Is There No Problem with Diagnosis of Vasospastic Angina in the Clinic?: We Should Learn a Case Who Was Admitted to Our Hospital from a Distant Place

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75-year-old female was admitted to our hospital from a distant region due to rest angina and syncope. She had been medicated as an atypical chest pain or ischemic heart disease for 20 years in the neighborhood hospitals. She complained of chest pain mainly at rest and sometimes had syncope. Although coronary arteriography including the ergonovine spasm provocation test was performed once time, she was not diagnosed as coronary spastic angina. After the internet search, she was admitted to our hospital to investigate her chest symptom and syncope. Pharmacological spasm provocation tests including acetylcholine or ergonovine provoked two vessel spasm. Her chest symptoms improved after the administration of another coronary vasodilator. If cardiologists had no solid technology about pharmacological spasm provocation tests, there are less cardiologists who are familiar with coronary spasm in the future especially even in Japan.

KEY WORDS: diagnosis, spasm provocation test, syncope, vasospastic angina

I. Introduction

Majority of cardiologists may perform the computed tomography coronary angiography (CTCAG) in diagnosing patients with rest angina in the clinic^{1,2)}. If patients had no stenosis by CTCAG, cardiologist may administer the calcium channel blocker (CCB) as suspecting of coronary spastic angina (CSA). They may perform the percutaneous coronary intervention (PCI) in patients with rest angina and significant organic stenosis without further examination of coronary artery spasm. Recent cardiologists less than 40 years old may miss the strict diagnosis of chest pain or oppression in patients with rest angina and organic stenosis.

Pharmacological spasm provocation tests are employed to diagnose the presence of coronary spasm in the cardiac catheterization laboratory^{3–6)}. However, recent cardiologists may have less opportunity to perform the pharmacological spasm provocation tests to diagnose the coronary artery spasm, because cardiologists had less chance of diagnostic and follow-up coronary arteriography due to the widespread of CTCAG.

In this case report, typical CSA was shown who had been medicated as an atypical chest pain or ischemic heart disease in

the neighborhood hospitals. This patient was super sensitive to acetylcholine (ACh) but not ergonovine (ER).

II. Case report

She was a 75-year-old woman and her chief complaint was chest pain at rest and syncope. Approximately 20 years ago, she complained of chest pain at rest for a couple minutes. She visited the general hospital to investigate her chest pain. However, she had no ischemia after the examination of myocardial scintigraphy. She sometimes complained of chest pain and her upper right back tooth pain especially at early morning or midnight at least once a year. She visited another hospital to investigate her chest pain and CTCAG disclosed normal coronary artery. Next year, she had syncope at early morning after usual chest pain. She was transferred to the neighborhood hospital on ambulance. Brain examinations and electrocardiogram (ECG) showed no abnormal findings. Coronary arteriography and ER spasm provocation test were performed before discharge and just nitrate tape was prescribed. Because her chest pain did not improve for more than 20 minutes after sublingual nitroglycerine, she admitted to the hospital on ambulance. After a couple days admission, minor tranquilizer was administered. Sublingual nitroglycerine was employed at least 4 or 5 times per year at midnight or morning. She complained of chest pain when she read the news paper at morning and had faintness with cold sweating. She admitted to the hospital and she was suspected of CSA. CCB (benidipine 2 mg) was administered at morning. However, she complained of

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Fig. 1 Electrocardiogram on admission.

chest pain many times irrespective of taking above CCB. No ischemic ECG changes were recognized during the 24-hour Holter monitoring on her chest pain attacks. Although she took CCB and sublingual nitroglycerine at her chest pain attack, she had syncope after her chest pain. She visited our hospital from a distant region (approximately 300 km apart from our hospital) after searching the internet.

On admission to our hospital as outpatient, she took medicine including diltiazem R 100 mg, benidipine 2 mg at morning and nitrate tape 40 mg/day. She had no history of smoking or diabetes mellitus (glycohemoglobin: 5.9%), while she had dyslipidemia (total cholesterol: 234 mg/dl & low-density-lipoprotein cholesterol: 145 mg/dl). ECG showed the slight horizontal ST depression in V3–6 leads (0.5 mm), as shown in Fig. 1. After consulting with patient and her family, she was admitted to our hospital to diagnose the presence of coronary artery spasm one month later. No ischemia was found after the examination of myocardial stress thallium adenosine scintigraphy. Her coronary arteriography was normal (Fig. 2D and Fig. 3D), and spasm provocation tests were performed. Prior to 24-hour cessation of CCBs and nitrate, intracoronary injection of acetylcholine (ACh) 20 or 100 μ g into the left coronary artery (LCA) disclosed no spasm. However, intracoronary administration of ACh 200 μ g into the LCA documented the slow flow in the left anterior descending (LAD) and focal spasm at segment 12 accompanied with usual chest pain before syncope (Fig. 2A), ischemic ECG changes (ST junctional depression in V3–6 leads (2.0 mm), or transient hypotension (50 mmHg). Intracoronary injection of ACh 20 or 50 μ g into the right coronary artery (RCA) had no spasm, while intracoronary injection of ACh 80 μ g into the RCA disclosed the distal diffuse spasm at atrioventricular node artery with compressing the throat and ischemic ECG changes (ST horizontal depression in V3–6 (1.0 mm) (Fig. 3A). However, intra-

coronary administration of ER 64/40 μ g into the LCA/RCA (Fig. 2B and Fig. 3B). Adding ACh 100 μ g after ER 64 μ g into the LCA disclosed focal spasm at segment 12 with chest pain and no ischemic ECG change (Fig. 2C), whereas adding ACh 50 μ g after ER 40 μ g into the RCA had focal spasm at segment 4 with no ischemic ECG change and slight squeezing at throat (Fig. 3C). She was diagnosed as definite CSA with two vessel spasm. After diltiazem R 100 μ g before sleep was added and sublingual nitroglycerine use at early precursor was recommended, she had no syncope but just some slight chest pain.

III. Discussion

This case was a definite CSA with syncope. However, for 20 years, cardiologists in neighborhood hospitals could not diagnose the presence of coronary artery spasm irrespective of rest angina or emergency admissions. Because CTCAG showed normal coronary artery trees and no ischemia on myocardial scintigraphy, CCB was not administered to her possibly due to atypical chest pain. Though she had typical rest angina with syncope, she was not diagnosed as CSA. Sublingual nitroglycerine uses on chest pain attacks or the administration of CCB was not completely to suppress her symptoms. However, she took medicine at morning but not before sleep. Although ER spasm provocation test was performed in this patient, CSA was not diagnosed and just nitrate tape was added. Intracoronary administration of ER may miss the presence of coronary artery spasm in this female patient. We already reported the super sensitivity of ACh in female patients with CSA⁷⁾. In the clinic, cardiologists should recognize the difference of coronary artery response between ACh and ER in the cardiac catheterization laboratory^{8,9)}. Optimal medication and good adherence after the precise diagnosis of definite CSA by the pharmacological spasm provocation test may lead to improve her chest symptoms. Recent cardiologists

Fig. 2 Coronary arteriography and ECG findings during spasm provocation tests in the left coronary artery.

A: intracoronary injection of acetylcholine 200 µg disclosed the focal spasm at segment 12 and ST junctional depression (2.0 mm) was observed in V3–6 leads.

B: neither provoked spasm nor ischemic ECG change was recognized after the administration of ergonovine 64 µg into the left coronary artery.

C: focal spastic change was observed at segment 12 after adding acetylcholine 100 µg after ergonovine 64 µg into the left coronary artery, while no ischemic ECG change was recognized.

D: no stenosis was found after the administration of nitroglycerine.

ACh: acetylcholine, ER: ergonovine

less than 40 years old may not be familiar with coronary spasm. Although mastering the percutaneous coronary intervention is one of the most necessary technique for cardiologists, they should get the technique for diagnosing coronary artery spasm precisely in the real world. A cardiologist before retirement recommends that cardiologists should have the knowledge about coronary spasm or CSA and the technique to diagnose coronary artery spasm in Japan. Cardiologists should learn to see through the truth in patients with rest angina in the clinic.

Approximately over ten years ago, Yasue et al reported the warning bell in the clinic all over the world¹⁰⁾. They mentioned that cardiologists now may be more interested in patients who are in needs of PCI and do not want to be bothered with coronary spasm. Many cardiologists consider the provocation test for

coronary spasm too cumbersome and time-consuming for the busy invasive-interventional laboratory and think that a trial of CCBs may be enough for the evaluation of possible spasm. Under these circumstances, it is possible that there will be less and less cardiologists who are familiar with coronary spasm in the future. Because PCI is not the right answer to the problem of coronary spasm, it is quite important for every clinician to be alert to the presence of coronary spasm, which may be silent and lethal.

In the future, Japanese Circulation Society should recommend the training on balanced cardiologists who are familiar to coronary spasm and organic coronary atherosclerosis in the field of ischemic heart disease. Furthermore, special cardiologists in Japan should have solid technology about pharmacological spasm

Fig. 3 Coronary arteriography and ECG findings during spasm provocation tests in the right coronary artery.

A: intracoronary injection of acetylcholine 80 µg disclosed the diffuse spasm at segment 4 and ST horizontal depression (1.0 mm) was observed in V4–6 leads.

B: neither provoked spasm nor ischemic ECG change was recognized after the administration of ergonovine 40 µg into the right coronary artery

C: focal spasm was observed at segment 4 after adding acetylcholine 50 µg after ergonovine 40 µg into the right coronary artery, while no ischemic ECG change was observed.

D: no stenosis was found after the administration of nitroglycerine.

ACh: acetylcholine, ER: ergonovine

provocation tests as one of necessary items as well as the technique about PCI. If not so, there are less cardiologists who are familiar with coronary spasm in the future especially even in Japan.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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