Frequency-domain optical coherence tomography assessment of very late vascular response after carotid stent implantation

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Intravascular optical coherence tomography is a high-resolution invasive imaging modality that allows the evaluation of vascular responses after stent implantation in a micron-scale level. We describe for the first time two patients with very late vascular response after carotid artery stenting that exhibit two different patterns of low-signal intensity (LSI), “ill-appearing” neointima: the first patient shows layered LSI neointima leading to stent restenosis, coupled with the presence of intraluminal thrombus, whereas the second patient demonstrates another pattern of non-restenotic LSI stent strut coverage, suggestive of lipid laden neointima (ie, “neoatherosclerosis”), recently associated with stent failure in coronary arteries. (J Vasc Surg 2013;58:201-4.)

Carotid artery stenting (CAS) has emerged as an alternative to carotid endarterectomy for the treatment of carotid artery disease. Our understanding of the mechanisms underlying CAS failure, however, remains limited because, as opposed to the coronary circulation, stent-vessel interactions in carotid arteries have not been extensively studied. The recent U.S. Food and Drug Administration clinical approval of frequency-domain optical coherence tomography (FD-OCT), a light-based intravascular imaging modality that provides an unprecedentedly detailed micron-level (10-μm axial resolution) evaluation of vascular response to the stent, may open a new avenue for assessment of plaque morphology and stent-vessel interactions in the carotid arteries.1 We recently demonstrated the feasibility of FD-OCT to image atherosclerosis and stent-vessel interactions in the carotid vasculature.2

Here we report two patients who illustrate novel features of abnormal very late vascular response to CAS that may be implicated in adverse clinical outcomes. Image acquisition was performed by means of an automated pull-back without proximal balloon occlusion. Blood clearance was obtained with the injection of 20 mL pure contrast. The studies reported here were done in the Baptist Heart and Vascular Institute after patients signed informed consent. The use of FD-OCT to facilitate clinical management in the reported patients and retrospective review and reporting of cases were approved by Baptist Hospital Institutional Review Board.

CASE REPORTS

Patient 1. A 62-year-old woman underwent carotid endarterectomy of the right internal carotid artery (RICA) in 2003, and 5 years later, she underwent CAS for the treatment of RICA high-degree asymptomatic surgical restenosis. Carotid ultrasound imaging in this asymptomatic patient 4 years later suggested severe stent restenosis, documented by peak systolic velocity of 436 m/s, peak diastolic velocity of 150 m/s, and internal carotid-to-common carotid artery ratio of 6.7. Subsequent angiography, however, demonstrated only a proximal 55% in-stent restenosis in the right common carotid artery, without signs of plaque instability or thrombus (Fig 1, A), whereas FD-OCT (C7-XRTM OCT Intravascular Imaging System; St. Jude Medical, St. Paul, Minn) imaging revealed different patterns of vascular reaction within the same stent (Fig 1, B, cross-sections 1-6), as follows: normal pattern (ie, high signal intensity) of neointimal hyperplasia, layered low signal intensity (LSI) in-stent tissue with organized thrombus and significant luminal narrowing (minimal cross-section area, 5.1 mm2; area stenosis, 70%), as well as intraluminal, nonorganized, thrombus.

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Given the findings of recurrent stenosis, the patient was treated with CAS using a Xact Carotid Stent System (Abbott Vascular, Santa Clara, Calif). FD-OCT pullback after stent implantation demonstrated that despite using a closed-cell stent design, a large amount of LSI tissue prolapse occurred (Fig 2). The patient remains asymptomatic.

**Patient 2.** A 76-year-old man underwent CAS in RICA for symptomatic stenosis (Carotid Revascularization Endarterectomy...
vs Stent Trial study protocol) in 2004. He presented 8 years later with left-sided weakness, with multiple small right middle cerebral artery distribution infarcts demonstrated by magnetic resonance imaging (not shown). Carotid angiography demonstrated an intraluminal filling defect (Fig 3, A) suggesting the presence of thrombus within the stent.

After a 6-week course of antiplatelet and antithrombin therapy, the patient returned for further studies to assess residual thrombus and underlying plaque morphology to help clarify the mechanisms of stent failure. Although angiography demonstrated almost complete resolution of the angiographic “haziness” (Fig 3, B), FD-OCT revealed intrastent plaque rupture, without overlying thrombus, and a nonobstructive uniform LSI tissue with signs of macrophage infiltration, diffuse borders, and high attenuation of light that limited adequate stent strut visualization (Fig 3, C–F). The patient has remained asymptomatic on medical therapy with clopidogrel and a statin.

DISCUSSION

The present report provides the first evidence of “ill-looking” in-stent tissue observed by FD-OCT very late (4 and 8 years) after implantation of bare-metal stents in
the carotid artery. The complex and heterogeneous arterial wall response observed in these two patients resembles the optical features of pathologic neointimal tissue after drug-eluting stent (DES) implantation in the coronary circulation.

Patient 1 showed layered LSI tissue suggestive of hypocellular matrix with abundant proteoglycan, similar to what we have described as a “black hole” in the coronary circulation. Despite the patient’s asymptomatic status, the presence of organized and intraluminal white thrombus is alarming because it suggests a “high-risk,” prothrombotic vascular milieu.

The second patient had homogeneous LSI in-stent tissue suggestive of lipid-laden neointima, with signs of inflammation, and two sites of rupture. There was no FD-OCT evidence of overlying thrombus, likely because of anticoagulation therapy. Although a cause-and-effect relationship cannot be extrapolated, similar OCT findings have been recently suggested as a possible underlying mechanism of stent thrombosis and acute coronary syndromes late after coronary stent implantation.

The potent antiproliferative cellular effects of DES, and inflammatory reaction to polymers or hypersensitivity to both have been blamed for similarly abnormal OCT findings in the coronary circulation. Although late abnormal neointimal proliferation has long been observed in coronary arteries treated with radiotherapy and DES, only recently has the term “neoatherosclerosis” been used to describe such vascular responses. The present patients revealed that these are neither exclusive to the coronary artery nor to DES.

Although FD-OCT is currently the best image modality to investigate vascular response to stents, it is important to recognize the limitations of the method because different materials may have similar optical properties. For example, proteoglycan-rich tissue, fibrin accumulation surrounding stents, excessive inflammation, and stent neoatherosclerosis may appear as LSI tissue in an FD-OCT assessment. Nevertheless, one can rely on optical properties coupled with additional morphologic characteristics (ie, layered vs nonlayered, regular vs irregular, well defined vs poorly defined borders) to differentiate normal from abnormal tissue in vivo based on previous histopathologic validation. To date, examination of intrastent tissue in the carotid vasculature has been largely by angiographic analysis that yields only gross quantitative data.

These seminal FD-OCT findings of late “high-risk” arterial reactions to CAS unravel a potentially important, yet unrecognized, mechanism of CAS failures that may have clinical relevance in a vascular tree where, unlike the coronary tree, symptoms are largely due to embolic events rather than to obstructive disease. Future prospective, large-scale studies are warranted to determine the frequency and treatment of very late pathologic arterial reaction after CAS.

REFERENCES

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