International Journal of Cardiology 165 (2013) 506–511

Contents lists available at SciVerse ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Presentations of acute coronary syndrome related to coronary lesion morphologies as assessed by intravascular ultrasound and optical coherence tomography

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ARTICLE INFO

Article history:
Received 1 July 2011
Accepted 6 September 2011
Available online 1 October 2011

Keywords:
Acute coronary syndrome
Intravascular ultrasound
Optical coherence tomography
Metabolic syndrome

ABSTRACT

Background: Pathologically, the lesions responsible for acute coronary syndrome (ACS) are ruptures of vulnerable plaques (and occasionally fibrous-cap erosions or calcified nodules) with a superimposed thrombosis. We aimed to clarify the clinical presentations related to the morphologies of coronary lesions of ACS using intravascular ultrasound (IVUS) and optical coherence tomography (OCT).

Methods and results: Seventy-five culprit lesions of ACS patients were clearly assessed with IVUS and OCT. Patients were classified into two groups based on the presence or absence of a rupture of a culprit plaque as identified by OCT. Clinical characteristics and lesion morphologies were compared between the two groups. Waist circumference was significantly greater ($p<0.02$) and prevalence of the metabolic syndrome (MS) higher ($p=0.0011$) in the rupture group. The prevalence of prodromal angina was higher in patients without plaque ruptures ($p<0.0001$). Using multivariate analysis, the MS and prodromal angina were independent predictors of rupture of a culprit coronary plaque (odds ratio (OR): 27.30, $p<0.003$ and OR: 0.04, $p=0.0004$, respectively). Among the components of the MS, the prevalence of abdominal obesity was a significant independent predictor of rupture of a culprit plaque (OR: 4.24, $p<0.02$).

Conclusions: There are two presentations related to the coronary lesion morphologies of ACS: we should understand these aspects of ACS.

1. Introduction

The lesions responsible for acute coronary syndrome (ACS) are sudden ruptures of vulnerable plaques [1–3] (and occasionally erosions or calcified nodules) with a superimposed thrombosis [4,5]. In general, vulnerable plaques are characterized as those having a thin inflamed fibrous cap over a large lipid core with activated macrophages near the fibrous cap [2,3]. Intravascular ultrasound (IVUS) has become a standard invasive method for diagnosing coronary artery disease. Reports have suggested that positive vascular remodeling and hypoechoic regions corresponding to lipid-rich tissue in coronary plaques on IVUS images are related to acute coronary events [6]. Furthermore, intravascular optical coherence tomography (OCT) has been proposed as a high-resolution imaging method for characterization of coronary plaques [7,8]. OCT can be used to detect the microstructure of vulnerable plaques such as thin fibrous caps, lipid cores, and intracoronary thrombi [9–11].

Acute myocardial infarction (AMI) caused by the rupture of culprit plaques is associated with a high degree of myocardial damage and poor functional recovery as compared with AMI without plaque rupture, even after successful primary angioplasty [12]. The etiology of ACS may affect outcome. However, the presentations related to differences in the clinical background of ACS patients with and without ruptures of vulnerable plaques are not known. The aim of this study was to clarify the different presentations of ACS related to the morphologies of coronary lesions using IVUS and OCT.

2. Methods

2.1. Study population

The study protocol was approved by the Ethics Committee of Hiroshima City Asa Hospital (Hiroshima, Japan). Written informed consent was obtained from all patients after receiving an explanation of the study protocol. We comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

This study involved patients with ACS who were admitted to the Coronary Care Unit of Hiroshima City Asa Hospital. Patients had ischemic chest discomfort with ST-segment elevation or depression of >0.5 mm or T-wave inversion in two or more leads. Among them, AMI was diagnosed by increased serum levels of creatine phosphokinase (more than twice the upper limit of normal) and creatine phosphokinase-MB fraction (>10% of total creatine kinase). Other patients without elevation of the creatine kinase-MB fraction were classified as having unstable angina. All patients underwent angiography within 24 h of the onset of chest pain to document the responsible coronary lesions. Patients with a history of a myocardial infarction or coronary artery bypass grafting were excluded. Other exclusion criteria were patients with: heavily calcified lesions; left main disease; tortuous lesions expected to cause difficulty in advancing the IVUS and OCT catheters; a reference diameter >4.0 mm by angiography (which was too large to occlude blood

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doi:10.1016/j.ijcard.2011.09.032

flow). We identified plaques based on coronary angiography, and analyzed each plaque using IVUS and OCT. Among them, lesions with massive thrombi were thrombolysed with a pulse infusion thrombolysis system (Nemoto Kyorindo, Tokyo, Japan) [13] or a thrombectomy was carried out with an aspiration system (Thrombuster, Kaneka Medix Company, Osaka, Japan) before IVUS and OCT.

Patients were divided into two groups based on the presence or absence of ruptures of culprit coronary plaques as identified by OCT. We assessed patient characteristics (age, sex, body mass index (BMI), waist circumference (WC)), the presence of atherosclerotic risk factors (hypertension, diabetes mellitus (DM), dyslipidemia, current smoking, ischemic family history, metabolic syndrome (MS)) and medications. Hypertension was defined as systolic blood pressure (SBP) ≥140 mm Hg, diastolic blood pressure (DBP) ≥90 mm Hg, or use of anti-hypertensive drugs. Dyslipidemia was defined as the presence of a low-density lipoprotein-cholesterol (LDL-C) level ≥140 mg/dL, fasting triglyceride (TG) level ≥150 mg/dL, a high-density lipoprotein cholesterol (HDL-C) level <40 mg/dL, or use of anti-hyperlipidemic drugs. DM was defined as any of the following: fasting serum glucose level ≥126 mg/dL, non-fasting glucose level ≥200 mg/dL, self-reported use of medications for DM, or a self-reported previous diagnosis from a physician.

The characteristics of MS were based on criteria from the third report of the National Cholesterol Education Program Adult Treatment Panel III (ATP III) [14]. Among those criteria, WC might not be suitable for Japanese subjects, and it was modified. One study [15] demonstrated that a visceral fat area of 100 cm^2 assessed by abdominal CT at the level of the umbilicus was identified in Japanese men with a WC of 85 cm and in Japanese women with a WC of 90 cm. According to that report, we defined the MS as the presence of ≥3 of the following factors: (i) WC ≥85 cm in men and ≥90 cm in women; (II) fasting TG level >150 mg/dL; (iii) HDL-C <40 mg/dL in men and <50 mg/dL in women; (4) hypertension (SBP ≥130 mm Hg, DBP ≥85 mm Hg or use of antihypertensive drug therapy); and (5) fasting glucose level ≥110 mg/dL. Blood sampling was evaluated at a hemodynamically steady state 5–7 days after the onset of ACS.

2.2. Coronary angiography

Aspirin (100 mg, p.o.), clopidogrel (300 mg, p.o.), and heparin (7000 U, p.o.) were administered before coronary intervention. Coronary angiography was undertkane by the standard Judkins technique using a 6-F sheath and catheters. Images were analyzed as previously described, with substantial lesions (vessel diameter narrowed by >50%) being measured quantitatively [16].

The location of the culprit lesion was determined by correlating the presence of a complex lesion with electrocardiographic and wall-motion abnormalities. In each patient, the coronary vasculature was reviewed to identify anatomically remote complex lesions. An anatomically remote lesion was defined as a lesion in an artery different from that containing the culprit lesion, in a different branch of the same artery, or in the same branch, but ≥5 cm from the culprit lesion with an intervening disease-free segment. The angiograms were analyzed by two independent angiographers (K.D. and S.S.). Results were compared, and the final decision made by consensus if there was disagreement.

2.3. Acquisition of intracoronary images

Lesions with a thrombolysis in myocardial infarction (TIMI) flow grade of ≤2 with thrombi were treated with aspiration thrombectomy and/or pulse infusion thrombolysis [17] before intracoronary imaging, but pre-dilatation with a balloon catheter was not allowed. After reperfusion with TIMI flow grade 3, the culprit lesion was observed using IVUS and OCT. First, an IVUS (Atlantis SR Pro 2.5 F, 40 MHz; Boston Scientific, Natick, MA, USA) examination was undertaken utilizing an anatomic pullback device at a rate of 0.5 mm/s. Then, a 0.016-inch OCT catheter (ImageWire, LightLab Imaging Incorporated, Westford, MA, USA) was advanced to the distal end of the culprit lesion through a 3-F occlusion balloon catheter. To remove blood from the field of view, the occlusion balloon was inflated to 0.5 atm at the proximal site of the culprit lesion, and lactated Ringer's solution infused into the coronary artery from the distal tip of the occlusion balloon catheter at 0.5 mL/s. The entire length of the culprit lesion was imaged with an automatic pullback device moving at 1 mm/s, and the OCT image clearly visualized the culprit lesion.

2.4. Image analyses

All images were recorded digitally and analyzed by two independent investigators (E.K. and Y.N.) blinded to the clinical presentation. Corresponding images from IVUS and OCT were identified by the distances from two landmarks (e.g., side branches). The change in the cross-sectional area of the external elastic membrane at the lesion site was the direct measure of arterial remodeling. The remodeling index was calculated as the lesion site divided by the reference cross-sectional area of the external elastic membrane [18, 19] and used to identify lesions as positive remodeling (remodeling index >1.1).

The presence of a plaque rupture or intracoronary thrombus was also noted. Plaque ruptures were identified by the presence of a discontinuity in a fibrous cap and cavity formation of the plaque (Fig. 1). Culprit lesions without plaque ruptures were identified as lesions without any fibrous-cap disruption or cavity formation (Fig. 2). Intracoronary thrombi were identified by images of an irregular mass protruding into the vessel lumen from the surface of the vessel wall. In OCT images, the thickness of the fibrous cap was measured at its thinnest part [20]. Red thrombi were identified as high-backscattering protrusions inside the lumen of the artery, with signal-free shadowing, whereas white thrombi were identified as low-backscattering projections in the OCT image [21]. Formation of a massive red thrombus indicated that more than half of the luminal cross-sectional area was occupied by a red thrombus. In non-ruptured plaques, the thickness of the fibrous cap was defined as the minimum distance from the lumen of the coronary artery to the inner border of the lipid pool, which was characterized by a signal-poor region in the OCT image. In ruptured plaques, the residual fibrous cap was identified as a flap between the lumen of the coronary artery and the plaque cavity, and its thickness was measured at the thinnest part [9]. Cap thicknesses for each image were measured at three times and the mean value used. A thin-cap fibroatheroma (TCFA) was defined as a plaque with lipid content in ≥2 quadrants and with the thinnest part of the fibrous cap measuring ≤65 μm. Inter-observer and intra-observer variability was assessed by evaluation of all

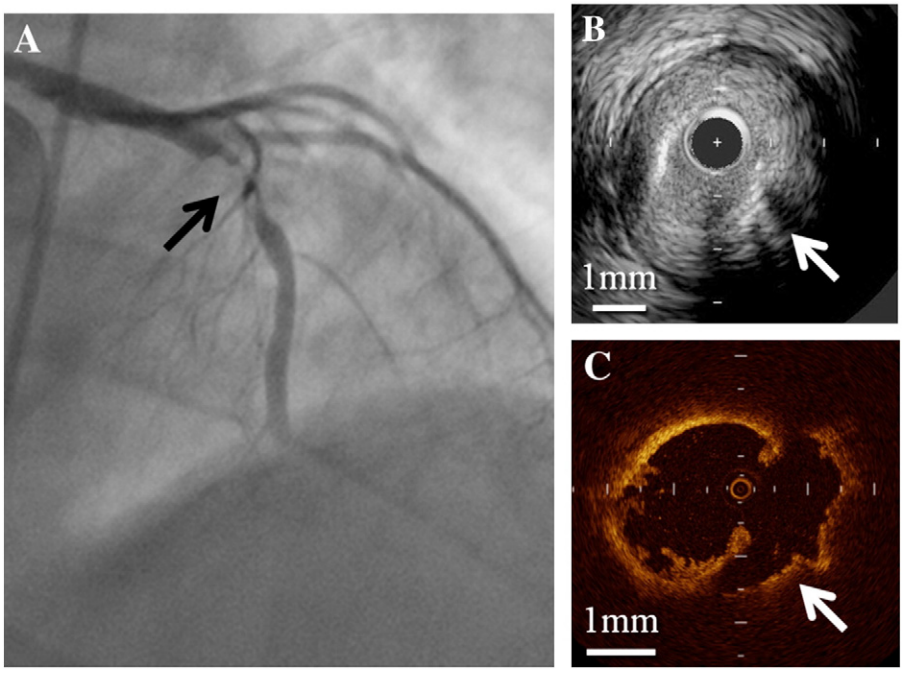

Fig. 1. Representative case with rupture of a culprit plaque. Rupture of a culprit plaque in the corresponding images as assessed by coronary angiography (A), intravascular ultrasound (B), and optical coherence tomography (C). (B) Formation of an eccentric ulcer with an intimal flap (arrow). (C) Localized disruption of a fibrous cap and ulcer formation (arrow).