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CASE REPORT

Improved vascular healing after the successful treatment of very late sirolimus-eluting stent thrombosis with a bare metal stent implantation — A serial optical coherence tomography study

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Abstract We present the case of a patient with non-ST-elevated myocardial infarction due to very late stent thrombosis 2 years after a sirolimus-eluting stent implantation (SES). Optical coherence tomography (OCT) imaging identified vessel wall destruction of the whole stented coronary segment with multiple cavity formations along the entire stent length, severe strut malapposition and thrombi. The patient was treated successfully with the implantation of a bare metal stent (BMS). Follow-up OCT imaging at 12 months revealed the improvement of vascular healing with complete re-endothelialization of the distal parts of the new BMS, while the stent body remained partly uncovered, suggesting vascular toxicity due to the old SES.

Short abstract: The current case is the first to demonstrate the vascular response to a bare metal stent (BMS) implantation inside an old sirolimus-eluting stent with very late stent thrombosis *in vivo* using optical coherence tomography (OCT). Treatment of very late stent thrombosis with a new BMS resulted in a favourable outcome with improved vascular h ealing at 12 months, as identified by OCT.

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Introduction

Clinical studies have shown that drug-eluting stents (DES) inhibit neointimal proliferation and dramatically reduce in-stent restenosis.[1,2] However, DES may affect the normal vascular healing process, resulting in delayed endothelialization and increased susceptibility to late stent thrombosis, an infrequent but life threatening complication.[3–5] Optical coherence tomography (OCT), which offers ultra-high image resolution, offers a unique opportunity for *in vivo* assessment of the vascular response to DES.[6] We present the case of a patient with non-ST-elevated myocardial infarction due to very late stent thrombosis 2 years after a sirolimus-eluting stent (SES) implantation. OCT identified vessel wall destruction of the stented coronary segment, suggesting a severe localized hypersensitivity reaction to SES. Follow-up OCT at 12 months after successful treatment with a bare metal stent revealed improved vascular healing.

Case report

A 44-year-old man without cardiovascular risk factors was admitted to our hospital because of a non-ST elevated myocardial infarction. The patient had a history of percutaneous coronary intervention (PCI) with a sirolimus-eluting stent (SES) that was 3.0 mm in diameter and 23 mm in length (Cypher stent, Cordis, Johnson & Johnson, Miami, Florida) and was implanted in the mid left anterior descending artery 2 years prior. During his current admission, coronary angiography revealed non-significant coronary artery stenosis. However, at the site of the old Cypher stent, peri-stent contrast staining was observed (Fig. 1A). OCT imaging found that along the entire stent length there was severe strut malapposition and multiple cavity formations between stent struts with a depth range of 0.5 to 2.1 mm (Fig. 1C and 1D). Moreover, at the proximal part of the stent, multiple red thrombi were observed (Fig. 1B) that almost obstructed the lumen of the vessel. Interestingly, most of the stent struts were totally covered by a layer of tissue similar to neo-endothelium (Fig. 1C, 1D). We decided to treat the patient with a new bare-metal stent (BMS) that was 2.75 mm in diameter and 30 mm in length. After stent implantation, we performed multiple dilatations with a 3.0 mm balloon under high atmosphere, with a good angiographic result (Fig. 2A). OCT imaging of the new BMS showed good expansion and apposition of the stent (Fig. 2B); however, some large cavities were still present between the stent struts (Fig. 2C and 2D). Notably,

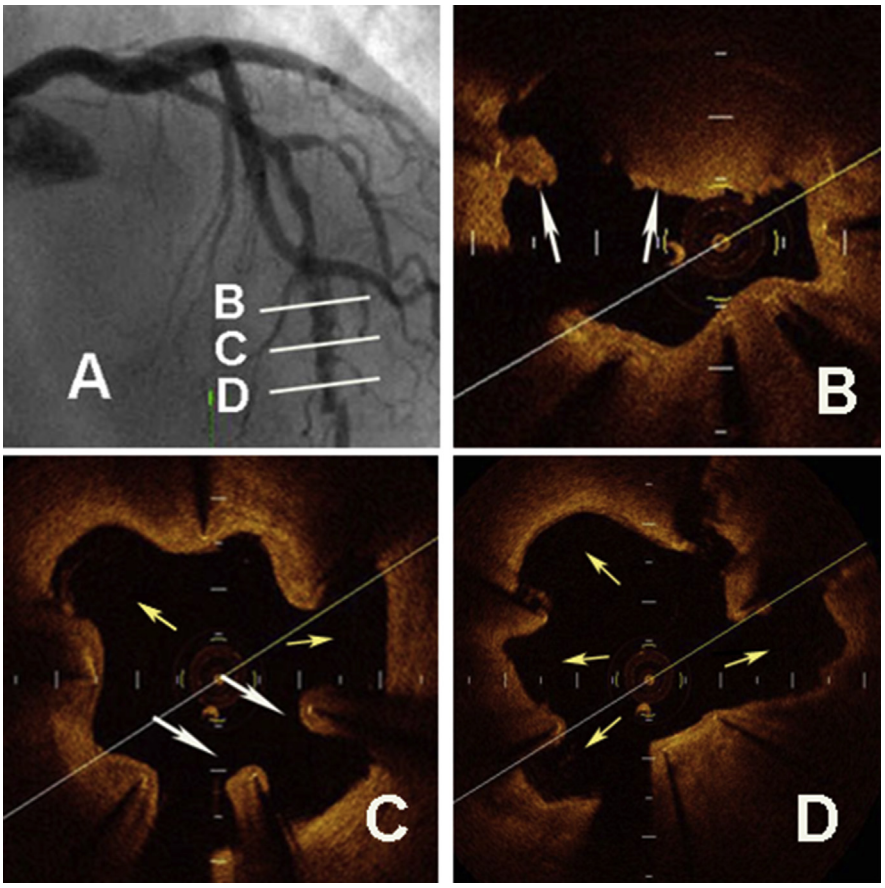

Figure 1 Baseline angiographic and OCT findings. A. Peri-stent contrast staining in mid LAD (the coronary artery segment between lines B and D). B, C and D. OCT images reveal: B. the proximal part of the old Cypher stent with multiple red thrombi (arrows) C. and D. Severe strut malapposition (white arrows) and multiple cavity formations (yellow arrows). Interestingly, most of the stent struts are covered by a layer of tissue similar to neo-endothelium.

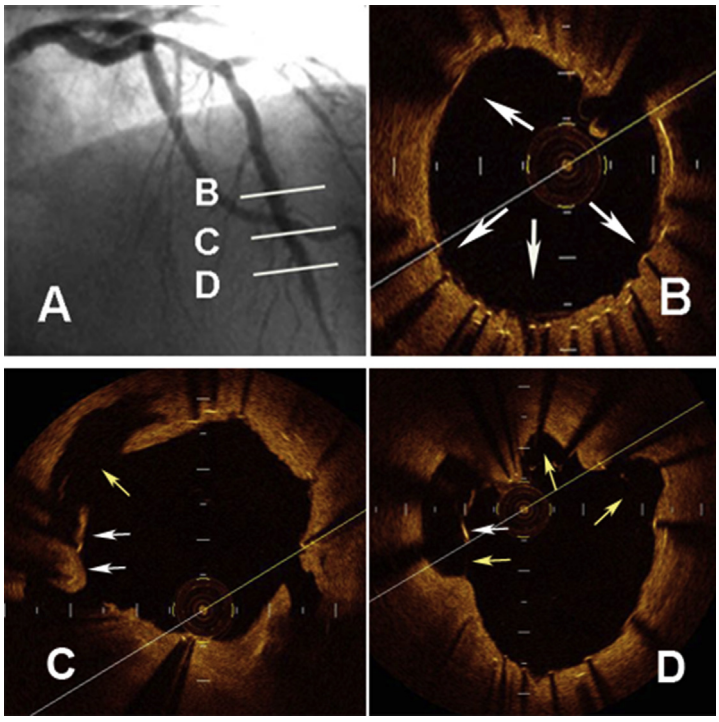

Figure 2 Angiographic and OCT findings immediately after PCI in mid LAD. A. Good angiographic results after BMS implantation (2,75 mm in diameter and 30 mm in length) in mid LAD. B, C and D. OCT images reveal: B. Well- expanded stent struts of the BMS with good apposition (arrows). C. and D. Regression of the number and the size of the cavity formations (yellow arrows) and the strut malapposition of the old Cypher stent (white arrows).

strut malapposition of the old Cypher stent became less severe (Fig. 2C).

A follow-up angiography at 12 months demonstrated that the good angiographic result was unchanged (Fig. 4A). OCT at 12 months showed that the distal and proximal edges of the BMS, which were outside of the old Cypher stent, had been totally covered by a thick layer of tissue (up to 650 μm), likely corresponding to neo-endothelium (Fig. 3A and

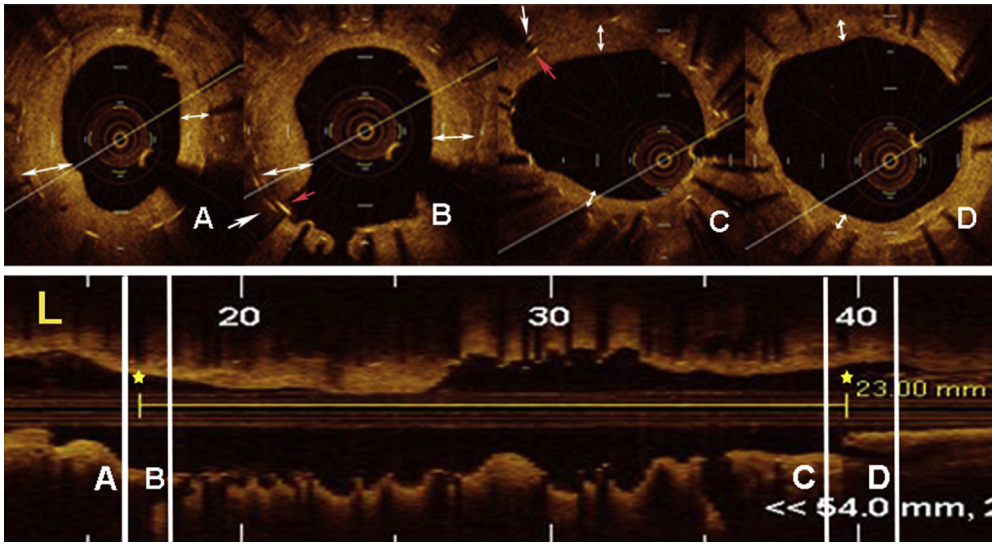

Figure 3 OCT findings at 12 months after the BMS implantation. The longitudinal OCT image reveals the whole BMS stent (lines A and D correspond to the BMS edges) as well as the old Cypher stent (yellow stars correspond to the Cypher edges). A and D. OCT images reveal the distal (A) and the proximal (D) edges of the BMS outside of the old Cypher covered with a thick layer of tissue (double arrows), likely corresponding to neo-endothelium. B and C. OCT images reveal the sites of the BMS covering the edges of the old Cypher stent which were covered by a tissue similar to neo-endothelium (double arrows). The struts of both stents, BMS (red arrows) and Cypher (white arrows) are visible. Disappearance of the cavity formations and the stent strut malapposition was noticed at this part of the stented vessel.

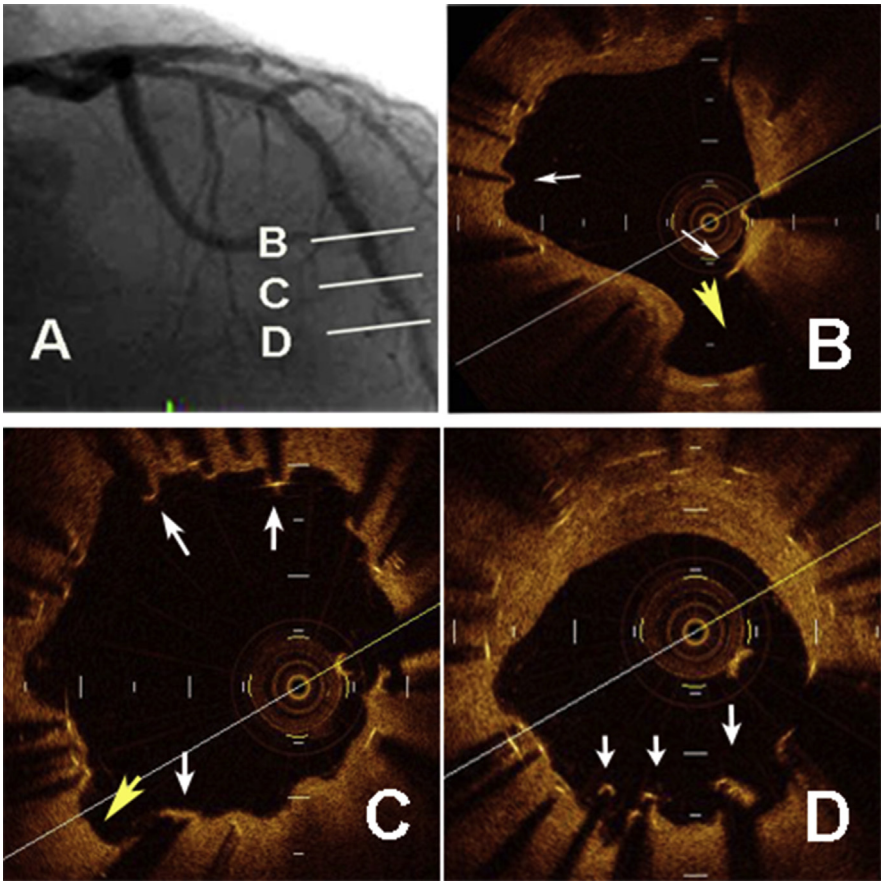

Figure 4 Angiographic and OCT findings at 12 months after the BMS implantation. A. Angiographic image reveals that the good PCI result remained unchanged. B, C and D. OCT images corresponding to the BMS body reveal several uncovered struts with mild malapposition (white arrows). Some cavity formations were still present at this part of the stented vessel (yellow arrows).

3D). Additionally, the part of the BMS that covered the edges of the old Cypher was also covered by a tissue similar to neo-endothelium (Fig. 3B and 3C). In contrast, most of the struts of the BMS body, which were inside the old Cypher, remained uncovered, suggesting vascular toxicity due to SES at this vessel segment (Fig. 4B, 4C, 4D). Furthermore, a significant regression of the size and the number of the interstrut cavity formations were observed along the entire length of the old Cypher stent (Figs. 3 and 4).

Discussion

Late stent thrombosis remains an infrequent but life threatening complication after DES implantation that is primarily attributed to delayed arterial healing (i.e., lack of re-endothelialization and poor strut coverage).[3] Autopsy studies[3–5] have shown that the underlying mechanism of late stent thrombosis for SES is localized strut hypersensitivity. Recently, Kon et al.[7] reported a case with peri-stent contrast staining associated with very late stent thrombosis after SES implantation. In that case, autopsy demonstrated an aneurysm-like focal dilatation of the stented segment with marked inflammatory cell infiltration. Additionally, collapse and loss of the intimal tissue was found, which caused stent malapposition. These pathological findings were consistent with localized hypersensitivity vasculitis.[7] Morino et al.[8] also reported a case with peri-stent contrast staining after SES implantation with multiple cavity formations between stent struts due to vascular positive remodelling, as detected by intravascular ultrasound. Surprisingly, in that case, OCT demonstrated entirely covered stent struts with no thrombus formation in these cavities.[8] A very recent study suggested that this phenomenon of multiple cavity formations after SES implantation seems to be a specific morphological footprint of early generation SES that is nearly absent in newer generation zotarolimus and everolimus-eluting stents.[9]

To our knowledge, the current case is the first to show the vascular response to a BMS implantation inside an old Cypher stent with very late stent thrombosis *in vivo* using OCT. OCT imaging of the Cypher stent thrombosis before PCI revealed destruction of the stented vessel wall with multiple cavity formations and severe strut malapposition. Immediate post-PCI OCT demonstrated regression of both strut malapposition and number and size of cavity formations. Follow-up OCT imaging at 12 months showed complete re-endothelialization of the distal parts of the new BMS covering the old Cypher, although the BMS body remained partly uncovered. This type of vascular healing is consistent with histopathological data reporting that endothelial coverage is generally more complete at the

extreme proximal and distal regions of a stent versus the middle segments.[10,11] Furthermore, experimental models have shown that re-endothelialization after BMS or DES implantation occurs from proliferation and migration of endothelial cells of the intact neighbouring coronary segments.[10,11] We speculated that the implantation of a BMS long enough to cover both entire length of the old Cypher and the intact neighbouring coronary segments might offer a stimuli for re-endothelialization of the whole stented vascular segment.

The optimal treatment for stent thrombosis has not been determined. Observational studies suggest that the primary PCI for treatment of stent thrombosis is less effective and long term clinical outcomes are unfavourable with high mortality and recurrence rate.[12–15] However, in our case, the implantation of a BMS was a safe and effective treatment for very late SES thrombosis with improved vascular healing at 12 months. Still, randomized trials are urgently needed to determine the optimal treatment strategy in these patients.

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