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Letter to the Editor

Title: Neoatherosclerosis – a cause of late stent thrombosis?

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Percutaneous coronary intervention (PCI) remains the primary revascularisation strategy for coronary artery disease [1]. While stent technology has advanced with several developments, stent thrombosis remains an infrequent but significant complication of PCI, and carries with it significant morbidity and mortality.

Tissue coverage of a stent over time contributes to in-stent restenosis, and previous studies suggest that this neointimal layer is subject to atherosclerotic forces similar to that of the native coronary vessels [2, 3]. Neoatherosclerosis (NA) is the subsequent development of atherosclerosis within the neointimal layer [3].

Neoatherosclerosis has been hypothesised to provide the substrate for late stent failure [2-4], including in-stent restenosis and late stent thrombosis. Nakazawa et al. have demonstrated in autopsy studies that high-risk plaques such as thin-cap fibroatheromas are able to develop within the neoatheromatous layer, with the risk of plaque rupture and subsequent acute coronary syndromes [2-4]. In an observational study, Kang et al demonstrated that very late stent thrombosis was associated with in-stent neointimal rupture, and this was associated with a higher frequency of ST-elevation myocardial infarction [4].

Neoatherosclerosis occurs in both drug eluting (DES) and bare metal stents (BMS), but it occurs much earlier and more frequently in DES [1]. The exact pathogenesis of NA remains unknown, but chronic inflammation and endothelial dysfunction are likely to play a role [1, 3]. Yonetsu et al have shown that risk

factors such as increased stent age, cigarette smoking and chronic kidney disease are strongly associated with the formation of NA, whereas the use of angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB) appears to be protective [5].

Optical coherence tomography (OCT) is a novel coronary imaging technique with a high resolution of 15 microns and permits the *in-vivo* visualisation and characterisation of the neointimal layer of an indwelling stent [6]. OCT is the modality of choice to detect subsequent atheromatous change [5, 6]. Its high-resolution is also able to detect individual stent struts and characterise their apposition to the vessel wall. OCT is therefore well positioned to investigate the causes of stent failure and provide insights to the pathophysiology and management of complications after PCI [6]. Guidelines on the standards for reporting these lesions are available [7].

We present a case of very late stent thrombosis in a young patient where OCT was used to demonstrate the various causative pathologies resulting in the clinical presentation.

A 42-year-old male presented with acute ischaemic chest pain at rest lasting for 6 hours. Electrocardiography showed ST-segment elevation in the precordial leads with associated Q-waves (Figure 1). 8 years prior, he had received percutaneous coronary intervention (PCI) with a BMS (Abbott Vascular USA Vision 3.0mm x 28mm stent) to the left anterior descending coronary artery (LAD) in the setting of an ST elevation myocardial infarction. His other

cardiovascular risk factors included a history of ongoing smoking, dyslipidaemia and a family history of ischaemic heart disease.

Peak troponin and creatine kinase levels were 20.55 microg/L and 613 U/L respectively at 11 hours.

Coronary angiography showed total occlusion of the proximal-mid segment of the previously implanted LAD stent. Gentle predilation of the lesion was undertaken to allow passage of the OCT wire. Optical coherence tomography revealed severe in-stent restenosis and significant neoatherosclerosis with evidence of stent thrombosis (Panel).

Subsequent coronary intervention (PCI) to the lesion with a drug eluting stent yielded an excellent result (Panel).

Stent thrombosis is an uncommon but serious complication after coronary intervention and is associated with a high mortality rate of up to 33% [8].

This case reinforces the hypothesis of neoatherosclerosis being a cause of late stent thrombosis as visualised on OCT. It also highlights the importance of optimising this patient's modifiable cardiovascular risk factors, especially his ongoing cigarette smoking. A possible mechanism is that nicotine enhances angiogenesis in endothelial cells, and cigarette smoke induces endothelial injury with subsequent atherosclerosis [5]. The predictors of neoatherosclerosis are reported to be a stent >48 months old, DES, smoking, and chronic kidney disease,

while therapy with ACE inhibitors or angiotensin receptor blockers reduced neointimal proliferation and restenosis [5]. It is speculated that the tissue renin angiotensin system inside the stent may play a role in neointima formation.

Early detection of neoatherosclerosis may be beneficial to improving the long-term outcome of patients with pre-existing stents [3]. OCT provides the imaging capabilities for long term follow up of such high-risk patients, and is able to shed light on the effect of therapies that aim to attenuate the risk of recurrence.

He remained free of ischaemic symptoms at his 1-month review.

References:

1. Nakazawa, G., et al., *The pathology of neoatherosclerosis in human coronary implants bare-metal and drug-eluting stents*. J Am Coll Cardiol, 2011. **57**(11): p. 1314-22.
2. Finn, A.V. and F. Otsuka, *Neoatherosclerosis: A Culprit in Very Late Stent Thrombosis*. Circulation: Cardiovascular Interventions, 2012. **5**(1): p. 6-9.
3. Park, S.J., et al., *In-stent neoatherosclerosis: a final common pathway of late stent failure*. J Am Coll Cardiol, 2012. **59**(23): p. 2051-7.
4. Kang, S.J., et al., *OCT analysis in patients with very late stent thrombosis*. JACC Cardiovasc Imaging, 2013. **6**(6): p. 695-703.
5. Yonetsu, T., et al., *Predictors for neoatherosclerosis: a retrospective observational study from the optical coherence tomography registry*. Circ Cardiovasc Imaging, 2012. **5**(5): p. 660-6.
6. Ferrante, G., et al., *Current applications of optical coherence tomography for coronary intervention*. Int J Cardiol, 2013. **165**(1): p. 7-16.
7. Tearney, G.J., et al., *Consensus standards for acquisition, measurement, and reporting of intravascular optical coherence tomography studies: a report from the International Working Group for Intravascular Optical Coherence Tomography Standardization and Validation*. J Am Coll Cardiol, 2012. **59**(12): p. 1058-72.
8. Windecker, S. and B. Meier, *Late Coronary Stent Thrombosis*. Circulation, 2007. **116**(17): p. 1952-1965.

Figure legends

Figure 1:

ECG at presentation

Figure 2:

1: Initial coronary angiogram showing total occlusion of the proximal LAD

(marked by red arrow).

2: OCT wire in situ with lines marking individual OCT image sites, proximal to

distal, A-C. Long dotted line marks length of the previously implanted stent.

3: Post PCI outcome with a widely patent LAD.

A: Severe neoatherosclerosis causing in-stent restenosis. All stent edges marked

with purple arrowheads.

B: Neoatherosclerosis with visible large red thrombus (white 'x').

C: Distal site of OCT with homogenous coverage of the indwelling stent.

Fig 1

Fig 2

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