver
ACS at the chronic phase of stent implantation

stent (3.5 mm × 15 mm, Fig. 2E and F). Serum creatine kinase rose to 1626 IU/ml 18 h after the onset of myocardial infarction.

Discussion

Here we report two cases of acute coronary syndrome that occurred after preoperative discontinuation of antiplatelet therapy in the chronic phase of stent implantation. There are no clear guidelines and definitive strategy for the treatment of patients who undergo stent implantation and have to discontinue antiplatelet therapy in preparation for an invasive treatment. According to the AHA/ACC guideline, in order to prevent in-stent thrombosis after coronary stent implantation, patients should be treated with clopidogrel and aspirin for at least 1 month after BMS implantation [3]. These are based on the anticipated time it takes for the stent struts to become adequately endothelialized. In the cases presented here, acute coronary syndrome occurred because of discontinuation of dual antiplatelet therapy; in Case 1 after 5 months and in Case 2 after 1.5 months. Based on these findings, care should be exercised when discontinuing antiplatelet therapy even in the chronic phase after stent implantation.

Thus far, several risk factors of in-stent thrombosis have been reported, morphological and procedural factors such as long stents, small vessels, and suboptimal stent results, as well as clinical factors such as advanced age, renal failure, diabetes, and the use of immunosuppressive agents that may promote endothelial dysfunction [4—8]. In Case 1, several factors such as relatively small stent (2.75 mm in diameter), renal failure, diabetes, and immunosuppressive agents might have contributed to the in-stent thrombosis. However, in Case 2, there seems to be no additional risk factors other than discontinuation of antiplatelet therapy. So we should reconsider the period of dual antiplatelet therapy after stent implantation, and take more care to avoid in-stent thrombosis even if the patient seems to have little risk for in-stent thrombosis.

Several pathological mechanisms of stent thrombosis have been reported [9]. In the two cases of our report, there is a possibility that plaque rupture occurred at the proximal portion of the stents, or there had been a plaque prolapse at stent struts, inducing stent thrombosis. It was also reported that thrombosis is closely related to the hyper-inflammatory state [10—12]. In both of our cases, inflammatory reaction might have been evoked at the stent sites by stopping aspirin. Anti-inflammatory drugs such as statins might be useful in such cases [13]. In any case, discontinuation of antiplatelet drugs might have been the most crucial trigger for stent thrombosis.

According to another AHA/ACC advisory regarding the discontinuation of dual antiplatelet therapy in patients with coronary artery stents [14], implantation of BMS or balloon angioplasty should be considered in patients who are undergoing preparation for PCI and are likely to require invasive or surgical procedures within the next 12 months. In both cases reported here, it might have been better to perform as a first treatment option PCI by balloon angioplasty only.

The AHA/ACC advisory described above also states that aspirin should be continued if possible for patients treated with coronary stents who are to undergo subsequent procedures that mandate discontinuation of thienopyridine therapy, and that thienopyridine should be restarted as soon as possible after the procedure [14]. In these two cases, it might have been better to perform kidney transplantation and esophageal bypass surgery with continuing aspirin if at all possible, or consider the use of other antiplatelets that have shorter half-life-time such as cilostazol and beraprost, etc. until a few days before the surgical procedure.

The AHA/ACC guideline also recommends perioperative beta-blocker therapy for patients with risk of coronary artery disease [15]. Beta-blocker therapy had been discontinued for 1 day in Case 1, and 14 days in Case 2 when stent thrombosis occurred. Discontinuation of the beta-blocker might also have contributed to the in-stent thrombosis. Administration of intravenous beta-blocker may be effective to prevent stent thrombosis when the patient cannot take oral therapy.

In conclusion, we encountered two cases of acute coronary syndrome that occurred after preoperative discontinuation of antiplatelet therapy in the chronic phase of stent implantation. This report provides a warning about the temporary discontinuation of antiplatelet therapy in the chronic state of coronary stent implantation.

References


