Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

Focal Vasa Vasorum Formation in Patients With Focal Coronary Vasospasm
– An Optical Frequency Domain Imaging Study –
Kensuke Nishimiya, MD, PhD; Yasuharu Matsumoto, MD, PhD; Hironori Uzuka, MD; Kazuma Ohyama, MD; Kiyotaka Hao, MD, PhD; Ryuji Tsuburaya, MD, PhD; Takashi Shiroto, MD, PhD; Jun Takahashi, MD, PhD; Kenta Ito, MD, PhD; Hiroaki Shimokawa, MD, PhD

Figure 1. Representative (A,B) coronary angiography and (C,D) optical frequency domain imaging (OFDI) showing markedly enhanced vasa vasorum (VV) formation (yellow arrows) in a vasospastic angina patient with focal spasm. VV area density was increased along with (E) extent of arterial wall thickening, represented by %([intima]+[media]) area, and (F) coronary vasoconstriction.

Coronary artery spasm plays important roles in the pathogenesis of a wide range of ischemic heart disease, not only in vasospastic angina (VSA) but also in other forms of ischemic heart disease.1 Although VSA is believed to be more prevalent in Asian compared with Caucasian subjects,2 it has been recently suggested that the prevalence of VSA could be similar in both populations.3 Thus, coronary spasm is an emerging issue in the world. Furthermore, given that 14% of VSA patients treated with appropriate medications have refractory angina,4 novel therapeutic strategies are warranted.

Editorial p ????
Coronary adventitia has attracted much attention as a source of inflammation because it harbors nutrient blood vessels,
Adventitial VV formation was significantly increased at the spastic focal segments compared with the proximal or distal reference segments (Figure 2A). Furthermore, there were significant positive correlations between the extent of adventitial VV formation and that of arterial wall thickening or coronary vasoconstriction (Figures 2B, C). Similar correlation was also noted between the extent of adventitial VV formation and that of arterial wall thickening at the reference segments (P<0.01, R=0.47).

To the best of our knowledge, this is the first report showing that adventitial focal VV formation coincides with the focal spastic segments in VSA patients. We have previously demonstrated in pigs that coronary hyperconstriction can be induced by adventitial inflammatory changes and after drug-eluting stent implantation, through Rho-kinase activation in the vascular smooth muscle. It was previously reported that adventitial VV formation precedes manifestation of coronary vasomotion abnormalities in hypercholesterolemic pigs. Thus, it is possible that enhanced adventitial VV formation initiates adventitial inflammatory changes with resultant coronary spasm.

In the present study, coronary vasospastic responses were noted at atherosclerotic lesions with focal spasm. We have previously demonstrated that coronary spasm can be induced at the atherosclerotic lesion in porcine models involving balloon injury and high-cholesterol diet. The extent of adventitial VV formation through hypoxia-induced angiogenesis was positively correlated with the severity of atherosclerotic changes in pigs. Indeed, in the present study, such positive correlations were noted between the extent of adventitial VV formation and that of arterial wall thickening at both the spastic and reference segments. No significant correlation was noted, however, between the extent of arterial wall thickening and that of the spasm (P=0.09, R=–0.28). Thus, it remains to be examined in future studies whether adventitial changes are involved in the enhanced VV formation at the focal spasm site. We
have recently demonstrated that atherosclerotic changes may not be correlated with adventitial VV formation at the diffuse spasm site. Thus, it is possible that the underlying mechanisms of VV formation are different between focal and diffuse spasm.

In the pathogenesis of VSA, the roles of other adventitial components remain to be elucidated. Indeed, we have recently demonstrated that coronary perivascular adipose tissue is also increased in VSA patients.15

In conclusion, adventitial focal VV formation coincides with focal spasm in VSA patients, for which atherosclerotic changes may be involved.

Disclosure
None.

References

Supplementary Files

Supplementary File 1

Table S1. Demographic characteristics and treatment
Table S2. Laboratory data
Table S3. Coronary angiography findings
Table S4. Morphometric analysis of OFDI

Figure S1. (A) Morphometric parameters, including lumen diameter, intimal (I)+medial (M) thickness, lumen area, vessel area and I+M area, were manually measured in off-line manner, at every 1 mm along the spastic segments and the proximal/distal references within 5 mm adjacent to the spastic segments.

Methods

Please find supplementary file(s); http://dx.doi.org/10.1253/circj.CJ-16-0580