The Return of the Vulnerable Plaque: Optical Coherence Tomography Imaging of a Case of a Late In-Stent Restenotic Chronic Total Occlusion

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Abstract

Keywords

- coronary artery disease
- interventional cardiology
- optical coherence tomography

Although the use of drug-eluting stents (DES) has dramatically decreased the incidence of in-stent restenosis (ISR), concerns regarding the late manifestations of ISR remain. Optical coherence tomography (OCT) imaging provides unique insights into characteristics and patterns of ISR. We report a case of late DES ISR with unusual heterogeneous intracoronary luminal characteristics suggestive of vulnerable atherosclerotic plaque activity by OCT imaging. This case demonstrates that late ISR after DES may involve more than mere neointimal hyperplasia with lesion-associated craters, septae, and neoatherosclerosis. The use of OCT provides novel insights into the mechanisms and potential biology of the late DES ISR.

Although the use of drug-eluting stents (DES) has dramatically decreased the incidence of in-stent restenosis (ISR),^{1,2} concerns regarding the late manifestations of ISR remain. Estimates of DES failure are reported to be between 5 and 10%³ with up to 60% of patients with ISR presenting with an acute coronary syndrome.^{4,5}

With the advent of novel high-resolution imaging modalities, such as optical coherence tomography (OCT), the in vivo intracoronary structure can be elucidated with unprecedented detail. Although traditional intraluminal imaging modalities, such as intravascular ultrasound, offer improved depth penetration for imaging lipid-rich and calcified plaques, the superior spatial resolution provided by OCT techniques provide the ideal imaging of thin cap plaque structures, including sites of rupture and vulnerability.

OCT imaging provides unique insights into characteristics and patterns of ISR.⁶ Although simple neointimal hyperplasia (NIH) is the leading cause of ISR, OCT can now identify heterogeneous neointimal materials including a thin fibrous cap under the intima, intimal rupture, and small (<15 μ m) thrombi suggesting neoatherosclerosis may be a contributor to late DESISR.⁷ Supporting this conjecture, we report a case of late DES ISR with unusual heterogeneous intracoronary luminal characteristics demonstrated by OCT imaging.

Case Presentation

An 82-year-old man, with previous three-vessel percutaneous coronary intervention (PCI) with DES (Xience; Abbott Laboratories, Abbott Park, IL) to the left anterior descending (LAD) artery, left circumflex (LCx) artery, and right coronary artery (RCA) in 2005, now complained of progressive angina. He refused coronary artery bypass graft surgery in 2005. He had 3 months of intermittent progressive left-sided substernal chest pressure, which was worse with exertion, relieved with rest and/or nitroglycerin use. The pain radiated to the left anterior neck and was associated with dyspnea on exertion, and decreasing exercise tolerance over this time period. The chest pressure and associated symptoms are similar to his previous episodes of unstable angina.

The patient is treated for hypertension, high cholesterol, and atrial flutter (on stable rate control strategy) on anticoagulation. Cardiac medication included metoprolol succinate (100 mg daily), rosuvastatin (10 mg daily), clopidogrel (75 mg daily), furosemide (10 mg daily), and rivaroxaban (15 mg daily).

The physical examination was normal except for an irregularly irregular cardiac rhythm. The patient's resting electrocardiogram (ECG) revealed rate controlled atrial flutter with variable block. The chest X-ray was normal without

cardiopulmonary abnormalities. A treadmill exercise stress test was abnormal with chest pressure at 2'41" with 1.5 to 3 mm down-sloping ST depressions in the inferior and anterolateral leads. The patient was referred for coronary angiography.

Coronary angiography demonstrated a widely patent left main and an LAD with diffuse nonobstructive luminal irregularities. The circumflex artery was diffusely calcified with 60% ISR of the previous proximal and mid vessel stents. There were left to right collaterals which fed the posterior descending artery (PDA) (►Fig. 1, I and II).

The RCA was a diffusely calcified and diseased vessel with proximal disease 50 to 60% and chronic total occlusion (CTO) of the mid to distal RCA stented segment (►Fig. 1, III). Previous distal stents of the CTO were visualized. Left ventriculography was performed showing a left ventricular ejection fraction of 30% with hypokinesis of the mid and distal anterior wall, the apex and the mid to distal inferolateral wall (►Fig. 1A, B).

A decision was made to attempt PCI of the RCA mid vessel CTO first, as it was felt to be the culprit vessel given the treadmill stress testing ECG results. PCI was performed with a JR4 guide catheter. A 0.014-mm guide wire (Cross-It; Abbott Laboratories, Abbott Park, IL) successfully crossed the mid vessel RCA CTO. Before stent implantation, the OCT catheter system (St. Jude Medical, St. Paul, MN) was then positioned to visualize the ISR segment with the recommended method.⁸ Intracoronary imaging (►Video 1) demonstrated a substantial amount of heterogeneous material with eccentricity of numerous crater-like ulcerations and septated intimal plaques with a marked intraluminal fibrous and thrombus, findings which strongly suggestive of recent plaque rupture (►Fig. 2A). The

minimum luminal area and diameter were calculated to be 2.25 mm² and 1.5 mm, respectively (►Fig. 2B). Using the three-dimensional (3D)-OCT imaging also provided more details of coronary branch points relative to the target lesion and deep cratered intimal plaques. The axial rotational and longitudinal 3D views are shown in ►Videos 2 and 3.

Video 1

OCT intracoronary imaging of the mid to distal RCA before coronary intervention. OCT, optical coherence tomography; RCA, right coronary artery. Online content including video sequences viewable at: <https://www.thieme-connect.com/products/ejournals/html/doi/10-1055-s-0036-1583764-ija-16-0008-v1.mp4>.

Video 2

3D OCT intracoronary imaging of the RCA in the axial view before coronary intervention. OCT, optical coherence tomography; RCA, right coronary artery; 3D, three-dimensional. Online content including video sequences viewable at: <https://www.thieme-connect.com/products/ejournals/html/doi/10-1055-s-0036-1583764-ija-16-0008-v2.mp4>.

Fig. 1 (I) Angiography of the left coronary artery imaged in the LAO view with cranial angulation. (II) Angiography of the left coronary artery imaged in the RAO view with caudal angulation. (III) Angiography of the right coronary artery imaged in the LAO view with cranial angulation. (A) Left ventriculogram in diastole. (B) Left ventriculogram in systole. LAO, left anterior oblique; RAO, right anterior oblique.

Fig. 2 (a) OCT intravascular imaging of the mid to distal RCA before coronary intervention. (b) Representative OCT intravascular images in the axial view depicting maximal measured cross-sectional area and diameter. "A to D" refers to positions in the coronary artery depicted in short axis at different positions "A to D" and, then correspondingly, the the same "A to D" positions are shown in the longitudinal axis of the same coronary artery. OCT, optical coherence tomography; RCA, right coronary artery.

Video 3

3D OCT imaging of the RCA in the longitudinal view before coronary intervention. OCT, optical coherence tomography; RCA, right coronary artery; 3D, three-dimensional. Online content including video sequences viewable at: <https://www.thieme-connect.com/products/ejournals/html/doi/10-1055-s-0036-1583764-ija-16-0008-v3.mp4>.

A 2.5 × 38 mm XIENCE (Abbott Vascular) DES was then deployed across the mid RCA lesion and postdilated with a 2.5 × 15 mm NC TREK balloon with a post-PCI stenosis of 0% with reconstitution of and TIMI 3 flow (►Fig. 3A). Post-PCI OCT imaging documented the stent struts were well apposed and fully expanded (►Fig. 4; ►Video 4). A repeat angiogram of the LCA revealed that the right collaterals were now absent

(►Fig. 3B, C). The remaining LCx lesion(s) were deferred for a staged procedure as clinically indicated.

Video 4

OCT intracoronary imaging of the RCA postcoronary intervention. OCT, optical coherence tomography; RCA, right coronary artery. Online content including video sequences viewable at: <https://www.thieme-connect.com/products/ejournals/html/doi/10-1055-s-0036-1583764-ija-16-0008-v4.mp4>.

Discussion

This case demonstrates that (1) late ISR after DES may involve more than mere NIH and (2) OCT showed lesion craters, septae, and neoatherosclerosis in the ISR lesion. Although these findings

Fig. 3 (A) Angiography of RCA after percutaneous coronary intervention of distal RCA. (B) Angiography of the left coronary artery postcoronary intervention in the right anterior oblique view with caudal angulation. Imaging reveals loss of left to right collateral vessels. (C) Angiography of the left coronary artery postcoronary intervention in the left anterior oblique view with caudal angulation. Imaging reveals loss of left to right collateral vessels. RCA, right coronary artery.

Fig. 4 Optical coherence tomography intravascular imaging of the right coronary artery postpercutaneous coronary intervention. "A to C" refers to positions in the coronary artery depicted in short axis at different positions "A to C" and, then correspondingly, the the same "A to C" positions are depicted in the longitudinal axis of the same coronary artery.

did not alter our current treatment, the use of OCT did provide novel insights into the mechanisms and potential biology of the late DES ISR. The gradual and progressive development of ISR in this patient led it to being perceived as a benign process. Our current understanding of mechanisms of DES ISR is somewhat

limited. Pathological examination of DES-treated arteries has shown incomplete reendothelialization, chronic inflammatory cell infiltration, fibrin deposition, and platelet activation.⁹ Potent antiproliferative strategies in DES delay the biologic response to injury and extend the time frame to develop clinical signs of

restenosis. Reports on the clinical presentation of ISR suggest that up to 66% present as unstable angina and 1 to 20% with myocardial infarction.¹⁰ Clinical ISR in the DES era has been reported between 3 and 20%.

Three mechanisms have been reported to play a role in late ISR: persistent inflammation, poor response to drugs due to genetic polymorphisms, neoatherosclerosis inside the neointima,⁷ or hypersensitivity response to stent components.¹¹ OCT evaluation of 50 DES ISR lesions suggested presence of thin cap fibroatheroma and neointimal rupture with prevalence increasing 20 months after DES implantation compared with the initial 20 months.⁷ Serial angioscopic examinations of sirolimus DES-implanted lesions suggested possibility of neoatherosclerotic neointima formation at the site of DES implantation.¹² This presence of neoatherosclerosis has also been suggested as possible cause of very late stent thrombosis, although incomplete stent apposition and incomplete lesion coverage have been suggested as major determinants.

Clinical Implications

The detailed OCT observation in this setting will provide additional understanding of late loss mechanisms associated with DES, thus directing our thinking toward specific therapies aim at these processes. The identification of neoatherosclerosis versus NIH will help individualize therapy for each ISR lesion.

Conflict of Interest

The authors declare that they have no conflict of interest or other disclosures.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

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