

CASE REPORT

Early definite stent thrombosis with everolimus-eluting stents

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Case Report

A 54-year-old Japanese male was referred to our hospital with a diagnosis of ST elevation myocardial infarction. An electrocardiogram revealed ST elevation in leads V₁₋₄, with reciprocal changes in the inferior leads. Echocardiography demonstrated a reduced left ventricular ejection fraction of 40% and akinesis extending from the mid-anteroseptal wall to the apex. Coronary angiography demonstrated an obstruction of the proximal segment of the left anterior descending artery (LAD) and a 90% stenosis of the second diagonal branch (Fig. 1A). Thrombus aspiration and balloon angioplasty were performed, and coronary flow of Thrombolysis in Myocardial Infarction (TIMI) grade 3 was attained (Fig. 1B). Following the procedure, angiography demonstrated that the lesion was complicated, as it was characterized by long length and a Medina type 0, 1, 1 bifurcation with the second diagonal branch. Considering that the area of myocardium supplied by the second diagonal branch was relatively wide, we decided to treat these lesions with DES after confirming the safety of dual antiplatelet therapy with aspirin and clopidogrel. After 14 days, percutaneous coronary intervention (PCI) with EESs was performed, using the Culotte technique for the bifurcated lesions. Xience Prime (Abbott Vascular, Santa Clara, CA),

Key Clinical Message

Stent thrombosis (ST) is a serious complication of percutaneous coronary intervention. Several factors are associated with ST, and combination of these factors increase the risk, even in everolimus-eluting stents, which have low risk of ST. We experienced a case of ST caused by limited coronary flow and resistance to antiplatelet agent.

Keywords

Coronary flow limitation, CYP2C19 polymorphism, everolimus-eluting stent, stent thrombosis.

2.75 × 33 mm, and Xience Prime, 2.25 × 23 mm, were each deployed to the proximal site of LAD and to the diagonal branch, respectively (Fig. 1C). Coronary angiography demonstrated no residual stenosis in either the culprit lesion or the diagonal branch, except for a 50% stenosis just below the stent in the second diagonal branch. Intravascular ultrasound performed following stent deployment did not demonstrate stent malapposition or stent underexpansion. The patient was discharged without any complications.

Seven days following stent implantation, the patient's chest pain at rest recurred. An electrocardiogram at a neighboring clinic revealed ST elevation in the anterior precordial leads. Coronary angiography demonstrated occlusion of the proximal segment of left anterior descending artery (Fig. 2). The patient was diagnosed with acute myocardial infarction due to early definite coronary stent thrombosis. Thrombus aspiration and balloon angioplasty were performed, and an EES (2.25 × 18 mm; Xience Prime) was deployed at the second diagonal branch, distal to the previously implanted stent, because that site had significant stenosis that may have limited coronary flow and caused stent thrombosis. PCI was performed without any complications (Fig. 3).

We examined the causes of stent thrombosis. First, premature discontinuation of dual antiplatelet therapy was

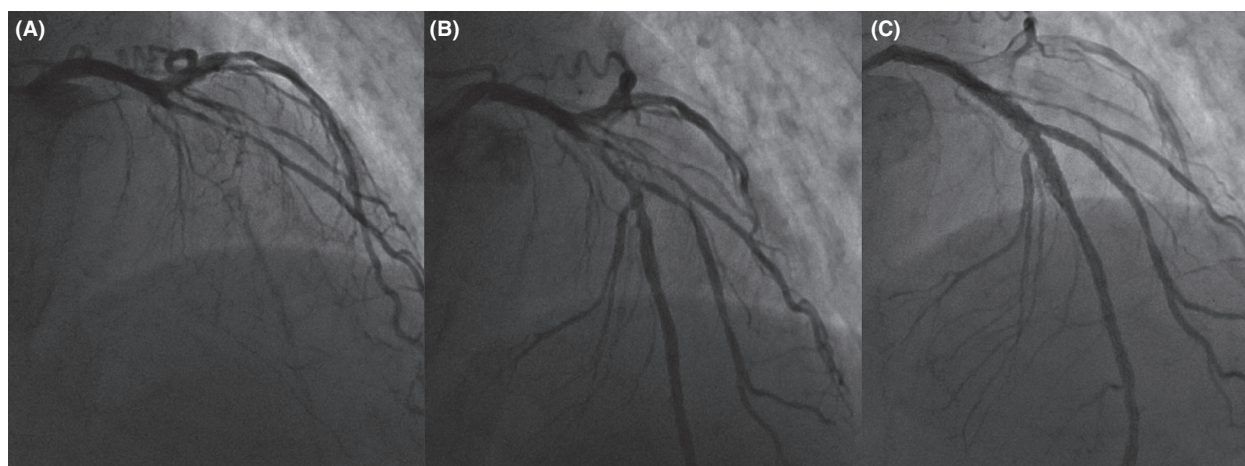


Figure 1. (A) Emergent coronary angiography for ST elevation myocardial infarction. Emergent coronary angiography demonstrated the occlusion of a proximal segment of the left anterior descending artery. (B) Coronary angiography after thrombus aspiration and balloon angioplasty. Coronary angiography demonstrated that the lesion was complicated with long lesion length and bifurcation with the second diagonal branch. (C) A final angiogram following EES implantation. A final angiogram following EES implantation demonstrated favorable blood flow in both the left anterior descending artery and a diagonal branch.



Figure 2. Coronary angiography at 7 days following the EES implantation. Definite stent thrombosis was diagnosed via coronary angiography at 7 days following the implantation of the EES.

excluded via history taking. Stent fracture, stent underexpansion, and stent malapposition were not observed via coronary angiography or intravascular ultrasound. Cilostazol was added because the patient was considered to be resistant to clopidogrel. Adenosine diphosphate (ADP)-induced platelet aggregation was preserved with a value of 45% (normal range, 30–70%), and collagen-induced platelet aggregation was reduced to 54% (normal



Figure 3. A final angiogram after PCI to definite stent thrombosis. A final angiogram following PCI to the site of definite stent thrombosis demonstrated favorable blood flow in both the left anterior descending artery and a diagonal branch.

range, 60–100%), secondary to treatment with aspirin and clopidogrel, as well as cilostazol. Additionally, platelet responses were evaluated using VerifyNow Aspirin, P2Y₁₂ assays (Accumetrics, San Diego, CA). The platelet reaction units (PRUs) for clopidogrel were 299 (therapeutic range, below 233), and the PRUs for aspirin were 420 (therapeutic range, below 550). Furthermore, we searched for

cytochrome P450 (CYP) 2C19 polymorphisms and discovered that the patient carried a wild-type allele and a CYP2C19 loss-of-function variant of the CYP2C19*2 allele, which indicated that the patient was an intermediate metabolizer of clopidogrel. The patient was discharged without additional cardiovascular events. Follow-up coronary angiography at 7 months following the occurrence of stent thrombosis demonstrated the preservation of blood flow in the left anterior descending artery.

Discussion

This is a case of early definite coronary stent thrombosis associated with ST elevation myocardial infarction at 7 days following EES implantation. Stent thrombosis is a serious complication of PCI with stenting and often presents with an acute coronary syndrome and carries a high mortality rate [1]. The advent of newer generation DES such as EES has made stent thrombosis less of a concern than it was with previous devices. However, stent thrombosis remains a clinically important issue given the high rates of both myocardial infarction and mortality following acute stent thrombosis, even in this new generation DES-era. There are several factors associated with the incidence of stent thrombosis, including patient- and procedure-related characteristics. In particular, premature discontinuation of dual antiplatelet therapy, diabetes, and procedure-related factors such as stent fracture, stent underexpansion, and stent malapposition are each related to the occurrence of early stent thrombosis [2]. EES have demonstrated a lower incidence of stent thrombosis compared with other DESs because of the rapid and complete re-endothelialization that occurs due to the EES having the thinnest stent struts among the available DES [3], as well as less thrombogenicity and inflammation due to the biocompatible polymer composition of the stent [4] and the resistance to fracture incurred by its cobalt–chromium design. However, it is difficult for even EES to prevent stent thrombosis in lesions with an inflow or outflow obstruction, which has been demonstrated to be a significant variable associated with early ST [5]. In this case, the combination of metallic overlapping by the Culotte stent and residual stenosis distal to the prior stent at the second diagonal branch may have caused inflow and outflow obstructions that resulted in early stent thrombosis. Regarding the use of the two-stents technique, safety concerns have been raised in the previous report. In a meta-analysis by Zhang *et al.* [6], two-stents strategy for treatment of bifurcation lesions was associated with a higher risk of early myocardial infarction compared with single stenting or provisional stenting of side branch for the side branch occlusion, although the rate of definite ST was similar between the two strategies. However, in

our case, the side branch had a significant stenosis with large area of myocardium supplied by the branch, we selected two-stents strategy using Culotte technique for the bifurcation lesion. Of interest, the patient's CYP2C19 polymorphism preserved platelet reactivity as determined by the VerifyNow, P2Y12 assay, in spite of the use of dual antiplatelet therapy, which may have caused stent thrombosis. In Asian people, the prevalence of the CYP2C19 gene polymorphism is higher compared with people living in other countries [7]. Although there are conflicting data regarding definite effects of CYP2C19 polymorphisms on the incidence of cardiovascular events [8, 9], a recent report demonstrated that residual platelet activity was associated with cardiovascular mortality [10], which supported the observed relationship between our case and the incidence of stent thrombosis.

In conclusion, stent thrombosis is a life-threatening condition that occurs following stent implantation. Although newer generation DES have reduced the incidence of stent thrombosis, there remain several factors associated with the occurrence of stent thrombosis. We must account for the patient-, lesion-, and procedure-related factors associated with the occurrence of stent thrombosis and minimize the impacts of these factors when performing PCI with stent implantation.

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Conflict of Interest

None declared.

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