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Editorial

Editorial: Silent myocardial ischemia due to coronary artery spasm

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Coronary artery spasm plays an important role in the pathogenesis of coronary artery disease and has been shown to be associated with adverse clinical outcomes, including acute coronary syndrome, heart failure, ventricular arrhythmias, and sudden cardiac death [1–5]. In particular, multivessel spasm has been reported to be a strong predictor of major adverse cardiac events in patients with vasospastic angina [1]. In this issue of the journal, Sueda et al. [6] report a patient in whom multivessel spasm was documented by acetylcholine provocation test, despite no symptoms suggestive of myocardial ischemia. Because coronary artery spasm can be associated with adverse events even if it is silent [4,5], its diagnosis is crucial.

Vasospastic angina is usually suspected based on symptoms, and noninvasive evaluations are the first step in its diagnosis. Because coronary artery spasm develops transiently, its diagnosis can be challenging in a clinical setting. Holter recording is a useful and important examination not only for the detection of ischemic attacks but also for estimating the frequency of such attacks [3,7]. Because its frequency can considerably fluctuate, Holter recording (multichannel recording desirable) repeated or for an extended period of time of 24–48 h can improve diagnostic accuracy [3]. In the present patient, data regarding Holter recording were not shown, but inferior ischemia was suspected on exercise tolerance testing. The results of exercise testing in patients with vasospastic angina have been shown to be influenced by the degree of disease activity [3,8] and are characterized by poor reproducibility caused by circadian variations in exercise tolerance. Importantly, the present patient had no symptoms suggestive of myocardial ischemia, i.e. chest pain/discomfort. Even symptoms of the jaw, throat, neck, back, shoulder, arms, and epigastric region were absent. The authors speculated that slight fatigue and cold sweating might be symptoms related to coronary artery spasm; however, objective evidence supporting this speculation is lacking. Caution is required because some patients with silent myocardial ischemia associated with multivessel spasm have no symptoms suggestive of myocardial ischemia, such as the present patient.

The underlying mechanism of silent myocardial ischemia remains unclear; however, several factors, such as differences in both peripheral and central neural processing of pain, autonomic neuropathy, or anti-inflammatory cytokines, have been proposed to play important roles in the pathogenesis of silent ischemia. It has been also reported that coronary collaterals immediately appear during coronary occlusion due to coronary artery spasm in patients with variant angina, and such collateral flow could prevent transmural myocardial ischemia, resulting in a lesser degree of ischemia [9]. In patients with vasospastic angina, chest pain accompanies about 20% to 30% of episodes of ischemic ST-T changes, and many episodes of coronary spasm are asymptomatic [3]. Egashira et al. [7] reported that the majority (76%) of ischemic events are completely silent in patients with variant angina.

Coronary angiography was performed in the present patient. Recently, the use of coronary computed tomography angiography to evaluate coronary artery disease has been increasing annually in Japan. Because coronary artery spasm cannot be diagnosed on coronary computed tomography angiography, coronary angiography must be performed in patients suspected to have coronary artery spasm. A drug-induced coronary spasm provocation test during coronary angiography has been established to be a useful diagnostic examination for coronary artery spasm [1,3,10]. Acetylcholine and ergonovine are most often used clinically as pharmacological agents in coronary spasm provocation tests in Japan. However, these tests are thought to have a potential risk of arrhythmic complications, including ventricular tachycardia, ventricular fibrillation, and bradyarrhythmias. A recent observational study evaluating 1244 patients with vasospastic angina who underwent coronary spasm provocation tests (acetylcholine 57% and ergonovine 40%) has reported that the overall incidence of arrhythmic complications was 6.8%, which is comparable to the 7.0% incidence during spontaneous angina events [1]. Furthermore, this study has also shown that mixed (focal and diffuse) type multivessel spasm was associated with major adverse cardiac events [1]. Thus, coronary spasm provocation tests are relatively safe and may be useful for risk stratification in patients with vasospastic angina. However, the Japan Circulation Society (JCS) guidelines recommend that acetylcholine or ergonovine provocation tests should be performed during coronary angiography in patients suspected to have vasospastic angina on the basis of symptoms, but who have not been diagnosed with coronary spasm by noninvasive evaluation (Class I) [3]. Detailed history taking is important in the diagnosis of coronary artery spasm. Because the incidence of vasospastic angina is higher in Japanese than in Westerners, the potential possibility of coronary artery spasm should be kept in mind when performing history taking and noninvasive evaluations, and it is important to assess the need for spasm provocation tests.

The final problem is terminology. The authors diagnosed "silent coronary spastic angina" in the present case. However, because a diagnosis of "angina" is based on the subjective evaluation of

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symptoms, it might have been more appropriate to give the patient a diagnosis of "silent myocardial ischemia due to coronary artery spasm". More importantly, the second is that the evidence supporting a diagnosis of silent myocardial ischemia was weak. In the present patient, the diagnosis of silent myocardial ischemia requires the objective findings such as a decrease in ischemic attacks with ST-T changes on Holter recording or the improvement of inferior ischemia on thallium exercise scintigraphy after starting treatment with a calcium-channel antagonist as compared with before treatment. However, the present case provides many informative suggestions with regard to the difficulty in medical history taking and the diagnosis of silent myocardial ischemia due to coronary artery spasm.

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