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CASE REPORT

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Usefulness of optical coherence tomography in the assessment of atherosclerotic culprit lesions in acute coronary syndromes. Comparison with intravascular ultrasound and virtual histology

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Abstract

In this paper, we present a case of a female patient with clinically unstable angina pectoris and a bordeline stenosis in the proximal segment of the left anterior descending coronary artery as assessed by coronary angiography and intravascular ultrasound. Virtual histology revealed morphological criteria of a vulnerable plaque forming the culprit lesion. Optical coherence tomography visualized both fibrous cap fracture and a significant stenosis of a coronary artery caused by soft structures identified as mural thrombus covering the plaque surface. The image of atherosclerotic plaque obtained by optical coherence tomography enabled explanation of the cause of coronary instability and influenced subsequent management. The presented case illustrates usefulness of optical coherence tomography as an imaging method complementary to virtual histology and intravascular ultrasound in the diagnostic evaluation of selected patients with acute coronary syndromes. Application of optical coherence tomography in the assessment of vulnerable atherosclerotic plaques is discussed as related to the presented case. (Cardiol J 2008; 15: 561–566)

Key words: optical coherence tomography, intravascular ultrasound, virtual histology

Case description

A 51-year old obese female patient with a history of smoking and hypercholesterolemia was transferred to our department from a community hospital for further evaluation and treatment due to episodes of resting retrosternal chest pain recurring for 8 days. An acute coronary syndrome with elevated troponin level was diagnosed (troponin I level at the local hospital was 0.74 ng/mL, with a cutoff level for the diagnosis of myocardial infarction at 0.78 ng/mL and the upper limit of normal values at 0.04 ng/mL). Despite full medical treatment according to current guidelines, including clopidogrel, aspirin, enoxaparin, beta-blocker, angiotensin-converting enzyme inhibitor, statin, trimetazidine and nitrates, recurrent episodes of resting chest pain lasting for several minutes were seen. Apart from small negative T waves in lead III and flat T waves in lead aVF, electrocardiogram was unremarkable. On admission to our department, troponin I level was normal at 0.013 ng/mL (normal values < 0.03 ng/mL). Coronary angiography performed in the first day of hospitalization revealed a borderline stenosis in the proximal segment of the the left anterior descending coronary artery

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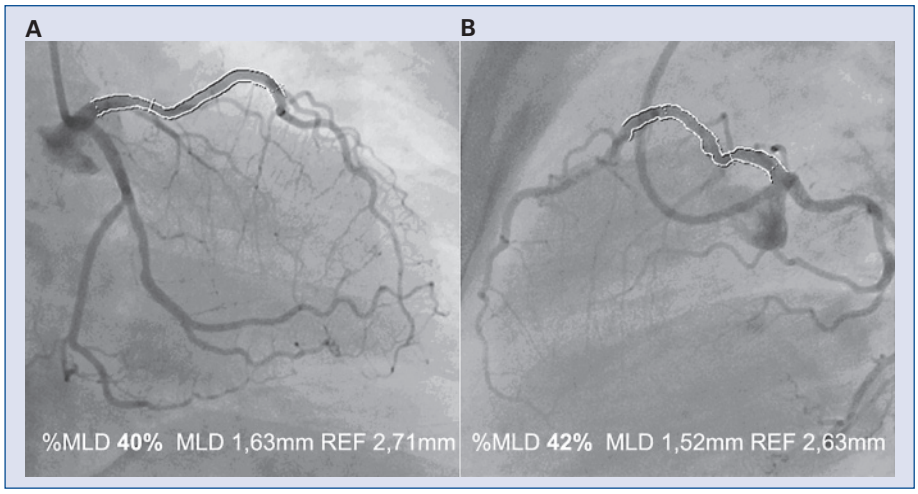

Figure 1. Coronary angiography, RAO 30° (**A**), and LAO 90° (**B**) views. A borderline 40–42% stenosis in the proximal segment of the left anterior descending coronary artery is seen in quantitative coronary angiography.

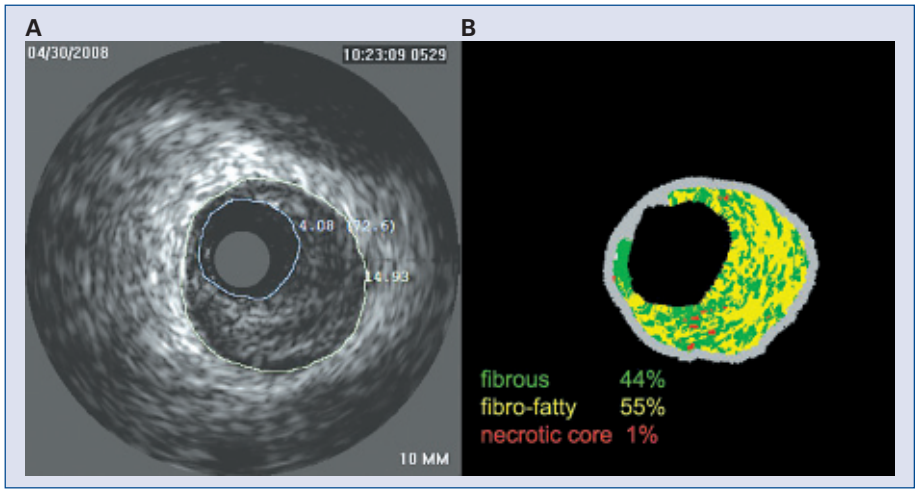

Figure 2. Intravascular ultrasound images acquired at the site of the minimal lumen area. **A.** Total vessel cross sectional area (14.93 mm^2) and lumen cross-sectional area (4.08 mm^2) measurement. **B.** Virtual histology analysis of the same cross-section.

(LAD) and a myocardial bridge in the middle segment of LAD. The maximal vessel stenosis by quantitative coronary angiography (QCA) was 42% in the left lateral view (Fig. 1).

At that stage, a decision was made to proceed with further diagnostic evaluation to assess functional significance of the LAD stenosis. An exercise test was clinically and electrocardiographically negative at the maximal workload of 8 METs. Due to unstable course of angina in the patient and prognostically important localization of the culprit lesion, repeat cardiac catheterization was performed with a view to evaluate the proximal LAD stenosis with intravascular ultrasound (IVUS) and, if necessary, optical coherence tomography (OCT). IVUS was performed with an EagleEye®Gold probe and analyzed using In-Vision Gold software (Volcano Therapeutics, USA). In the area of angiographically borderline stenosis, IVUS revealed a soft atherosclerotic plaque with luminal borders that were difficult to delineate (Fig. 2). Minimal lumen area (MLA) measured planimetrically in cross-sectional view was 4.08 mm^2; maximal vessel stenosis relative to the vessel area within the external elastic membrane was 72.6%, and lumen dimensions at the site of maximal stenosis were 2.2 × 2.5 mm (Fig. 2). Thus, the LAD stenosis was of borderline significance also by IVUS and the latter technique did not

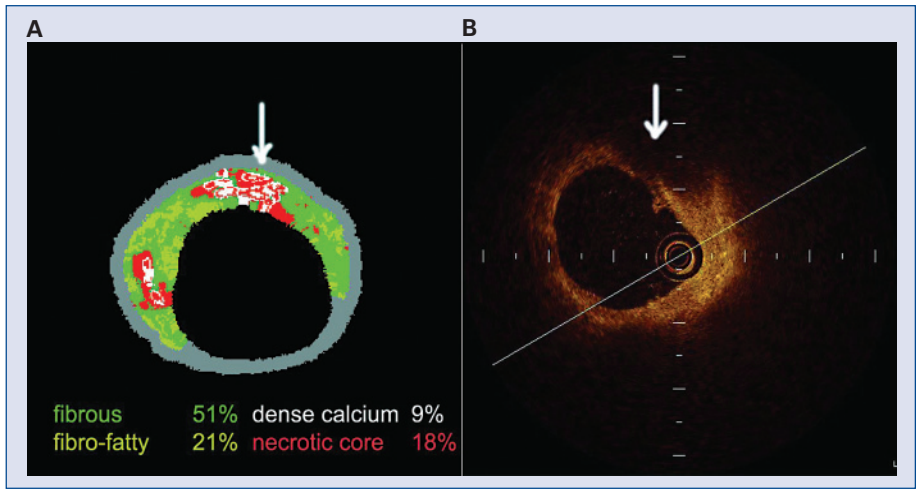

Figure 3. An image of vulnerable (unstable) atherosclerotic plaque by virtual histology (**A**) and optical coherence tomography (**B**). Arrows indicate plaque area with large necrotic core and thin, ruptured fibrous cap.

indicate that revascularization is necessary [1]. Virtual histology at the site of ultrasonographically determined MLA revealed partially fibrous and partially fatty-fibrous plaque with a negligible necrotic core (Fig. 2).

Distally to the site ultrasonographically determined of MLA, a segment of the plaque was noted that fulfilled the criteria of an unstable plaque by virtual histology: the area of the necrotic core was 18% (threshold > 10%) of the total plaque area, with relative plaque area of 53% (threshold > 40%) of the total cross-sectional vessel area and a direct contact between the necrotic core and the lumen (Fig. 3) [2, 3]. The presence of a plaque with such characteristics could be considered a substrate for an acute coronary syndrome. However, with no significant vessel stenosis and no visible thrombus, the mechanism of recurrent resting angina seen in the patients could not be easily explained.

Subsequently, OCT was performed using a M2x system and a ImageWire 0.019" catheter with a Helios occlusive balloon catheter (LightLab™, USA). Image acquisition was performed using a mechanical pullback system at the speed of 3 mm/s. During image acquisition, normal saline was infused to the investigated artery to provide blood flushing and adequate visualization. MLA measured during OCT, estimated at 1.86 mm^2 (Fig. 4), was much smaller compared to IVUS estimate, likely resulting from visualization of soft thrombi covering plaque surface that could not be seen in the ultrasonographic study due to their echogenicity similar to that of blood. In addition, a plaque rupture in an area of thin fibrous cap covering soft, fatty-necrotic core was visualized slightly distally to the site of MLA. The site of a plaque rupture seen by OCT corresponded to the unstable plaque as determined by virtual histology (Fig. 3). Arrows in Figure 4 indicate the necrotic core as visualized using both imaging modalities.

Notably, most cross-sectional views showed high concordance between IVUS images, virtual histology and OCT (Fig. 5, cross-sections 1, 2, and 4). Only soft thrombus forming on the plaque surface was not clearly visible by IVUS (Fig. 4 and cross-section 3 in Fig. 5), resulting in overestimation of MLA by IVUS.

Due to unstable clinical course and the presence of ruptured plaque in LAD, a decision was made to perform an *ad hoc* coronary angioplasty. The likely cause of recurrent angina was thought to be dynamic variability of the size of thrombi on the surface of ruptured plaque and/or resultant coronary embolism. A Xience™ 3.0/15 mm (Abbott, USA) everolimus-eluting stent was implanted. The procedure was optimalized using OCT and IVUS, with additional stent dilatation using 3.5 mm balloon at 18 bar. The clinical condition of the patient stabilized following coronary intervention, with no recurrent angina seen during the subsequent month.

Discussion

The presented case may form a basis for some more general conclusions regarding diagnostic evaluation and treatment of patients with acute coronary syndromes. First, this case confirms well-known limitations of conventional coronary angiography in the evaluation of hemodynamic significance of detected coronary stenoses [4]. Second, unsuccessful medical treatment in the setting

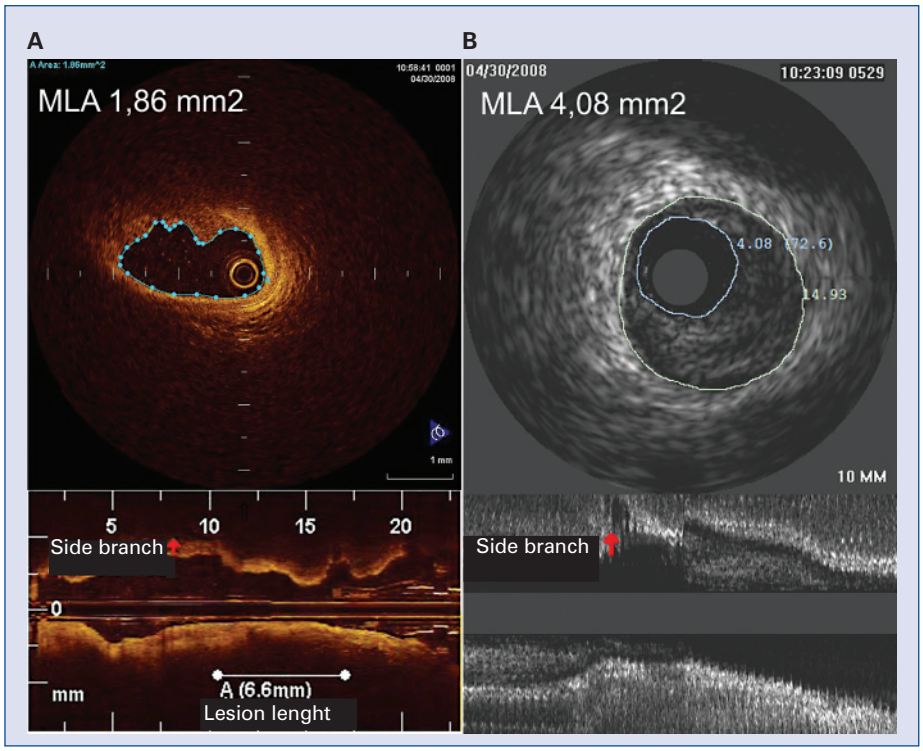

Figure 4. Cross-section of the left anterior descending coronary artery at the site of minimal lumen area. Optical coherence tomography showed significantly smaller minimal lumen area (1.86 mm^2; **A**) compared to intravascular ultrasound (4.08 mm^2; **B**). Intravascular ultrasound underestimated minimal lumen area due to its inability to visualize soft structures corresponding to intraluminal thrombus.

of equivocal angiographic picture, even with negative stress test, suggests a need for further invasive evaluation of the coronary vasculature using additional imaging modalities.

Subsequent evaluation of the potential culprit lesion using IVUS and virtual histology resulted in identification of an unstable plaque. However, precise visualization of the coronary lumen at the site of MLA was not possible due to a relatively low spatial resolution of these techniques and their low sensitivity for the detection of fresh thrombus. In contrast, OCT allowed more precise visualization of the unstable atherosclerotic plaque and also revealed the site of ruptured fibrotic cap with resultant formation of a platelet-rich thrombus leading to significant lumen obstruction. Finally, our data confirm the ability to obtain successful mechanical stabilization of a atherosclerotic plaque using a drug-eluting stent [5].

To date, only a few papers have been published that reported on the use of this combination of two novel imaging modalities, i.e. virtual histology and OCT, to identify unstable coronary plaques in humans *in vivo* [3]. Simultaneous use of these complementary imaging modalities may result in increased diagnostic precision, and also affect subsequent therapeutic decisions as illustrated by our case. Technological advance regarding OCT eliminated or reduced problems related to low penetration in indiaphanous tissue and slow image acquisition [6], making OCT a clinically useful and safe alternative to other methods of imaging coronary plaques *in vivo* [6, 7]. OCT allows precise evaluation of the structure and content of atherosclerotic plaques as shown by comparing OCT with histological evaluation [6, 8]. Image resolution with OCT catheters used in clinical practice is 10–20 μm, and experimental systems offer prospects of increasing spatial resolution to 4 μm [6, 9]. Typical OCT catheters do not contain signal transducers and thus are relatively cheap and of limited size [6]. Currently, 0.016–0.019" catheters are uses, and in the near future 0.014" catheters are likely to be introduced. In comparison to IVUS, OCT is characterized by high reproducibility of findings, both between- and within-observer [8]. In addition, OCT allows much higher image resolution and capacity to differentiate various elements of the vessel wall, as well as higher precision of the measurements compared to IVUS [6, 9–11]. Main drawbacks of this modality

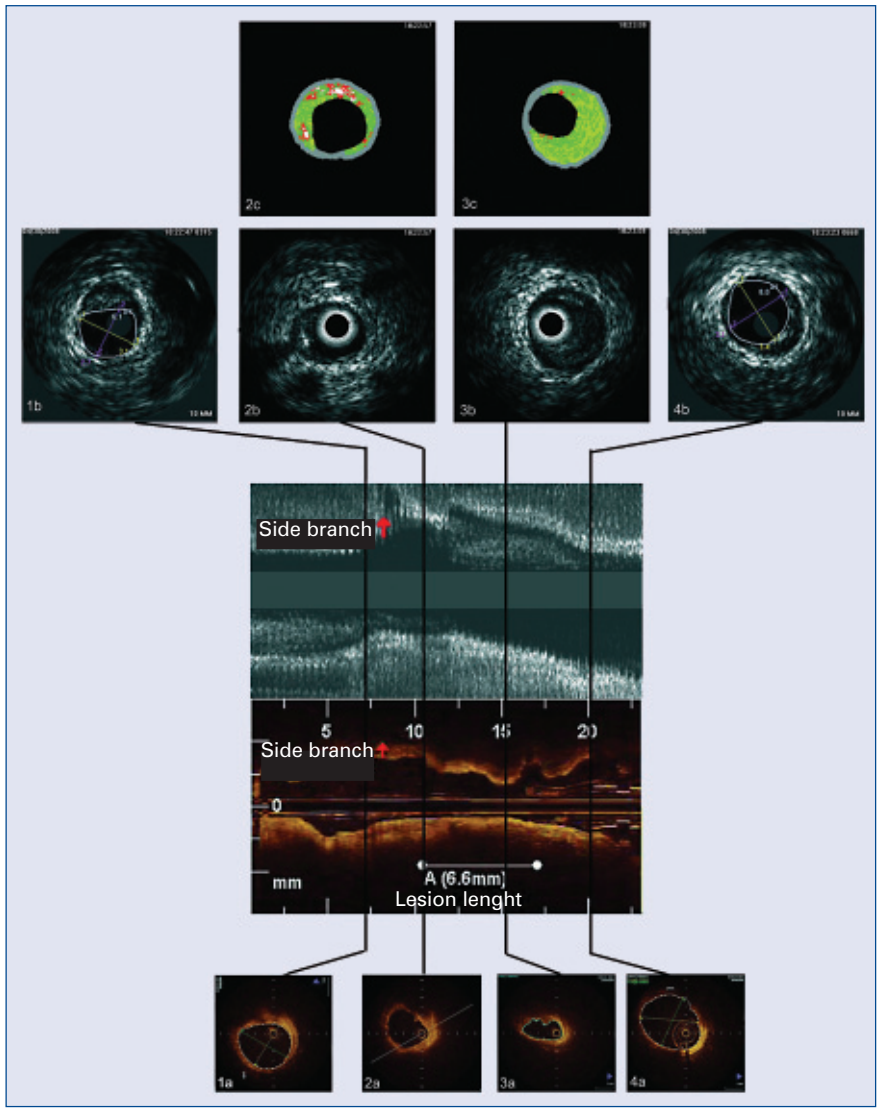

Figure 5. Corresponding images of cross-sections (1–4) and longitudinal reconstructions (pictures in the middle of the figure) obtained by different methods of atherosclerotic plaque imaging: optical coherence tomography (a), intravascular ultrasound (b) and virtual histology (c). Note the concordance of vessel lumen assessment by all imaging methods in reference cross-sections 1 and 4, as well as in cross-section 2 with vulnerable plaque. However, intravascular ultrasound underestimated the degree of lumen stenosis in cross-section 3 at the site of minimal lumen area.

include limited penetration of light into tissue (maximally for 2–3 mm) and the necessity of replacing blood in the examined vessel with optically translucent fluid (most commonly normal saline, Ringer solution, dextran or radiological contrast medium) [6, 7]. *Ex vivo* studies in animals and humans allowed defining OCT images of fibrous plaques, calcified fibrous plaques and lipid-rich lesions [8]. Current research on the use of OCT in clinical practice focuses on visualization of morphological features of unstable atherosclerotic plaques that determine their vulnerability, i.e. rupture-prone characteristics [6, 11–13]. The unique capabilities of OCT allow measurements of fibrous cap thickness, evaluation of foam cell content in the plaque, and visualization of sites of plaque rupture or erosion [6, 14]. Fibrous cap thickness threshold considered an indicator of plaque instability and vulnerability is $\leq 65\,\mu$m [9, 12, 13]. *In vivo* studies using OCT allowed, for the first time, to show correlation between an unstable clinical course of coronary artery disease and fibrous cap thickness. Proportion of atherosclerotic plaques with thin fibrous cap was higher, and the mean fibrous cap thickness was smaller in patients with myocardial infarction and unstable angina pectoris (72% and 47.0 μm, and 50%

and 53.8 μm, respectively) compared to patients with stable angina (20% and 102.6 μm) [12]. In addition, correlation was shown between elevated systemic inflammation markers, accumulation of inflammatory cell within atherosclerotic plaque, and lower fibrous cap thickness [14]. The ability to visualize intravascular thrombi using OCT was shown both in experimental models and in humans [11, 15]. This is a significant advantage of OCT, particularly in regarding to visualization of small, new, soft, unorganized platelet-rich thrombi that might not be seen or clearly delineated by other imaging modalities as illustrated by our case. Other authors also highlighted improved capacity of OCT to visualize lumen borders in comparison to IVUS [7]. Considering the above unique advantages of visualization of coronary lesions using OCT, this imaging modality may be very useful in clinical practice, guiding therapeutic decisions in selected patients with acute coronary syndromes. Our case illustrates feasibility of the use of OCT in the diagnostic evaluation in difficult cases and settings, when other commonly used invasive imaging methods cannot adequately explain the cause for an unstable clinical course of coronary artery disease. In our patient, OCT allowed visualization of morphologic characteristics of a coronary plaque consistent with its instability the were unable to be determined using other imaging techniques.

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