Very late thrombosis of sirolimus-eluting stent due to late malapposition: Serial observations with optical coherence tomography

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Abstract

A 54 years old man underwent directional coronary atherectomy in segment 7 with a partial deep cut injury. A sirolimus-eluting stent (SES) was implanted at the restenosed post-atherectomy lesion. Six months after SES implantation, intravascular ultrasound (IVUS) examination revealed slight vessel enlargement although there were no malapposed struts. Optical coherence tomography (OCT) revealed partial stent malapposition. Ticlopidine was discontinued 3 months after SES implantation, but aspirin was continued. Twenty-nine months after SES implantation, after discontinuing aspirin for 7 days for colon polypectomy, the patient suffered an acute myocardial infarction at the SES implantation site. IVUS revealed further positive vessel remodeling and slight stent malapposition, and OCT revealed extension of the previous stent malapposition and ulcer-like appearance around the stent struts. This case demonstrates that even a small partial SES malapposition that can be detected only by OCT has the potential to enlarge over time and the late malapposition may result in late thrombosis when anti-platelet therapy is discontinued.

(158 words)

Introduction

Sirolimus-eluting stent (SES) is now commonly used for percutaneous coronary intervention (PCI) because they dramatically reduce the rates of restenosis, even in small vessels and long lesions [(1)]. Their long-term efficacy and safety, however, have not been satisfactory [(2)]. A major concern of SES implantation is late stent thrombosis. Late thrombosis is a very rare, but fatal complication of SES because it may result in acute myocardial infarction or sudden cardiac death [(3)]. Here, we report very late stent thrombosis 29 months after SES implantation due to late malapposition. Serial changes of the SES structure were observed using optical coherence tomography (OCT), which provide high resolution images of intra-stent structures [(4,5)].

Case report

Directional atherectomy was performed in the mid-left anterior descending artery in a 54 years old man with 90% stenosis in March 2004. At that time, PCI was performed without the use of any stents because the coronary angiogram (CAG) revealed good dilatation and intravascular ultrasound (IVUS) examination showed a partial laceration of the intima-media complex due to the deep atherectomy. Six months later, in September 2004, we performed a follow-up CAG, which showed 90% focal, tandem restenosis at the previous debulking lesion site (except for the deep cut area) (Figure 1-a). We implanted a 3.5×28mm SES (Cypher®; Cordis, Johnson and

Johnson Company) to cover the total area of the restenosed lesion. The post PCI angiogram revealed good dilatation (Figure 1-b) and IVUS revealed good stent apposition. Both aspirin (100 mg/day) and ticlodipine (200 mg/day) were prescribed. Three months after SES implantation, the ticlodipine was discontinued, but aspirin therapy was continued.

In March 2005, 6 months after the SES implantation, a follow-up CAG was done. In-stent restenosis was not observed by CAG (figure 1-c). IVUS (Atlantis SR Pro2®,Boston Scientific Corporation) and OCT (ImageWire®, LightLab imaging) were indicated for better visualization of the SES. IVUS revealed almost no change in the stent cross-sectional area (CSA) and slight enlargement of the vessel CSA (from 22.1 mm^2 to 22.7 mm^2) compared with those immediately after SES implantation. Further, on IVUS examination all struts seemed to be well apposed (Figure 2-a). OCT visualized partial small stent malapposition at the previous deep cut injury site, but thin neointimal tissue was present on almost all of the struts (Figure 3-a).

In February 2007, 29 months after SES implantation, aspirin therapy was temporarily discontinued because of a planned colon polypectomy. Seven days after discontinuing the aspirin, the patient suddenly experienced severe chest pain after taking a bath and presented at our hospital emergently. An electrocardiogram demonstrated ST-segment elevation on the V2-V6 leads. The patient underwent an emergent CAG on suspicion of acute myocardial infarction. The CAG revealed total occlusion at the mid SES (Figure 1-d), and emergent PCI was performed.

After guide-wire passage, a thrombectomy was performed using an aspiration catheter (Rebirth®; Goodman Co., Ltd.) and a red thrombus was aspirated. A 3.0×14 mm bare metal stent (BMS) (Duraflex®, Avantec Vascular Corp.) was implanted directly, overlapping the distal part of the residual SES. At this time, IVUS was not performed because of the emergent nature of the case.

After 3 weeks, just before discharge, we performed a follow-up CAG, IVUS (Eagle Eye® Volcano Therapeutics Inc.), and OCT. CAG revealed no change of SES condition (Figure 1-e). IVUS revealed an increased vessel CSA (22.7mm^2 to 31.1mm^2) without a change in the SES CSA and visualized slight stent malapposition mainly at the previous deep-cut site (Figure 2-b, Table 1). OCT more clearly revealed an expansion of the previous stent malapposition and the ulcer-like appearance around the stent struts from the mid SES to the distal edge, which overlapped the BMS (Figure 3-b).

Discussion

SESs are now widely used in PCI because they significantly reduce the rates of restenosis and target lesion revascularization compared with BMS [(1)]. Despite reduced revascularization, SES does not ensure long-term safety due to the persistent risk of stent thrombosis [(2)].

In the present case, we implanted the SES at a previous deep cut injury site. After 6 months, although IVUS showed slight vessel enlargement, no stent malapposition was observed. OCT,

however, revealed partial stent malapposition at that site. After thrombosis, although we did not perform pre-balloon angioplasty before implanting BMS, IVUS revealed further enlargement of vessel and slight stent malapposition at there, and OCT also revealed a progression of the stent malapposition and ulcer-like appearance around the struts expanding over the previous deep cut injury site.

The mechanism of late stent thrombosis of the SES may be multi-factorial. A recent case report suggested that the mechanism of SES late thrombosis is late malapposition and cessation of a short course of double anti-platelet therapy [6,7]. In the present case, the combination of the temporary discontinuation of aspirin therapy and the progression of late stent malapposition might have contributed to the development of late thrombosis.

Late stent malapposition also may be due to many different factors. We previously reported that 2.2% of SES struts were malapposed at a 6-month follow-up by OCT and the predictors of SES malapposition were choronic total occlusion (CTO) and overlapped stenting [4]. We postulate that the mechanism for the increased malapposition in a CTO lesion may be positive vessel remodeling or the absorption of thrombi with suppressed neointimal hyperplasia. As for overlapping SES segments, excessive inhibition of neointimal hyperplasia due to the doubled dose of sirolimus may be a factor. In the present case, a single SES was implanted and there was no CTO lesion, but a partial stent malapposition was detected around the previous deep cut

injury site at first, and enlarged over time. Nakamura et al reported late malapposition of BMS was associated with vessel enlargement due to mechanical injury from directional atherectomy by serial IVUS study. They speculated that vessel wall injury due to aggressive plaque removal might alter the focal vessel wall compliance and the resultant effects of tensile stress from stretching cause chronic vessel enlargement [8]. We reported a similar change when an SES was implanted into an intramural hematoma [5]. As shown in table 1, this case also expressed positive vessel remodeling at six months follow-up study. Therefore, we speculate that the mechanism of a first stent malapposition is the combination of arterial wall fragility and sirolimus-induced inhibition of intimal hyperplasia.

In this case, furthermore, the late malapposition proceeded to the distal edge of the SES over the previous deep cut injury site, leading to thrombosis. Therefore, the persistent late malapposition was not only due to deep cut injury. Virmani et al reported that localized hypersensitivity vasculitis in response to an SES implanted in a human coronary artery led to late stent malapposition and thrombosis in a pathology study [9]. They observed significant malapposition in both proximal and distal stents and this peculiar vascular response between the polymer and the vessel may cause positive remodeling and be involved in late malapposition and thrombogenicity between 8 and 18 months. Although we did not examine the possibility of an allergic reaction and malapposition was not observed at the proximal edge, we speculate that

localized hypersensitivity vasculitis might also have been involved in late malapposition and thrombosis.

We think that not all late malappositions are likely to result in late thrombosis, but we have an opinion that patients with late stent malapposition should be encouraged to continue at least one long-term anti-platelet therapy.

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Legends

Figure 1

a. Coronary angiogram (CAG) showed 90% focal, tandem restenosis at the previous debulking lesion site (except for the deep cut area).

b. Post-percutaneous coronary intervention CAG. A 3.5×28mm sirolimus-eluting stent (SES) (Cypher®) was implanted and good dilatation was observed.

c. Six month follow up CAG. The CAG revealed no restenosis at the SES implanted site.

d. Emergency CAG revealed total occlusion in the middle of the SES implanted site

e. The follow up CAG revealed no change of SES condition.

Figure 2

a. The IVUS (Atlantis SR Pro2®) examination of six month after SES implantation. IVUS revealed almost no change in the stent cross-sectional area (CSA) and slight enlargement of the vessel CSA (from 22.1 mm^2 to 22.7 mm^2) compared with those immediately after SES implantation. Each IVUS image revealed good apposition. Numbers 3 indicates the previous deep-cut injury site.

b. The IVUS (Eagle Eye®) visualized the small stent malapposition and showed an increased vessel CSA (22.7mm^2 to 31.1mm^2) without a change in the stent CSA compared with that at the 6-month follow-up. The white arrow indicates the SES malapposition.

Figure 3

a. Optical coherence tomography (OCT) images of 6 months after SES implantation. OCT visualized thin neointimal tissue on almost all of the well apposed stent struts, but revealed some partial stent malapposition at the previous deep-cut injury site (indicated by white arrows).

b. OCT images of 29 months after SES implantation (post late thrombosis). OCT revealed more extensive malapposition than that observed at the 6-month follow-up and it was expanding over the previous deep cut injury site (from the mid to distal edge of the SES, which were overlapping bare metal stent). Numbers 3, 4, 5 indicate the ulcer-like appearance around the SES struts (indicated by white arrows).

Figure 1

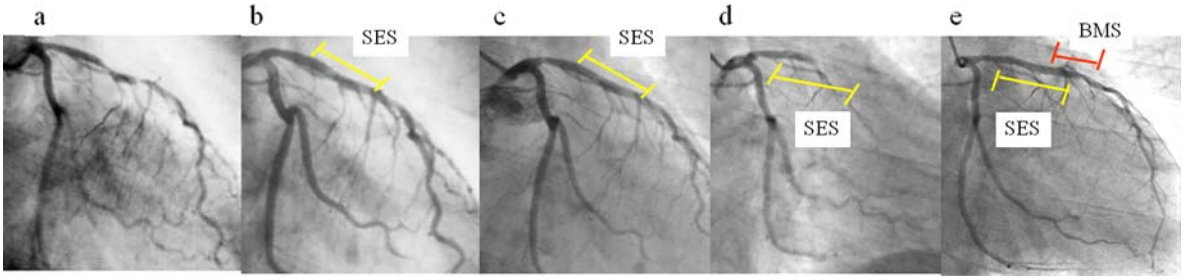
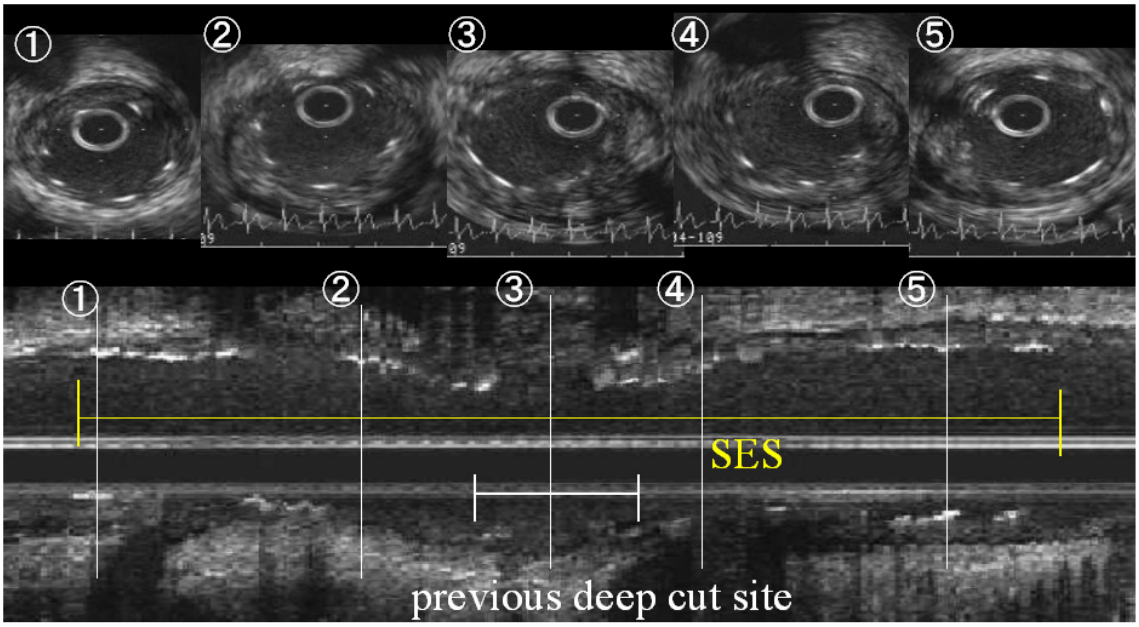


Figure 2

a.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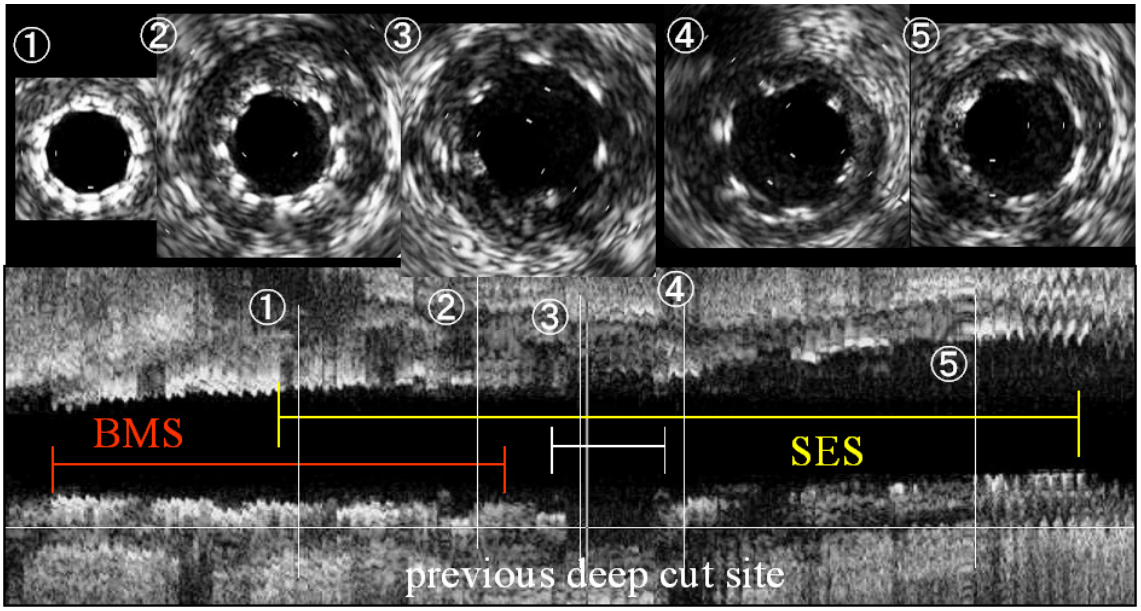
SES
previous deep cut site

b.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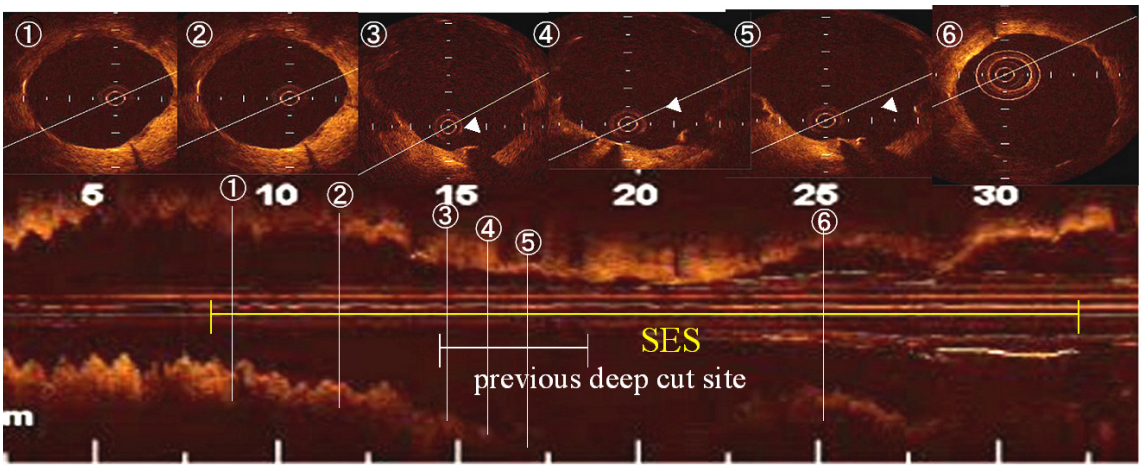
BMS
SES
previous deep cut site

Figure 3

a.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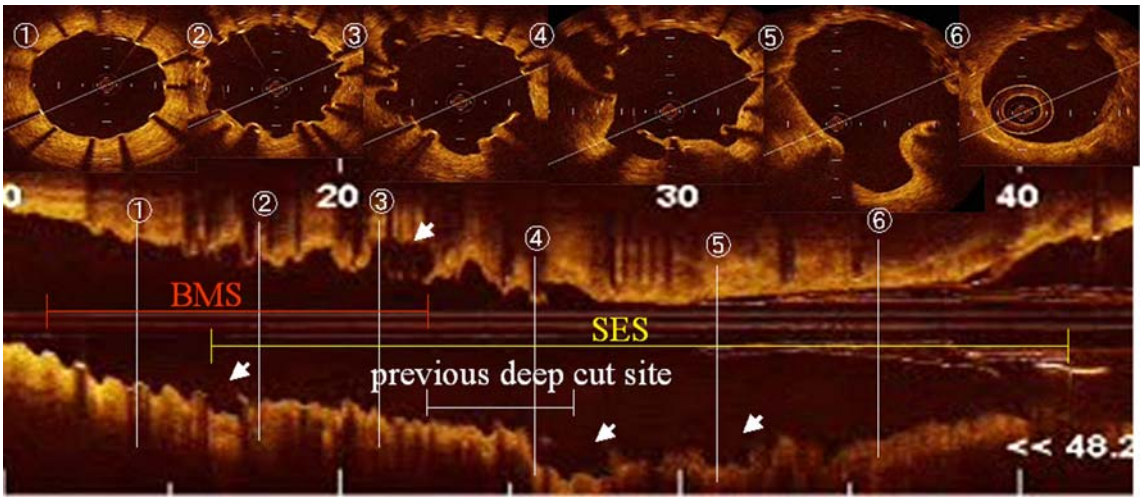
25
30
SES
previous deep cut site

b.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BMS
SES
previous deep cut site
<< 48.2