Case Report

Complete disappearance of red thrombi in a drug-eluting stent despite discontinuation of antiplatelet therapy: Angioscopic confirmation

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Summary We present the case of a 48-year-old man with unstable angina who underwent drug-eluting stent (DES) implantation for the left circumflex artery (LCx). Red thrombi within the stent were clearly found by coronary angioscopy. Dual antiplatelet therapy was orally given before the stenting. Twenty-two months after the procedure, the patient visited because of severe chest pain. The patient had stopped taking all prescriptions including antiplatelet drugs for the previous 18 months. The occurrence of late stent thrombosis (LST) derived from previously implanted DES in the LCx was strongly suspected. Unexpectedly, the left coronary angiograms showed neither in-stent restenosis nor thrombotic occlusion. Angioscopic images for the DES segment showed that there were no uncovered stent struts without neointimal coverage. Notably, red thrombi identified immediately after stenting by angioscopy had completely disappeared. Mural red thrombi at the first observation completely disappeared despite premature cessation of dual antiplatelet therapy. Early neointimal coverage may occasionally occur even under the condition of acute coronary syndrome. The leading cause of LST was not only the cessation of dual-antiplatelet therapy and multiple factors contribute to LST of DES. Relatively early and adequate neointimal stent coverage may reduce the risk of thrombus formation including LST even though anti-platelet therapy was discontinued prematurely.

Keywords Stent thrombosis; Dual antiplatelet therapy; Drug-eluting stent; Coronary angioscopy
Introduction

In recent years, late stent thrombosis (LST) after drug-eluting stent (DES) implantation has become a major clinical concern. A long-term follow-up study revealed that LST occurs at a constant rate of 0.4—0.6% per year for up to four years after DES implantation [1]. Up to now, optimal duration of dual antiplatelet treatment after DES implantation for prevention of LST is unclear. However, premature discontinuation of antiplatelet therapy is an established predictor of subacute thrombosis and LST [2]. A previous serial angioscopic study demonstrated new thrombus formation in the DES despite continuous administration of dual antiplatelet therapy (DAPT) [3]. The influence of premature discontinuation of antiplatelet therapy on appearance or disappearance of thrombus in DES is uncertain.

Case report

A 48-year-old man with unstable angina underwent coronary stenting under guidance with intravascular ultrasound (IVUS) for severe stenosis in the left circumflex artery (LCx). He was a current smoker and diagnosed as having impaired glucose tolerance (IGT; glycated hemoglobin A1c 5.2%), hypertension, dyslipidemia, and renal insufficiency (creatinine 1.16 mg/dl). After balloon angioplasty (Quantum Maverick™, 3.25/15 mm; Boston Scientific, Natick, MA, USA), a sirolimus-eluting stent (Cypher stent™, 3.5/18 mm; Cordis, Bridgewater, NJ, USA) was deployed at a pressure of 20 atm (Fig. 1B). Red thrombi within the stent were clearly found by coronary angioscopy (Fig. 1C and D). DAPT, aspirin 200 mg, and ticlopidine 200 mg/day, were orally given before the stenting. Atorvastatin (20 mg/day), nicorandil (15 mg/day), enalapril (10 mg/day), and azelnidipine (8 mg/day) were also given for control of coronary risk factors and his low-density lipoprotein cholesterol level was 102 mg/dl before discharge. Twenty-two months after the procedure, the patient visited our hospital because of severe chest pain. The patient had stopped taking all prescriptions including antiplatelet drugs by his own judgment for the previous 18 months. The occurrence of LST derived from previously implanted DES in the LCx was strongly suspected and we performed emergent coronary angiography (CAG). Unexpectedly, the left coronary angiograms showed neither in-stent restenosis nor thrombotic occlusion (Fig. 2B) and angiographic late loss in the stent segment was 0.2 mm. Alternatively, there was an atherosclerotic lesion progressing mild to severe stenosis in the right coronary artery (Figs. 1A and 2A). Angioscopic images for the DES segment showed that there were no uncovered stent struts without neointimal coverage. Notably, red thrombi identified immediately after stenting by angioscopy completely disappeared (Fig. 2C and D). The 3rd CAG was planned to assess whether the thin-layer structures identified by macroscopic diagnosis had an adequate endothelial function, and endothelium-dependent coronary vasomotion was estimated by intracoronary infusion of incremental doses of acetylcholine (ACh), 0.3 μg/min, 3 μg/min, and 30 μg/min, into the ostium of left coronary artery. Abnormal vasoconstriction to ACh was not induced in this case (Fig. 3), it was therefore proven that the neointima had a good endothelial function with anti-thrombotic effect.

Discussion

Long-term follow-up observations focusing on neointimal coverage after DES implantation showed that uncovered struts and subclinical thrombus formation remained occasionally [3]. In the current case, angioscopy could not identify any uncovered struts and the majority of struts were fully covered by thin neointima. No thrombi were recognized at the second observation by angioscopy. In other words, mural red thrombi at the first observation completely disappeared despite immature cessation of DAPT.

According to a recent analysis of optical coherence tomography, the frequency of uncovered struts was correlated with abnormal vasoconstriction by intracoronary ACh provocation after zotarolimus-eluting stent implantation [4]. In a previous report with angioscopy, 13% of SESs had complete coverage that means stent struts were visible but not translucent or struts were not visible (grade 2

Figure 1  (A) Coronary angiography (CAG) revealed a mild stenosis in the distal of right coronary artery. (B) CAG revealed a severe stenosis in the distal of left circumflex artery. The vessel was successfully treated with a sirolimus-eluting stent (Cypher 3.5/18 mm, blue arrow). (C and D) Coronary angioscopy showed mural reddish thrombi with yellow plaque.
Figure 2  (A) The second coronary angiogram (CAG) revealed a progressive stenosis in the distal of the right coronary artery. (B) The second CAG showed no significant in-stent stenosis and no thrombotic occlusion in the left circumflex artery. (C and D) Coronary angioscopy showed most of the stent struts were visible under a thin neointima and some struts were invisible by the thick neointima. There was no complete exposure without neointima. There were also no massive protruding and mural thrombi.

or 3, respectively) following 3–6 months of their implantation [5]. In the present case, neointimal coverage on all struts was regarded as grade 2 or 3. Moreover, the thin-layer structures identified by macroscopic diagnosis with angioscopy have an adequate endothelial function including anti-thrombotic effect. Probably, the neointima sufficiently might have covered over the struts in relatively early phase because LST did not occur in the present case despite immature DAPT discontinuation.

It is meaningful to consider the mechanism of the unexpected phenomena without stent thrombosis. First, the deployed stent had large diameter with satisfactory attachment to the vessel wall, so-called good apposed stent on IVUS findings. Adequate stent dilatation to the vessel contributes to the complete neointimal coverage by angioscopy after SES implantation [6].

Second, stent length was not so long because the culprit lesion was discrete. Longer stenting is one of the predictors of stent thrombus formation.

Third, the pre-existing yellow plaque and mural thrombi might be associated with decreased neointimal coverage of SES [7]. Otherwise, it was recently reported that acute coronary syndrome might promote neointimal coverage after SES implantation [8]. Early neointimal coverage could occasionally occur even under the condition of acute coronary syndrome including unstable angina as in this case.

Diabetes mellitus (DM) is an independent predictor of early ST which occurs within 30 days after stent deployment. By contrast, neointimal coverage and its thickness are greater in DM than in non-DM after SES implantation [9]. DM and IGT show similar characteristics of vessel pathophysiology, therefore IGT might contribute to early neointimal coverage in this case.

The mechanisms of stent thrombosis after DES implantation are multi-factorial and include the patient, lesion, and procedural factors, as well as the drug compliance or the reactivity to antiplatelet therapy. Similarly, the leading cause of LST was not only the cessation of DAPT and multiple factors contribute to LST of DES. As this case suggested, relatively early and adequate neointimal stent coverage may reduce the risk of thrombus formation including LST even though anti-platelet therapy was discontinued immaturely. LST of first-generation DES constantly occurs at an annual rate of 0.4–0.6%, we should therefore be aware of

Figure 3  (A–C) There were no vasoconstrictive responses to intracoronary acetylcholine (Ach) infusion. GTN, glyceryl trinitrate.
the possibility of LST after discontinuation of anti-platelet treatment. Nevertheless, the present case may support DES safety in specific patients regardless of immature cessation of DAPT.

References


