Short communication

Absence of adventitial vasa vasorum formation at the coronary segment with myocardial bridge - An optical coherence tomography study

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A B S T R A C T

Background: Myocardial bridge (MB) is a myocardial bundle through which coronary segment tunnels and could compress coronary arteries causing myocardial ischemia. However, the characteristic structural findings of MB remain to be fully elucidated. Recently, we demonstrated that optical coherence tomography (OCT) enables us to visualize adventitial vasa vasorum (VV) formation in humans. In this study, we examined adventitial VV formation at the coronary segment with MB in humans using OCT.

Methods: We examined 15 consecutive patients with suspected angina pectoris and MB in the left anterior descending (LAD) coronary arteries but no angiographic coronary stenosis. MB was detected on coronary angiography as a segment with milking effect. We performed intracoronary OCT imaging along the entire LAD. Morphometric analysis was performed at MB and proximal/distal segments at every 1 mm.

Results: OCT examination showed the absence of adventitial VV formation at MB in the LAD, while VV was clearly noted at both the proximal and distal reference segments. Adventitial VV area was significantly less at MB compared with the proximal or distal references.

Conclusions: These results with OCT imaging indicate that coronary segments with MB lack adventitial VV formation in humans, suggesting that MB could influence morphological and functional changes of the coronary artery.

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1. Introduction

Myocardial bridge (MB) is a myocardial bundle through which coronary segment tunnels, and is likely to develop in the mid to distal portion of the left anterior descending coronary arteries (LAD) [1]. Although MB could compress coronary arteries causing myocardial ischemia depending on the thickness and length [2], its clinical relevance varies substantially to imaging approaches. While “half-moon” sign on intravascular ultrasound has been anticipated to show better clinical evaluation of MB [3], the characteristic findings of MB on optical coherence tomography (OCT) with a highest resolution of 10 μm still remain to be elucidated. In the histological validation studies, we demonstrated that a newer generation OCT enables us to visualize adventitial VV formation in humans [4,5] in association with coronary artery spasm [6]. This type of OCT has another feature of angiographic co-registration during pullback of the light-core of OCT that allows us to detect the exact location by a radiopaque marker [4]. In this study, we thus examined adventitial VV formation at the coronary segments with MB in human using OCT.

2. Methods

The study protocol was approved by the ethics committee of Tohoku University Graduate School of Medicine (2014-1-640) and was performed in compliance with the Declaration of Helsinki. Written informed consent was obtained from all patients before study entry.

2.1. Study patients

We examined 15 consecutive patients with suspected angina pectoris (13 at rest and 2 on effort) and MB in the LAD but no angiographic coronary stenosis >25% (age, 67.0 ± 2.5 year-old; male, 47%). After provocation test for coronary spasm, we administered isosorbide dinitrate (ISDN) (2 mg) intracoronarily to diagnose MB as an angiographic milking phenomenon (Fig. 1A) [1,2]. Subsequently, we performed serial OCT imaging to examine the structure of MB.

2.2. Coronary spasm provocation test

We performed provocation test for coronary spasm with intracoronary acetylcholine [6,7]. Diffuse spasm was diagnosed when luminal narrowing was noted continuously from the proximal to the distal segment of the coronary artery as we previously described [8].

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2.3. Acquisition of OCT

After intracoronary ISDN, serial OCT imaging (LUNAWAVE, Terumo, Tokyo, Japan) was performed along the entire LAD with an automatic pullback speed (40 mm/s) [4–6].

2.4. Morphometric analysis on OCT

At MB and proximal/distal segments adjacent within 10 mm, morphometric analysis was performed at every 1 mm by 2 independent investigators. Wall thickness was expressed by [intimal plus medial thickness]. Adventitial area was calculated by the following formula: [area outside the external elastic lamina within a distance of the thickness of intima plus media — vessel area] [5,6], where adventitial VV area was manually traced. Adventitial VV area density was calculated by following formula: [adventitial VV area / adventitial area] [5,6]. The 3D-volume rendering of OCT was constructed by Osirix (Pixmeo, Bernex, Switzerland).

2.5. Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics 23 (IBM, New York, USA). Statistical differences were examined using one-way analysis of variance and post-hoc analysis with the Turkey’s honestly significant difference. A value of P < 0.05 was considered to be statistically significant. Results are expressed as mean ± SEM.

3. Results

3.1. Patient characteristics

All patients showed diffuse spasm of LAD during the provocation test with acetylcholine.

3.2. Absence of adventitial VV formation at MB

In all patients, OCT examination showed the absence of adventitial VV formation at MB in the LAD (Fig. 1C), while VV was clearly noted at both the proximal and distal reference segments (Fig. 1B and D). Furthermore, the 3D-OCT enabled us to visualize the 3D structural pattern of VV around MB (Fig. 1E).

3.3. Morphometric analysis of adventitial VV formation at MB

In all patients, adventitial VV area and VV area density were significantly less at MB compared with the proximal and distal references (Fig. 1F and G). In contrast, wall thickness was significantly greater at the proximal reference as compared with MB or the distal reference (proximal, 0.23 ± 0.01 mm; MB, 0.16 ± 0.00 mm; distal, 0.16 ± 0.05 mm; P < 0.01).

4. Discussion

To the best of our knowledge, this is the first report with OCT that demonstrates the absence of adventitial VV formation at the coronary segment with MB in humans.

4.1. Absence of adventitial VV formation at MB

The epicardial coronary artery is surrounded by pericoronary adipose tissue (PCAT) that harbors VV as nutrient blood vessels [7]. VV plays an important role as a conduit that diffuses inflammatory cells and cytokines derived from PCAT in the pathogenesis of coronary artery disease [6,7]. Given that coronary segments under MB may have less contact with PCAT [9], VV is unlikely to develop at MB. Separation of coronary segments under MB from VV could be protective against atherosclerotic changes. Conversely, coronary arteries without atherosclerosis under MB may not develop adventitial VV formation.

4.2. Adventitial VV formation at the reference segments

Adventitial VV formation is increasingly noted at the proximal references, which may be induced by hypoxic condition due to thickened arterial wall and altered blood flow [1]. Another possibility is that PCAT enhances VV formation by secreting pro-angiogenic cytokines. Neo-vessels arising from VV could be a trigger of plaque disruption [10]. VV formation is also consistently noted at the distal references that...
are predisposed to diffuse coronary artery spasm [11]. Indeed, we recently demonstrated that enhanced VV formation is associated with coronary spasm [6].

4.3. Study limitations

VV becomes thinner and loses its visibility when MB compressed. Although OCT imaging that covers the segments around MB was obtained at diastole, the significance of the present study remains to be examined in future studies. Second, while it has been demonstrated that focal spasm is frequently noted at the segment with MB in its relationship with endothelial dysfunction [12], no patients with focal spasm were enrolled in the present study. In order to address this remaining issue, the newer OCT with a high resolution of 1 μm [13] may be useful for visualization of endothelium at the segment with MB.

5. Conclusions

We were able to provide the first direct evidence using OCT that coronary segments with MB lack adventitial VV formation in humans, suggesting that MB could influence morphological and functional changes of the coronary artery.

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Conflict of interest

None.

References


