Rapid progression of nonculprit coronary lesions six weeks after successful primary PCI in culprit artery: a case report

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Abstract

We report a case of a 49-year-old man who was admitted with a 3-hour history of sudden onset of substernal chest pain. Coronary angiography revealed that the left circumflex artery (LCX) was acutely and totally occluded at the mid-portion. In addition, the proximal and mid-portion of the right coronary artery (RCA) had a 60% occlusion. We inferred that the LCX was the culprit artery and primary PCI was successfully performed. Six weeks later, the patient had an eventful course with recurrence of chest pain. Coronary angiography showed no significant stenosis in the previous LCX lesion, while the proximal and middle portion of the RCA had a 90% occlusion. Our case demonstrates the systemic nature of acute coronary syndromes and highlights the inherent instability of coronary artery disease.

Keywords: acute coronary syndrome, percutaneous coronary intervention, nonculprit coronary lesions

INTRODUCTION

Plaque rupture or endothelial erosion with subsequent occlusive thrombus formation is the primary cause of acute coronary syndrome (ACS)<sup>1-2</sup>. It has been generally accepted that plaque vulnerability is an underlying mechanism for this local phenomenon. However, plaque instability may reflect a pan-vascular process with the potential to destabilize the plaques in nonculprit areas<sup>3</sup>. Several studies have suggested that vulnerable plaques exist at nonculprit lesions, as well as in the culprit site in ACS patients<sup>4</sup>. Moreover, ACS patients who underwent percutaneous coronary intervention (PCI) had a similar recurrent adverse cardiac event rate in culprit lesions and nonculprit lesions (12.9% versus 11.6% during a 3-year follow-up period)<sup>5</sup>. Therefore, detection of these non-obstructive, vulnerable plaques may play an important role in the prevention of acute myocardial infarction (AMI) and sudden cardiac death.

CASE REPORT

A 49-year-old man was admitted with a 3-hour history of sudden onset of substernal chest pain. The pain started while he was doing exercise. It was sharp, substernal and associated with shortness of breath and diaphoresis. He had an irregular medical history of hypertension for 5 years and hypertriglyceridemia for 12 years, and had a long history of smoking and drinking. He had no history of spontaneous bleeding, diabetes mellitus, stroke, atrial fibrillation, or family...
history of coronary artery disease. On admission, his cardiac enzymes, including myoglobin, were normal. His initial electrocardiogram (ECG) showed ST-segment elevation in the inferior (II, III, and avF) and posterior (V7–V9) leads (**Fig. 1**), while there was ST-segment depression in the anterior (V1–V4) leads, which may indicate acute inferior and posterior myocardial infarction. The patient underwent primary angioplasty after receiving aspirin (300 mg) and clopidogrel (300 mg). Coronary angiography revealed that the left circumflex artery (LCX) was acutely and totally occluded at the mid-portion (**Fig. 2A**) and the proximal and mid-portion of the right coronary artery (RCA) had a 60% occlusion (**Fig. 2B**). We inferred that the LCX was the culprit artery and intervention was performed. After percutaneous transluminal coronary angioplasty (PTCA) was carried out in the LCX, lesions of the LCX had a hazy filling defect, which suggested an acute thrombus, and thrombus aspiration was conducted. Then, the patient had a successful stent in the culprit LCX. The patient’s symptoms and postoperative ECG results were significantly improved. One day later, laboratory tests showed: total cholesterol (TC) 3.83 mmol/L, triglycerides (TG) 5.35 mmol/L, high density lipoprotein (HDL) 0.75 mmol/L, low-density lipoprotein cholesterol (LDL) 2.25 mmol/L, lipoprotein a (Lp(a)) 179 mg/L, uric acid (UA) 445 μmol/L, and NT-proBNP 759 ng/L. A 2D-echocardiogram was performed and showed left ventricular ejection fraction (LVEF) of 67.8%, with no regional wall motion or valvular abnormalities. He remained stable throughout his hospital stay and recovered without any symptoms. The patient was discharged home 12 days later on aspirin (100 mg qd), clopidogrel (75 mg qd), atorvastatin (20 mg qn), ezetimibe (10 mg qd), and trimetazidine (20 mg tid).

Three weeks post discharge, he recovered without any symptoms and the test results showed values of: TC 2.89 mmol/L, TG 3.31 mmol/L, HDL 0.82 mmol/L, LDL 1.76 mmol/L, Lp(a) 45 mg/L, and UA 460.3 μmol/L. However, one week later, the patient had an eventful course with recurrence of chest pain. ECG showed that R waves of II, III, and avF leads were flat, and exhibited QS model of V7–V9 leads. His cardiac enzymes were still normal. 2D-Echocardiography examination showed that left ventricular lateral wall motion had decreased and LVEF was 57.1%. ECT showed myocardial ischemia and regional wall motion abnormalities in the left ventricular lateral wall, as well as inferior wall. Coronary angiography showed no significant stenosis in the previous LCX lesion, while the proximal and middle potion of the RCA had a 90% occlusion (**Fig. 2C**). Two coronary stents were implanted in the RCA. After the procedure, the patient

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**Fig. 1** Initial electrocardiogram of a 49-year-old man with a 3-hour history of sudden onset of substernal chest pain.

**Fig. 2** Coronary angiography. A: The left circumflex artery was acutely and totally occluded at the mid-portion. B: The proximal and mid-portion of the right coronary artery had a 60% occlusion. C: The proximal and mid-portion of the right coronary artery had a 90% occlusion.
had a stable course with no recurrence of chest pain. He was discharged six days later.

DISCUSSION

It is known that ACS patients are at high risk for recurrent ischemic events caused by a lesion that is anatomically unrelated to the initial event[6]. Our case supports the concept that ACS is a pan-vascular process with a higher prevalence of vulnerable plaques in nonculprit sites, leading to recurrent ischemic events in the future. Most (83.3%) of the plaque ruptures of nonculprit artery in a previous study were observed in ST-elevation MI patients[7]. Rioufol et al. reported plaque ruptures somewhere other than the culprit lesion in 79% of patients with ACS[8]. PCI patients with nonculprit coronary lesions underwent additional clinically driven PCI at rates of 7.7% at 1 year, 14% at 2 years, and 16% at 3 years because of the progression of pre-existing nonculprit coronary lesions[9].

Because of the rarity of the condition, no management guidelines exist. Nonculprit artery in AMI slows flow globally, which is associated with adverse outcomes[10]. Fractional flow reserve assessed by intracoronary pressure wire is useful in deciding whether to revascularize angiographically moderate nonculprit lesions in patients with ACS[11-12]. Previous studies have shown that inflammation plays a pivotal role in the development of atherosclerosis and inflammation factors such as C-reactive protein are involved in the progression of nonculprit lesions[13-14]. ACS correlates with systemic markers of inflammation, so high recurrent events may be related to additional vulnerable lesions distant from the culprit lesion. These observations support the concept that plaque instability is not merely a local vascular accident but rather probably reflects more generalized pathophysiological processes with the potential to destabilize atherosclerotic plaques throughout the coronary tree.

Despite achieving very low levels of LDL-C, many patients continue to show disease progression[15]. Poor lipid profiles at baseline PCI confer significant risks for clinically driven PCI[16]. On-treatment TG <150 mg/dl was independently associated with a lower risk of recurrent coronary heart disease (CHD) events, lending support to the concept that achieving low TG may be an additional consideration beyond low LDL-C in patients after ACS[17]. Hyperinsulinemia is associated with an increased lipid content and a greater plaque volume of nonculprit intermediate lesions in nondiabetic patients with ACS, suggesting that plaque vulnerability is increased in this subgroup of patients[18]. ACS, multivessel diseases, HDL-C and smaller increases in HDL-C were associated with the progression of nonculprit coronary lesion[3,6,17]. This finding highlights the need for intensive modification of global risk in patients with coronary artery disease.

Thrombus was identified more frequently in infarct-related arteries than non-infarct-related artery lesions in the previous study[7]. However, 5.0% of the nonculprit coronaries also exhibited thrombus[3,19]. These reports all primarily showed that lesion-specific morphologies determined plaque instability and patient symptoms.

Pathological studies have reported that healed ruptured plaque is associated with lesion progression. Subclinical episodes of plaque disruption, local thrombin activation, and subsequent healing with incorporation of thrombus into the vessel wall may represent one pathway for episodic progression superimposed on the slower systemic process[20]. This concept is supported by previous angiographic studies showing rapid progression of stenosis with complex angiographic features. After successful PCI of all angiographically significant lesions, overall untreated atherosclerotic burden remains high, and plaque burden lesions are frequently present in the proximal and mid-coronary tree. Patients with plaque burden lesions have greater atherosclerosis throughout the coronary tree, have more thin-cap fibroatheromas, and are at increased risk for future cardiovascular events[21].

To sum up, plaque disruption and healing occur not only at the culprit lesion but may be a pan-coronary process in patients with AMI. We identified some questions regarding the nonculprit coronary. The first concerns vulnerable plaques identified by the imaging tools. Three such devices have emerged and received the USA Food and Drug Administration approval with “tool” claims that are theoretically capable of identifying certain characteristics of a thin cap fibroatheroma: radiofrequency intravascular ultrasound (RF-IVUS), optical coherence tomography (OCT), and near-infrared spectroscopy (NIRS). However, each has its advantages and disadvantages[22]. So, how should these imaging tools be validated as potential detectors of vulnerable plaque? Secondly, most patients with coronary atherosclerosis are already prescribed high-dose statins. Despite attainment of an LDL-C level of less than 1.8 mmol/L, nonculprit coronary lesions had still progressed, mainly in preexisting nonculprit artery lesions rather than de novo nonculprit artery lesions. One previous study demonstrated that early aggressive lipid-lowering therapy, via atorvastatin for 6 months, significantly reduced the plaque volume in patients with ACS[23]. We recommend intensive treatment for the culprit lesion and other severe lesions after careful consideration, in a staged fashion if necessary. Thirdly,
multivessel PCI for patients during AMI is currently controversial. One meta-analysis supports current guidelines discouraging performance of multivessel primary PCI for STEMI. When significant nonculprit vessel lesions are suitable for PCI, they should only be treated during staged procedures. One study suggests that multivessel PCI is effective and safe for Chinese patients with ST-segment elevation AMI and simple lesions in nonculprit arteries. However, other research showed that initial multivessel PCI was associated with significantly increased risk of in-hospital death, all-cause death, and MACCE.

In conclusion, randomized trials must ultimately be undertaken in patients with high-risk plaques to evaluate the use of either new more potent systemic therapies or focal/regional interventional therapies to demonstrate that treating vulnerable plaques before rupture is effective in preempting future ACS. Here, we describe the clinical presentation and interesting angiographic findings in a case of rapid progression of RCA lesions six weeks after successful primary PCI in the totally occlusion of the mid-portion of the LCX with a brief discussion of a possible mechanism in the context of current management options. This case report demonstrates the systemic nature of acute coronary syndromes, highlights the inherent instability of coronary artery disease, and supports the notion of aggressive secondary prevention in these patients.

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