

Open Access

Late Stent Thrombosis After Drug-Eluting Stent Implantation: A Rare Case of Accelerated Neo-Atherosclerosis and Early Manifestation of Neointimal Rupture

Young-June Yang, MD¹, Mihyun Kim, MD¹, Choongki Kim, MD¹, Junbeom Park, MD¹,
Jaewon Oh, MD¹, Hoyoun Won, MD¹, Byeong-Keuk Kim, MD¹, and Myeong-Ki Hong, MD^{1,2}

¹Division of Cardiology, Severance Cardiovascular Hospital, ²Severance Biomedical Science Institute, Yonsei University College of Medicine, Seoul, Korea

ABSTRACT

An 80-year old woman suffered from sudden onset of chest pain and dyspnea, and visited the emergency room. She received stent implantation with a biolimus A9-eluting stent (Nobori® 3.0×24 mm) at the mid-portion of the left anterior descending artery 5 months prior to admission. The emergency 5-month follow-up angiogram was performed under the impression of late stent thrombosis. The follow-up angiogram showed subtotal occlusion at the mid-portion of the left anterior descending artery, which was the same segment of previous stent implantation 5 months ago. Immediately after thrombus aspiration with the thrombus aspiration catheter, the optical coherence tomography showed layered appearance of neointimal hyperplasia and neointimal rupture within the previously stented segment. Thus, neointimal rupture within accelerated growth of neointimal tissue was observed within a relatively shorter period (i.e., about 5 months) after stent implantation. (**Korean Circ J 2011;41:409-412**)

KEY WORDS: Stents; Thrombosis; Neointima.

Introduction

Implantation of 1st generation drug-eluting stents (DESs) has significantly reduced the incidence of restenosis and the need for repeat revascularization, compared to previously used bare-metal stents.^{1,2} However, increased use of DESs has raised safety issues regarding the occurrence of stent thrombosis.^{3,4} In the 1st generation DES, persistence of polymer even after complete elution of drugs may cause either hypersensitivity reaction or inflammation in the stented coronary segments, and both these conditions are associated with increas-

ed risk for stent thrombosis.⁵ To overcome this life-threatening complication, many newly designed DESs have been developed. Compared to previous DESs, the biolimus A9-eluting stent (BES, Nobori®, Terumo Corporation, Tokyo, Japan) has the characteristics of abluminally applied drug polymer matrix and biodegradable polymer (i.e., polymer degradation over the period of 6 to 9 months).⁶ We experienced a rare case of late stent thrombosis in patients who underwent implantation of a BES and follow-up optical coherence tomography (OCT) for investigation of late stent thrombosis.

Case

An 80-year old woman suffered from sudden onset of chest pain and dyspnea, and visited the emergency room. She had a history of hypertension, hyperthyroidism and major depressive disorder. Five months prior to admission, she visited the cardiology outpatient clinic for the further evaluation of syncope. The coronary computer tomography and coronary angiography revealed significant stenosis at the mid-portion of the left anterior descending artery (mLAD; B2, 80%, III, 0) (Fig. 2A) and a BES (Nobori® 3.0×24 mm) was success-

Received: March 3, 2011

Accepted: April 11, 2011

Correspondence: Myeong-Ki Hong, MD, Division of Cardiology, Severance Cardiovascular Hospital, Yonsei University College of Medicine, 250 Seongsan-ro, Seodaemun-gu, Seoul 120-752, Korea
Tel: 82-2-2228-8458, Fax: 82-2-2227-7732
E-mail: mkhong61@yuhs.ac

• The authors have no financial conflicts of interest.

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

fully deployed, without residual narrowing (Fig. 2B) at that time. Pulmonary congestion in both lung fields, suggestive of pulmonary edema, was noticed on the chest X-ray; newly de-

veloped Q wave was visible at leads V1-4 on the electrocardiogram (Fig. 1); recent regional wall motion abnormality (i.e., akinesia without thinning) was detected in the left anterior de-

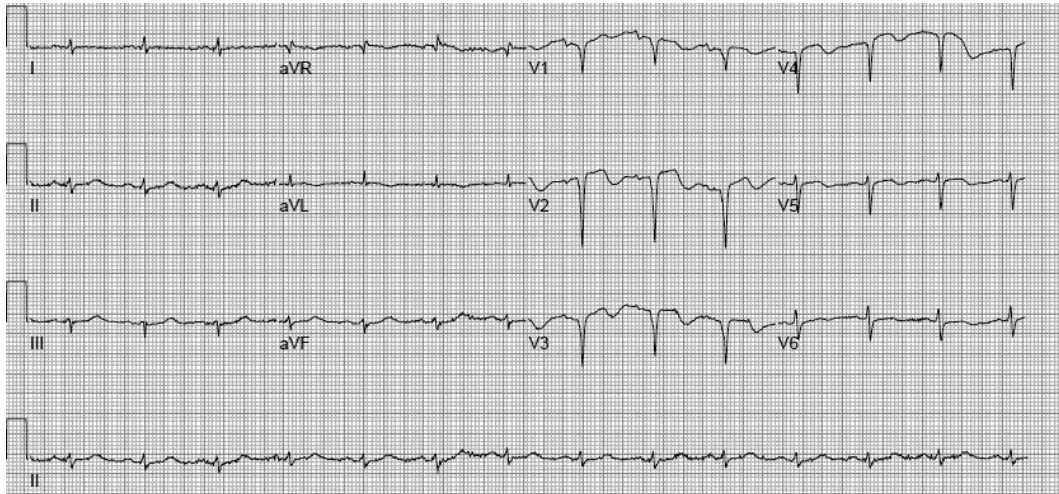


Fig. 1. First electrocardiogram at recorded in the emergency room; the Q wave was visible at on leads V1-4.

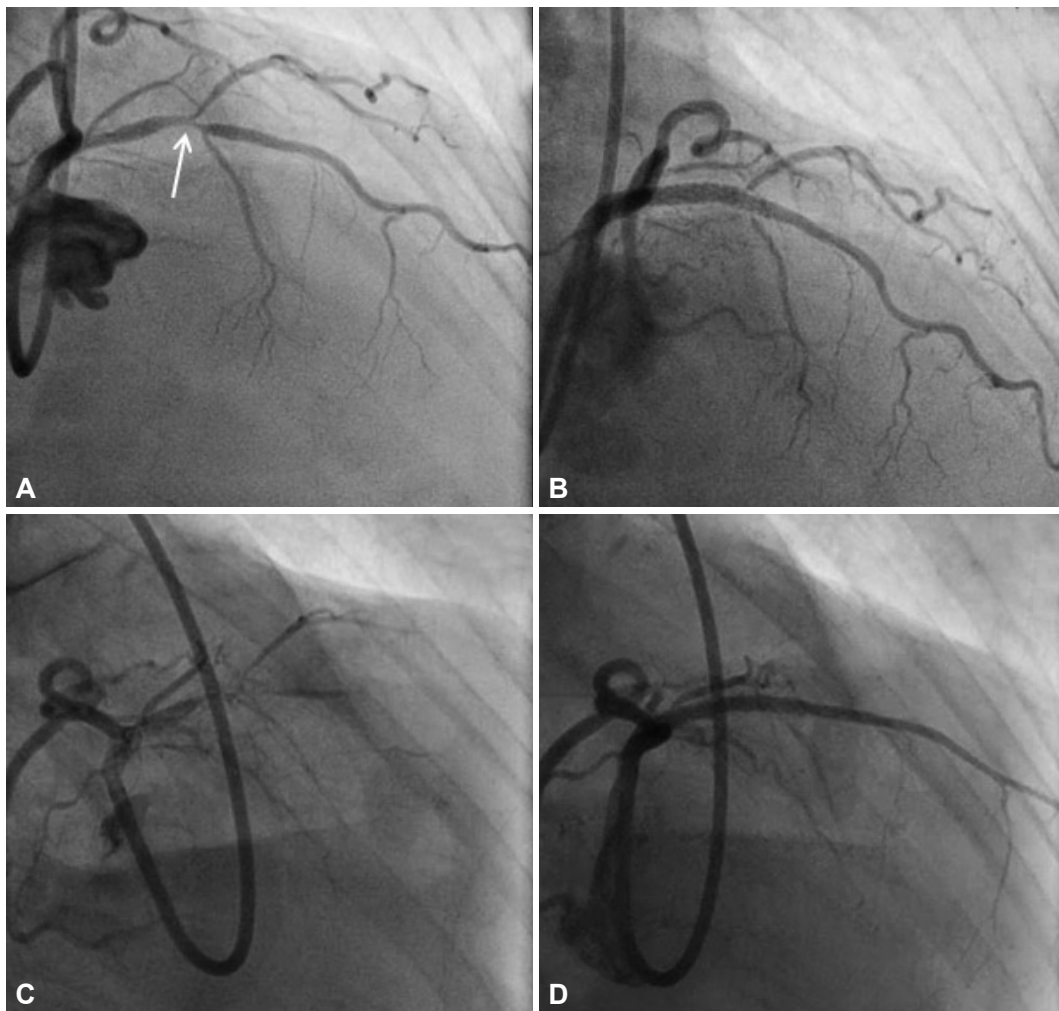


Fig. 2. Pre-intervention (A) and post-intervention (B) angiographic findings in lesion of the left anterior descending artery (arrow in A) are shown 5-months before the onset of late stent thrombosis. At the onset of late stent thrombosis, emergency follow-up angiogram showed sub-total occlusion at the mid-portion of the left anterior descending artery (C). The final angiogram, performed after balloon angioplasty with a drug eluting balloon, showed no residual stenosis at the mid-portion of the left anterior descending artery and a jailed diagonal branch (D).

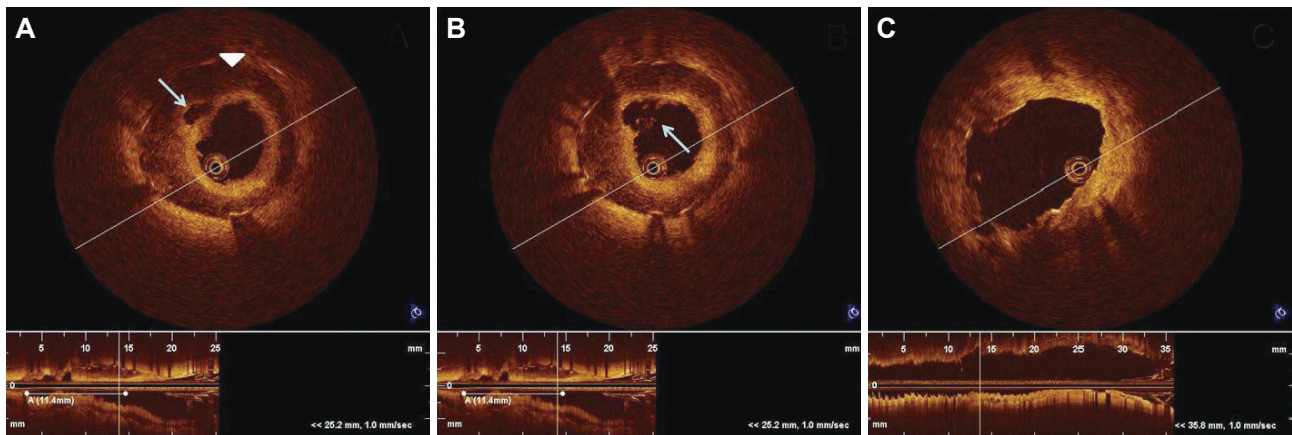


Fig. 3. The optical coherence tomography (OCT) showed layered appearance (arrowhead) of neointimal hyperplasia and neointimal rupture (arrow) within the previously stented segment (A and B). OCT image after balloon angioplasty with a drug eluting balloon (C).

scending artery territory, and the left ventricular ejection fraction was reduced by 30% on the echocardiogram at this time. Cardiac enzyme was slightly elevated (Troponin-T 0.124 ng/mL). Emergency follow-up angiogram was performed under the impression of non-ST elevation myocardial infarction, caused by late stent thrombosis. The follow-up angiogram showed subtotal occlusion at the mid-portion of the left anterior descending artery, the same segment of previous stent implantation 5 months ago (B2, 99%, II, 0) (Fig. 2C). Immediately after thrombus aspiration with the thrombus aspiration catheter (Thrombuster II®, Kaneka Corp. Japan), OCT was performed for investigation of both morphologic features and underlying cause of late stent thrombosis. The OCT showed layered appearance of neointimal hyperplasia and neointimal rupture within the previously stented segment (Fig. 3A and B). Considering that the stent thrombosis was not due to delay of stent strut endothelialization, balloon angioplasty with a drug eluting balloon (SeQuent please®, B. Braun Melsungen AG, Germany) was successfully performed at the mid-portion of the left anterior descending artery with no residual stenosis, however jailed diagonal branch (Figs. 2D and 3C). After the surgical procedure, she was discharged 3 days later, without any significant complications.

Discussion

Occurrence of stent thrombosis has been the major concern after implantation of 1st generation DESs. Iakovou et al.³⁾ reported 1.3% incidence of stent thrombosis in patients who received DES implantation. In addition, 45% of the patients who experienced stent thrombosis died. Daemen et al.⁴⁾ also reported that stent thrombosis occurring within 30 days after DES implantation increases 0.6% annually. While occurrence of acute or subacute stent thrombosis (i.e., onset of stent thrombosis within 30 days after stent implantation) is mainly related to procedural factors, development of late or very late stent thrombosis has different characteristics. Previous pa-

thologic studies showed that delayed stent strut endothelialization and potential prothrombotic properties of the DES itself (i.e., persistence of polymer even after complete elution of drugs) are important factors that may lead to late stent thrombosis.^{7,8)} A recent intravascular ultrasound study by Lee et al.⁹⁾ showed that neointimal rupture within the stent area was observed in 43.5% of 23 patients with very late stent thrombosis, after 1st generation DES implantation. A pathologic study reported that DES therapy may accelerate atherosclerosis, while reducing restenosis.¹⁰⁾ Therefore, new DESs with a biodegradable polymer have been developed to avoid complications caused by persistence of polymer. Several studies compared the outcomes (i.e., cardiac death, myocardial infarction, and stent thrombosis) of BESs with those of 1st generation DESs and concluded that BESs were not inferior to 1st generation DESs and that both suitable alternatives and long term outcomes were needed.¹¹⁾

Despite of these favorable conditions of a BESs compared to 1st generation DESs, accelerated neointimal proliferation, abnormal neointimal morphology (i.e., layered appearance of the neointima) and additional neointimal rupture were observed in this patient with late stent thrombosis within a relatively shorter period of time (i.e., about 5 months) after implantation of a BES. Due to high resolution images of the OCT, the cause of stent thrombosis was more precisely diagnosed than in previous cases using IVUS or other modalities.

REFERENCES

- 1) Moses JW, Leon MB, Popma JJ, et al. *Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery.* *N Engl J Med* 2003;349:1315-23.
- 2) Stone GW, Ellis SG, Cox DA, et al. *A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease.* *N Engl J Med* 2004;350:221-31.
- 3) Iakovou I, Schmidt T, Bonizzoni E, et al. *Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents.* *JAMA* 2005;293:2126-30.
- 4) Daemen J, Wenaweser P, Tsuchida K, et al. *Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in*

- routine clinical practice: data from a large two-institutional cohort study. Lancet* 2007;369:667-78.
- 5) Cook S, Ladich E, Nakazawa G, et al. *Correlation of intravascular ultrasound findings with histopathological analysis of thrombus aspirates in patients with very late drug-eluting stent thrombosis. Circulation* 2009;120:391-9.
 - 6) Chevalier B, Silber S, Park SJ, et al. *Randomized comparison of the Nobori biolimus A9-eluting coronary stent with the Taxus Liberté paclitaxel-eluting coronary stent in patients with stenosis in native coronary arteries: the NOBORI 1 trial: phase 2. Circ Cardiovasc Interv* 2009;2:188-95.
 - 7) Finn AV, Joner M, Nakazawa G, et al. *Pathological correlates of late drug-eluting stent thrombosis: strut coverage as a marker of endothelialization. Circulation* 2007;115:2435-41.
 - 8) Farb A, Burke AP, Kolodgie FD, Virmani R. *Pathological mechanisms of fatal late coronary stent thrombosis in humans. Circulation* 2003;108:1701-6.
 - 9) Lee CW, Kang SJ, Park DW, et al. *Intravascular ultrasound findings in patients with very late stent thrombosis after either drug-eluting or bare-metal stent implantation. J Am Coll Cardiol* 2010;55:1936-42.
 - 10) Nakazawa G, Vorpahl M, Finn AV, Narula J, Virmani R. *One step forward and two steps back with drug-eluting-stents: from preventing restenosis to causing late thrombosis and nouveau atherosclerosis. JACC Cardiovasc Imaging* 2009;2:625-8.
 - 11) Garg S, Sarno G, Serruys PW, et al. *The twelve-month outcomes of a biolimus eluting stent with a biodegradable polymer compared with a sirolimus eluting stent with a durable polymer. EuroIntervention* 2010;6:233-9.