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【 CASE REPORT 】

Acute Heart Failure Due to Multi-vessel Coronary Spasm

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Abstract:
A 46-year-old man presented to our hospital with chest pain followed by coughing and dyspnea. His myocardial enzyme levels were almost normal, and electrocardiography and echocardiography showed no obvious abnormalities. Chest radiography revealed congestion. He was diagnosed with heart failure with a preserved ejection fraction (HFpEF). Although subjective symptoms improved with intravenous diuretics, the patient was admitted to the hospital for a close examination. Coronary angiography showed no obvious stenosis, and a subsequent spasm provocation test demonstrated the presence of multi-vessel and diffuse spasms. Coronary spasm should be considered as a differential cause of heart failure, even in patients with HFpEF.

Key words: acute heart failure, vasospastic angina, coronary spasm, heart failure with preserved ejection fraction (HFpEF), multi-vessel spasm

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Introduction

Coronary spasm or vasospastic angina (VSA) is caused by the transient vasoconstriction of the epicardial coronary arteries, leading to myocardial ischemia (1, 2). It has been widely accepted that coronary spasm is the pathogenesis of not only rest angina but also other types of coronary artery disease (CAD), including exertional angina, acute coronary syndrome, and ischemic sudden death (3). Consequently, coronary spasm is considered a possible cause of heart failure (HF) (4-8). In such reports (4-8), coronary spasm was associated with the presence of HF with a reduced ejection fraction (HFrEF) or transient left ventricular (LV) dysfunction.

We herein report a case of VSA that caused acute heart failure with a preserved ejection fraction (HFpEF).

Case Report

A 46-year-old man was brought to our hospital by ambulance because of resting chest pain lasting 1 h starting at 8:00 a.m., followed by coughing and dyspnea. The patient had experienced but neglected chest pain for 10 min one morning 6 months prior to the arrival at our hospital and chest pain with cold sweats lasting for 1 h in the morning 1 month before this visit. The patient had no significant personal or family history and was an occasional alcohol drinker with no history of smoking.

The patient was 177 cm tall, weighed 104 kg, and had a body mass index (BMI) of 33.2 kg/m^2. His consciousness was not impaired, and the blood pressure was 112/69 mmHg with a pulse 109/min. The oxygen saturation was 91% with oxygen administered via mask at 5 L/min, and his body temperature was 36.1°C. No jugular vein distention was observed. Auscultation revealed no heart murmur; however, a mild coarse crackle was observed in the right lung field. No abnormalities in the abdomen or edema of the extremities were observed. A COVID-19 antigen test showed negative results, and blood tests showed a mildly elevated white blood cell count of 9,830/mm^3. The patient's high-sensitivity troponin T level was 0.013 ng/mL, and the N-terminal pro-brain natriuretic peptide (NT-proBNP) level was 49 pg/mL, which was almost within normal limits; however, the high-sensitivity troponin T level increased to 0.044 ng/mL after 4 h, and the NT-proBNP level was 137 pg/mL the next day.

Electrocardiography (ECG) revealed sinus tachycardia with no obvious ST-T changes (Fig. 1). Although the image quality was poor, echocardiography showed no LV enlargement, a normal LV wall motion with an interventricular septum thickness of 8 mm, a posterior LV wall thickness of 9 mm, an LV end-diastolic diameter of 45 mm, an LV end-

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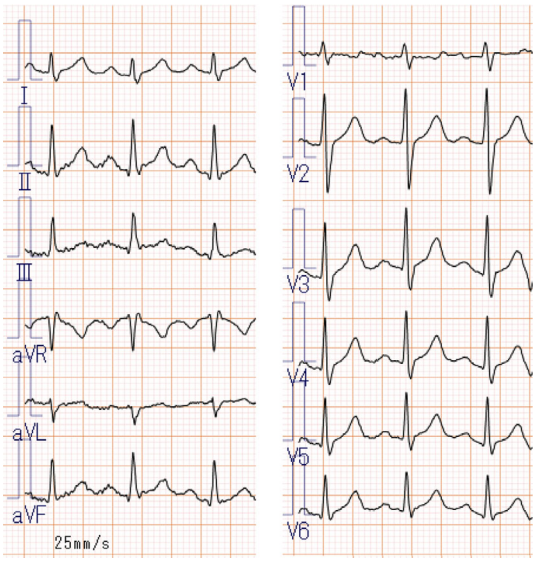

Figure 1. **Electrocardiogram findings on admission showing sinus tachycardia but no significant ST-T changes.**

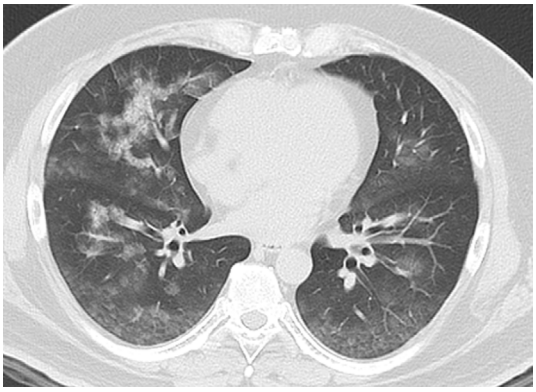

Figure 3. **Chest CT on admission showed frosted and infiltrating shadows predominantly in the right lung with scattered thickening of the interlobar septal wall. There was no pleural effusion or cardiac enlargement, but the findings were consistent with pulmonary edema. CT: computed tomography**

systolic diameter of 30 mm, and an LV ejection fraction (LVEF) of 62%. Chest radiography showed congestion (Fig. 2), which was confirmed using computed tomography (CT) (Fig. 3). The patient's symptoms worsened; however, after the intravenous injection of furosemide (20 mg), the subjective symptoms improved.

The patient was admitted to the hospital for a thorough examination on the same day. Cardiac catheterization was performed two days after admission to assess the cardiac function and discern CAD. Swan-Ganz catheterization showed a normal pulmonary wedge pressure with a mean of 11 mmHg and a normal cardiac index of 2.40 L/min/m^2. Initial coronary angiography showed no obvious stenosis in the coronary arteries, and the coronary spasm provocation test (SPT) was continued. Severe diffuse and moderate coronary spasm were observed in the left anterior descending coronary artery (LAD) and left circumflex coronary artery (LCX) at 50 μg of acetylcholine (ACh, Fig. 4), respectively,

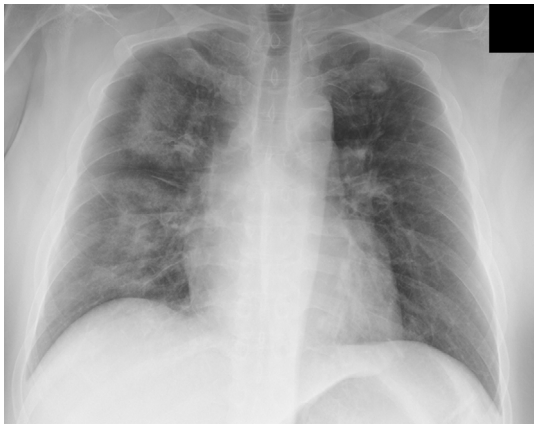

Figure 2. **Chest X-P findings on admission. The CTR was 49.6%. Pulmonary congestion was dominant in the right lung field. X-P: X-ray, CTR: cardiothoracic ratio**

accompanied by chest pain that was similar to the usual chest pain but mild in degree. In addition, ECG showed sustained right ventricular pacing. Intracoronary administration of 0.3 mg nitroglycerin (NTG) dilated the coronary spasms. Following ACh provocation of the right coronary artery (RCA), focal coronary spasm was induced in the distal RCA, which was dilated with a second intracoronary infusion of NTG (Fig. 4). Subsequently, we evaluated the LAD microvascular function; the coronary flow reserve was 5.2, and the index of microcirculatory resistance was 20.16, which were considered normal findings.

Given that the patient developed HF due to multi-vessel spasms, calcium channel blocker (CCB) therapy was initiated. Myocardial scintigraphy with 201-thallium and ^{123}I-betamethyl-p-iodophenyl-pentadecanoic acid (BMIPP) on day 5 of admission showed a moderate perfusion defect in the inferior LV on 201-thallium and a severely reduced uptake in the anterior and inferior LV on BMIPP (Fig. 5), indicating the presence of a perfusion-metabolic mismatch. Echocardiography on day 5 showed that the LVEF was 56%, E/e' was 12.3, septal e' was 5.2 cm/s, tricuspid regurgitant velocity was 2.9 m/s, and left atrial volume index was 25 mL/m^2. The patient was discharged on day six. Thereafter, the patient had no chest pain or recurrence of HF, including no elevation of NT-proBNP levels.

Discussion

We herein report a case of acute HF due to coronary spasms, confirmed by SPT, with multiple vessels and diffuse spasms. Coronary spasm can cause any type of CAD, so it may be the cause of HF mediated by coronary spasm-induced myocardial ischemia. However, in the present case, we strongly reaffirmed the association between coronary spasm and HF.

It has been considered that the anginal attack due to coronary spasm tends to be longer than that due to established CAD (3), and it has been reported that several severe

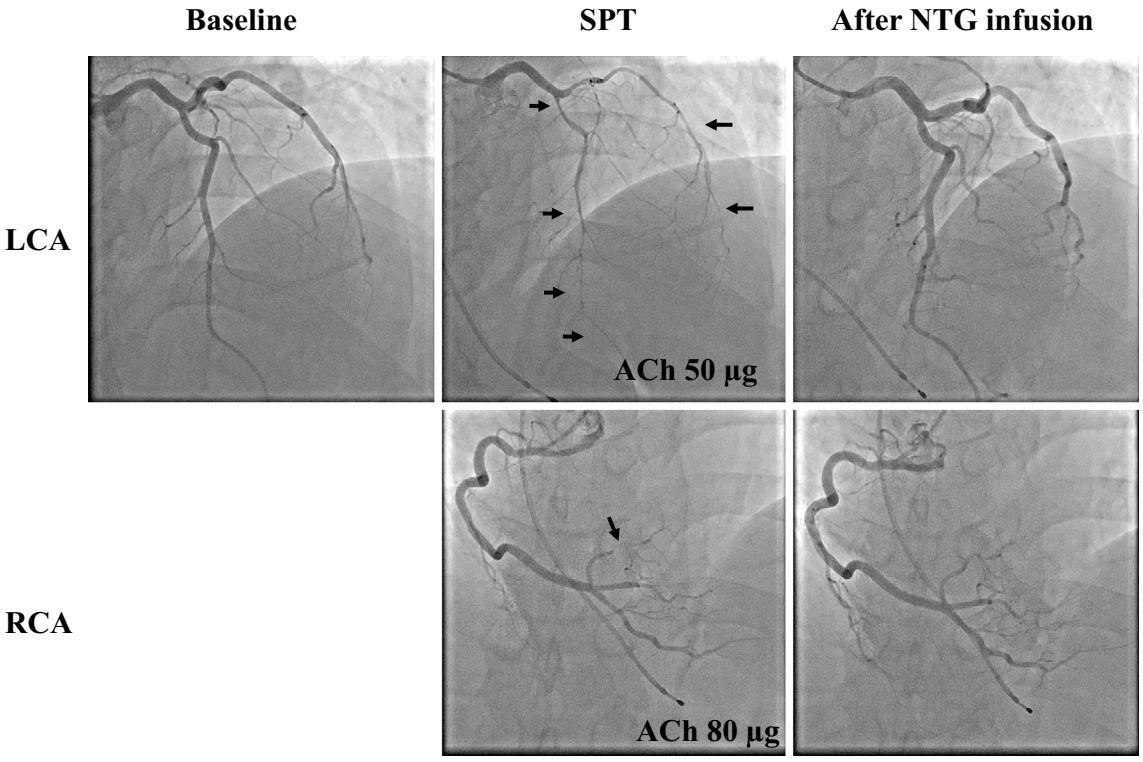

Figure 4. **Coronary angiography and SPT. There was no significant coronary stenosis in either coronary artery. On SPT, there were diffuse coronary spasms in the LAD and LCX, which were dilated after an intracoronary administration of 0.3 mg NTG. There was a focal spasm in the distal portion of the RCA. The sites of coronary spasm are indicated by black arrows. ACh: acetylcholine, LAD: left anterior descending coronary artery, LCX: left circumflex coronary artery, NTG: nitroglycerin, RCA: right coronary artery, SPT: spasm provocation test**

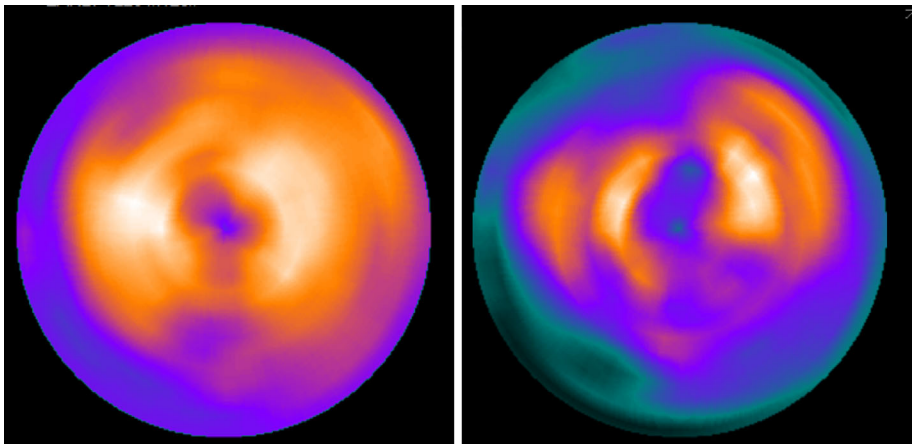

Figure 5. **Myocardial scintigraphy with 201-thallium and ^{123}I-BMIPP showed a mild defect in the inferior LV on 201-thallium and moderately reduced uptakes in the anterior and inferior LV on BMIPP. BMIPP: betamethyl-p-iodophenyl-pentadecanoic acid, LV: left ventricle**

angina-related symptoms, such as cold sweats or syncope, are more frequently observed in patients with VSA than in those with established CAD (9-11). Our previous study showed that approximately 30% of patients with VSA had chest-related symptoms that lasted for more than 15 minutes (11) and that VSA patients with prolonged chest symptoms had severe coronary spasm-related symptoms and elevated VSA activities. Such prolonged anginal attacks in VSA may be due to the finding that the triggers of anginal attacks due to coronary spasms are often unclear or absent; it is likely that the triggers cannot be controlled, so anginal attacks tend to be prolonged. Indeed, in the present case, the

patient presented with chest symptoms that lasted for one hour.

The relationship between coronary spasms and HF has also been discussed (4-6). The common denominator in these reports is that all types of coronary spasms were diffuse (4-6). Sakata et al. reported 9 of 9 cases (100%) (4), Sueda et al. reported 11 of 12 cases (92%) (5), and Inami et al. reported 20 of 20 cases (100%) (6) of multi-vessel spasm. One case by Sueda et al. (5) also involved coronary spasm in the proximal part of the LCX. Overall, HF may occur when myocardial ischemia occurs extensively owing to multi-vessel coronary spasms. In the present case, the patient also had multi-vessel and diffuse coronary spasms in the LAD and LCX, findings consistent with the above reports (4-6). Although the coronary spasm that occurred in the RCA in this case was focal, it was evaluated using a reprovocation test after NTG administration and may not have been accurately assessed.

However, what differentiates this case from others (4-8) is the LVEF at the onset of HF. While other reports have described cases of HFrEF (4-8), this patient had a preserved LVEF, and detailed echocardiography performed during the stable period after hospitalization (day 5) did not show a typical HFpEF image. The elevation of the NT-proBNP levels in this case was not high, suggesting that this case corresponded to one of mild HF. The frequency or duration of coronary spasm, extent of myocardial ischemia, duration of the disease, or comorbidities may have contributed to the relatively low LVEF. Furthermore, one of the characteristics of patients with HFrEF and coronary spasms is the low frequency of chest pain; the frequency of chest discomfort was 33% in the study conducted by Sueda et al. (5), and that of chest pain was 35% in the study conducted by Inami et al. (6). The infrequency of subjective symptoms may be related to the onset of HFrEF due to repeated or prolonged coronary spasms. In contrast, patients with chest symptoms, as in the present case, may be less likely to be exposed to repeated myocardial ischemia than in patients with an infrequency of subjective symptoms and may have HFpEF. Furthermore, the relationship between HFpEF and coronary microvascular dysfunction (CMD) has recently been considered (12). CMD is known to coexist in patients with VSA (13, 14); however, in the present case, an LAD evaluation did not reveal CMD coexistence. Although the presence of CMD could not be evaluated in either the LCX or RCA, CMD seemed unlikely to be involved in the cause of HFpEF in our patient. Nevertheless, this case showed that coronary spasm could be a cause of HFpEF, and it may be possible to include coronary spasm as a possible cause of HFpEF.

In general, HFpEF is often associated with clinical characteristics such as older age, atrial fibrillation, CAD, diabetes mellitus, and obesity (15); however, in the present case, the only risk factor present was obesity. Patients with VSA tend to be younger than those with obstructive coronary artery stenosis (3); therefore, the clinical characteristics of patients with coronary spasm-induced HFpEF may differ from those of patients with HFpEF often experienced in clinical practice. It is necessary to clarify the clinical characteristics of patients with HFpEF induced by coronary spasm by including such cases in the future.

The present patient did not have troponin levels elevated above the 99th percentile value (0.44 ng/mL <0.52 ng/mL), which by definition does not correspond to a significant transient elevation of myocardial enzymes (16) and does not imply myocardial infarction with non-obstructive coronary artery (MINOCA). However, the possibility of MINOCA in the present case cannot be completely ruled out, since the limited interval between blood drawing may have missed the maximal rise in troponin levels. Although MINOCA-related HF has been reported in a small percentage of patients with MINOCA (17-19), the frequency of coronary spasms in MINOCA-related HF is not well understood. Further multicenter registries should clarify the extent to which coronary spasms are involved in HF associated with MINOCA.

In conclusion, we encountered a case of acute HF with a preserved ejection fraction caused by multi-vessel and diffuse coronary spasm. Coronary spasm should be considered as a differential cause of HF.

Written informed consent for this case report was obtained from the patient.

The authors state that they have no Conflict of Interest (COI).

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