Acute Heart Failure Triggered by Coronary Spasm With Transient Left Ventricular Dysfunction

Yusuke ADACHI,¹ MD, Kenichi SAKAKURA,¹ MD, Tatsuro IBE,¹ MD,
Nanae YOSHIDA,¹ MD, Hiroshi WADA,¹ MD, Hideo FUJITA,¹ MD,
and Shin-ichi MOMOMURA,¹ MD

SUMMARY

Coronary spasm is abnormal contraction of an epicardial coronary artery resulting in myocardial ischemia. Coronary spasm induces not only depressed myocardial contractility, but also incomplete myocardial relaxation, which leads to elevated ventricular filling pressure. We herein report the case of a 55-year-old woman who had repeated acute heart failure caused by coronary spasm. Acetylcholine provocation test with simultaneous right heart catheterization was useful for the diagnosis of elevated ventricular filling pressure as well as coronary artery spasm. We should add coronary spasm to a differential diagnosis for repeated acute heart failure. (Int Heart J 2017; 58: 286-289)

Key words: Coronary spastic angina, Acetylcholine provocation test, Right heart catheterization

Coronary spasm is defined as abnormal contraction of an epicardial coronary artery resulting in myocardial ischemia.^{1,2)} The prevalence of coronary spasm is greater in Japan than in Western countries, because of genetic and environmental factors.^{1,2)} Coronary spasm induces not only depressed myocardial contractility, but also incomplete myocardial relaxation, which leads to elevated ventricular filling pressure.¹⁾ We herein report a case of repeated acute heart failure caused by coronary spasm, which was diagnosed by acetylcholine provocation test with simultaneous right heart catheterization.

CASE REPORT

A 55-year-old Japanese woman was admitted to our hospital with acute heart failure accompanied by CO₂ narcosis. Her blood pressure was 154/92 mmHg and her heart rate was 111 beats/min on admission. Her arterial blood gas analysis showed a pH of 6.83, pCO₂ of 117.0 mmHg, and pO₂ of 98.3 mmHg at a fraction of inspired oxygen of 70% with non-invasive positive pressure ventilation on admission. Chest X-rays showed pulmonary edema (Figure 1), an electrocardiogram (ECG) showed poor R progression in leads V1–V3 (Figure 2), and echocardiography showed diffuse severe hypokinesis with a global left ventricular ejection fraction (LVEF) of 35%. Serum creatine kinase (CK) and serum creatine kinase MB isoenzyme (CK-MB) levels were 347 IU/L and 38 IU/L, respectively. The brain natriuretic peptide level was 450 pg/mL. Although she had no risk factors for coronary artery disease except age and current smoking, she had a history of 2 emer-

gent admissions in 4 months: the first one at another hospital and the second one at our hospital. In the first admission, she had acute respiratory failure accompanied by CO₂ narcosis, which needed mechanical ventilation. Neither echocardiography nor coronary angiography (CAG) was performed during the first admission. Although the cause of her acute respiratory failure was not elucidated, the tentative diagnosis at the hospital was acute exacerbation of bronchial asthma. In the second admission, she had acute decompensated heart failure and was admitted to our hospital. Although blood analysis showed an increased CK level (5234 IU/L), the CK-MB level (78 IU/L) did not reach 10% of the CK level. ECG showed negative T waves in precordial leads. We performed CAG carefully under prophylactic use of steroids, which showed no organic stenosis in her coronary artery. Left ventriculography was not performed at that time. Echocardiography just before discharge showed normal systolic and diastolic function.

In the present admission, echocardiography revealed transient left ventricular dysfunction, which improved from LVEF of 35% to 60% in 24 hours. ECG on day 2 showed negative T waves in precordial leads (Figure 2), which had improved on day 4 and day 7 (Figure 2). Although she did not have chest pains in her daily life, chest discomfort preceded acute heart failure in this admission. Considering the above clinical course, we regarded severe coronary spasm as the probable diagnosis, and stress cardiomyopathy or bronchial asthma as possible diagnoses. To differentiate stress cardiomyopathy such as Takotsubo cardiomyopathy from severe coronary spasm, we conducted Iodine 123 β -methyl-p-iodophenyl-pentadecanoic acid (BMIPP) and thallium 201 chloride (²⁰¹TlCl) dual myocardial single photon emission computed tomography (SPECT) myo-

From the ¹ Division of Cardiovascular Medicine, Saitama Medical Center, Jichi Medical University, Saitama, Japan.

Address for correspondence: Kenichi Sakakura, MD, Division of Cardiovascular Medicine, Saitama Medical Center, Jichi Medical University, 1-847 Amanuma, Omiya, Saitama City, Japan 330-8503. E-mail: ksakakura@jichi.ac.jp

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cardial scintigraphy on day 7 (Figure 3). Impaired metabolism exclusively in the apical region, which is a typical finding for Tako-tsubo or stress cardiomyopathy,³⁾ was not observed. Furthermore, we performed a bronchodilator reversibility test to rule out bronchial asthma. The result of the test revealed that the patient did not have bronchial asthma, whereas she had chronic obstructive pulmonary disease with GOLD stage III. Based on these results, we considered severe coronary artery spasm as the most likely diagnosis. However, it was not clearly explained that the severe coronary artery spasm caused acute heart failure. One possible explanation was that the severe coronary artery spasm impaired left ventricular systolic and diastolic function and caused transient elevation of the left ventricular filling pressure, which could be the cause of the pulmonary edema. Therefore, we performed acetylcholine provocation testing and right heart catheterization simultaneously in order to confirm elevation of pulmonary capillary wedge pressure (PCWP) during coronary spasm.

Figure 1. Chest X-ray on admission. Chest X-ray showed pulmonary edema.

First, the patient was inserted a Swan-Ganz catheter as well as a temporary pacing catheter via femoral veins, and underwent a control CAG. There was no organic stenosis, and control mean PCWP was 7 mmHg (Figure 4, left). Following 50 μ g administration of acetylcholine chloride into the left coronary artery, significant coronary spasm accompanied by chest pain was provoked, and mean PCWP increased sharply from 7 mmHg to 14 mmHg (Figure 4, middle). The coronary spasm and chest pain were immediately relieved by administration of intracoronary nitroglycerin, and mean PCWP decreased to 9 mmHg (Figure 4, right). Transient occlusion (> 90% narrowing) of the coronary arteries with chest pain revealed a positive response to the acetylcholine provocation test.⁴⁾ Additional acetylcholine chloride administration was not performed after taking into consideration the safety and severity of the coronary spasm.⁵⁾ Finally, we diagnosed severe coronary artery spasm as the cause of her transient pulmonary edema. Although her chronic obstructive pulmonary disease was also associated with the exacerbation of CO₂ narcosis, severe coronary artery spasm was deemed as the primary cause of her acute respiratory failure. We prescribed oral calcium channel blockers, and she has been followed-up without recurrence for 12 months.

DISCUSSION

It is well known that acute myocardial ischemia impairs both left ventricular systolic and diastolic function and that left ventricular diastolic dysfunction precedes systolic dysfunction.⁶⁾ Thus, myocardial ischemia induced by coronary spasm triggers diastolic dysfunction in advance of systolic dysfunction. Therefore, coronary spasm can be a cause of acute pulmonary edema via acute elevation of left ventricular filling pressure. Acetylcholine provocation testing with right heart catheterization enables us to detect PCWP elevation by acute myocardial ischemia triggered by coronary spasm.

Alcalde and colleagues previously reported the usefulness

Figure 2. Time course of ECG changes. Negative T waves in precordial leads were improved in one week.

Figure 3. BMIPP and $^{201}\text{TlCl}$ dual SPECT myocardial scintigraphy. There was no mismatch between perfusion ($^{201}\text{TlCl}$) and BMIPP.

Figure 4. Results of acetylcholine provocation testing and right heart catheterization. Control coronary angiography (CAG) and baseline pulmonary capillary wedge pressure (PCWP) (Left). CAG and PCWP after 50 µg administration of acetylcholine chloride (Ach) to left coronary artery (Middle). CAG and PCWP after administration of nitroglycerin (NTG) (Right).

of the acetylcholine provocation test with Swan-Ganz catheterization to detect coronary spasm in a case of acute pulmonary edema.⁷⁾ Their patient was diabetic and dyslipidemic, whereas our patient did not have coronary risk factors except age and current smoking. Because smoking is closely associated with endothelial dysfunction⁸⁾ and current smoking is significantly associated with the prevalence of coronary spasm,⁹⁾ we should consider coronary spasm as a possible cause of pulmonary edema in patients with smoking habits, even when there are no other risk factors such as diabetes mellitus or dyslipidemia. While all patients with coronary spasm theoretically have the risk of elevated ventricular filling pressure during an attack, most spasm attacks do not induce severe pulmonary edema in our daily practice. The onset of pulmonary edema caused by coronary spasm probably depends on the patient's original diastolic and systolic function and the severity of the coronary spasm. Further clinical and basic studies are thus warranted. To our knowledge, this is the first case that reports acute heart failure induced by coronary spasm in a Japanese patient. Since coronary spasm is more common in Japan than in Western countries,^{1,2)} quite a few similar cases may potentially exist in Japan. We should add coronary spasm to a differential diagnosis for repeated acute heart failure. Furthermore, acetylcholine provocation testing with simultaneous right heart catheterization would be the best method to demonstrate the direct relationship between coronary spasm and elevated ventricular filling pressure.

DISCLOSURE

The authors declare no conflicts of interest in association with this study.

REFERENCES

1. Yasue H, Nakagawa H, Itoh T, Harada E, Mizuno Y. Coronary artery spasm--clinical features, diagnosis, pathogenesis, and treatment. *J Cardiol* 2008; 51: 2-17. (Review)
2. Yasue H, Kugiyama K. Coronary spasm: clinical features and pathogenesis. *Intern Med* 1997; 36: 760-5. (Review)
3. Matsuo S, Nakajima K, Kinuya S, Yamagishi M. Diagnostic utility of 123I-BMIPP imaging in patients with Takotsubo cardiomyopathy. *J Cardiol* 2014; 64: 49-56.
4. JCS Joint Working Group. Guidelines for diagnosis and treatment of patients with vasospastic angina (Coronary Spastic Angina) (JCS 2013). *Circ J* 2014; 78: 2779-801.
5. Yoneyama K, Akashi YJ, Ashikaga K, *et al.* Severity of myocardial fatty acid dysmetabolism induced by coronary spasm does not differ with Thrombolysis in Myocardial Infarction (TIMI) grade during intracoronary acetylcholine provocation tests. *Int Heart J* 2014; 55: 416-21.
6. Labovitz AJ, Lewen MK, Kern M, Vandormael M, Deligonal U, Kennedy HL. Evaluation of left ventricular systolic and diastolic dysfunction during transient myocardial ischemia produced by angioplasty. *J Am Coll Cardiol* 1987; 10: 748-55.
7. Alcalde O, Domingo E, Figueras J. Recurrent severe acute pulmonary edema caused by transient left ventricular insufficiency with mitral regurgitation related to severe coronary artery spasm. *Circ Heart Fail* 2010; 3: 332-5.
8. Lavi S, Prasad A, Yang EH, *et al.* Smoking is associated with epicardial coronary endothelial dysfunction and elevated white blood cell count in patients with chest pain and early coronary artery disease. *Circulation* 2007; 115: 2621-7.
9. Lee SN, Shin DI, Jung MH, *et al.* Impact of cystatin-C level on the prevalence and angiographic characteristics of vasospastic angina in Korean patients. *Int Heart J* 2015; 56: 49-55.