Coronary Stenosis as an Innocent Bystander in Acute Coronary Syndrome

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Figure 1. (A) Angiographic and (B–H) corresponding optical frequency-domain imaging (OFDI) slices. (A) Left cranial angiographic view of the proximal left anterior descending artery, showing intermediate stenosis followed by an intramyocardial bridge. In (H) the corresponding OFDI slice, a smooth, mainly fibrotic coronary plaque was found, without any sign of rupture and/or erosion; the calculated minimum lumen area at this point was 3.4 mm², indicating a non-significant stenosis. (H) The slice at the point of the intramyocardial bridge indicated diffuse intimal thickening.
A 56-year-old Asian man who was a smoker and had hypertension, and who had a family history of sudden cardiac death, presented to the emergency department with stuttering chest pain that had started approximately 6 h beforehand. The patient had not been on medication before admission. High sensitive-troponin T concentration was 0.149 ng/ml on admission, peaking at 0.211 ng/ml on the first day before trending down. Electrocardiogram (ECG) showed negative, ischemic T waves in leads V1–V4. The pain subsided shortly after admission and did not recur during hospitalization. Medical therapy for non-ST-elevation acute coronary syndrome (ACS) was initiated: drugs included low-dose aspirin, ticagrelor, statins and angiotensin-converting enzyme inhibitors. Coronary angiography was performed 24 h after admission, and indicated intermediate stenosis of the proximal left anterior descending artery (LAD) followed by a segment presenting phasic, systolic compression in the mid-distal LAD, which was interpreted as an intra-myocardial bridge (Figure 1).

Given that we were unsure about the underlying mechanism of the ACS, we elected to use high-resolution intracoronary imaging. Optical frequency-domain imaging (Terumo, Tokyo, Japan) showed, in the proximal tract of the LAD, a smooth, mainly fibrotic coronary plaque, without signs of rupture and/or erosion, and a diffuse intimal thickening of the entire LAD, more evident in the bridge area. Calculated minimum lumen area was 3.4 mm², indicating a non-significant stenosis (Figures 1A–F). According to the systematic algorithm of investigation of patients with acute myocardial infarction with no obstructive coronary atherosclerosis (MINOCA), intracoronary acetylcholine was administered at increasing dosages. Notably, the low dose (50 µg in 10 ml saline) elicited occlusive focal spasm, which did not involve the atheromathous area of the vessel, but was confined to the mid-distal part of the LAD, including the area of myocardial bridge (Figure 2). The patient experienced chest pain that was described as identical to that occurring before admission, and ECG showed peaking transient anterior T-waves. High-dose intracoronary nitrates were rapidly administered, which relieved the spasm and chest pain (Figure 2), with complete regression of the ECG changes. Diltiazem was added to the drug regimen and titrated up to 300 mg/daily, with no symptom recurrence for up to 6 months.

Flow-limiting coronary artery stenosis and its complications are the leading cause of ACS, supporting the concept that (mainly percutaneous) revascularization should be rapidly performed in order to improve symptoms and outcomes. A sizeable proportion of individuals presenting with ACS,
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However, are found to have absent or only angiographically mild coronary lesions. These patients are often mistakenly classified as being at low risk, and may not receive adequate secondary prevention or specific medical therapy such as calcium antagonists.

Dynamic change in epicardial coronary artery tone, alone or in combination with abnormalities of coronary microcirculation, is an important cause of MINOCA. The susceptibility to spasm can be unmasked by selective intracoronary ergonovine or acetylcholine; the latter is an endothelium-dependent vasodilator and a direct constrictor of vascular smooth muscle cells (VSMC).

Intriguingly, in the present patient, low-dose acetylcholine triggered focal coronary spasm not at the level of the proximal atherosclerotic plaque, but rather downstream. This suggests (albeit indirectly) that endothelial dysfunction is not responsible per se for coronary spasm, given that its anatomical hallmark (diffuse intimal thickening) was present along the entire course of the LAD and was probably even more severe at the site of the proximal atherosclerotic plaque. Endothelial dysfunction may thus merely favor spasm at the site of predisposed segments characterized by hyperreactivity of VSMC. Marked VSMC hyperreactivity, linked to enhanced Rho kinase activity, seems particularly prevalent in Asian subjects, such as the present patient.

Thus even large coronary plaques might act as mere “innocent bystanders” in ACS patients. The prevalence of these innocent bystanders is unknown because it can be unmasked only on ergonovine or acetylcholine treatment. Careful elucidation of the specific pathophysiological mechanism operating in each individual patient (regardless of ethnicity) with ACS, is crucial for risk stratification and implementation of the most appropriate therapy.

Disclosures

None.

References