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Vasospasm-induced ST-segment elevation myocardial infarction in a premenopausal woman with endothelial dysfunction

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Abstract

ST-segment elevation myocardial infarction (STEMI) can be caused by coronary artery vasospasm (VSA) due to endothelial dysfunction. However, the clinical role of endothelial function tests in VSA-induced STEMI is not fully understood. We present the case of a 43-year-old woman with atypical chest pain and no coronary risk factors. STEMI caused by VSA was diagnosed. Flow-mediated vasodilatation (FMD) and EndPAT tests were performed; the FMD and reactive hyperaemia index were 3.8% and 1.23, respectively. Endothelial dysfunction is the putative cause of STEMI. FMD and EndPAT tests might be useful for predicting adverse outcomes in young premenopausal women with VSA.

INTRODUCTION

Coronary artery vasospasm (VSA) can cause anterior ST-segment elevation myocardial infarction (STEMI) which is relatively infrequent manifestation of myocardial infarction with nonobstractive coronary artery (MINOCA; [1, 2]). VSA has been reported to be more common in male smokers with significant coronary risk factors who are over the age of 50–60. VSA is less common among young adult premenopausal women. Oestrogen prevents coronary spasm while vascular endothelial dysfunction may develop into VSA in adolescent and young adult patients without coronary risk factors [3, 4].

We have recently experienced VSA-induced STEMI in MINOCA in a premenopausal woman without coronary risk factors who had atypical chest pain and endothelial dysfunction. Since understanding of the pathophysiology of STEMI in MINOCA, and provocative testing for VSA has not always been recommended in STEMI in MINOCA [1], it is extremely important to discuss the role of systemic endothelial function tests in VSA-induced STEMI in MINOCA.

CASE REPORT

A 43-year-old woman (158 cm, 41 kg) visited our outpatient clinic because of intermittent atypical chest wall pain lasting for > 20 min from the day before presentation. Pain was not associated with effort or any triggers. Present history revealed that pain was sharp and intermittently occurred for all day long. She first visited other clinics and was referred to our hospital the next day. She did not have chest pain or any other symptoms when she visited our outpatient clinic, her heart rate was 80 beats/min and regular and her blood pressure was 120/70 mmHg. There were no risk factors for coronary artery disease. Relevant past medical history was negative, including the absence of any gynaecological problems and on no medications including birth control pills. She also denied a menstrual period at the time of the clinic visit and had a regular menstrual cycle. Electrocardiogram (ECG) revealed ST-segment elevation in leads V2–5 with super-acute tall T waves (Fig. 1). The chest radiograph was normal. Laboratory data showed positive troponin T (>0.1 ng/ml; TROP T sensitive R [Roche Diagnostic Inc. Tokyo, Japan]) and the other positive data were as follows: aspartate aminotransferase, 89 U/l; alanine aminotransferase, 29 U/l; creatine phosphokinase, 758 U/l; white blood cell count, 10 500/μl and serial changes are illustrated in Fig. 2. The other parameters were within the normal range. Echocardiography revealed segmental anterior severe hypokinesis, and Takotubo cardiomyopathy
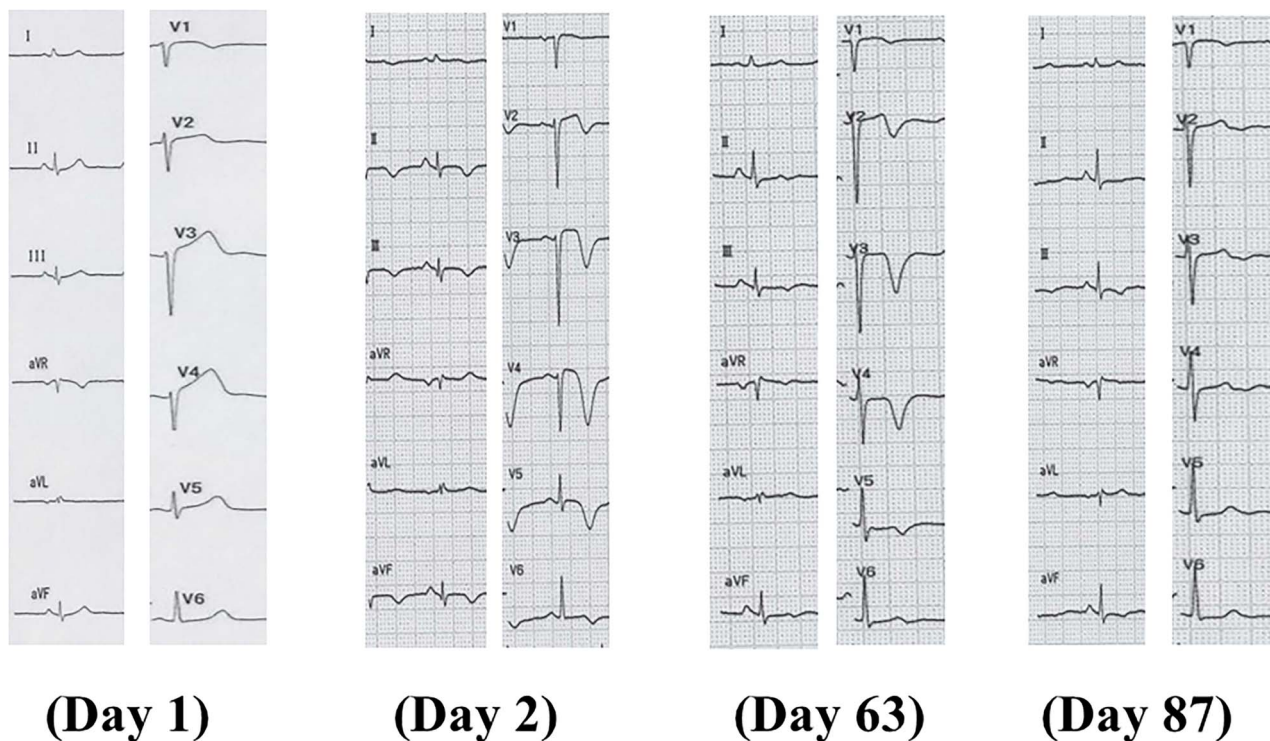
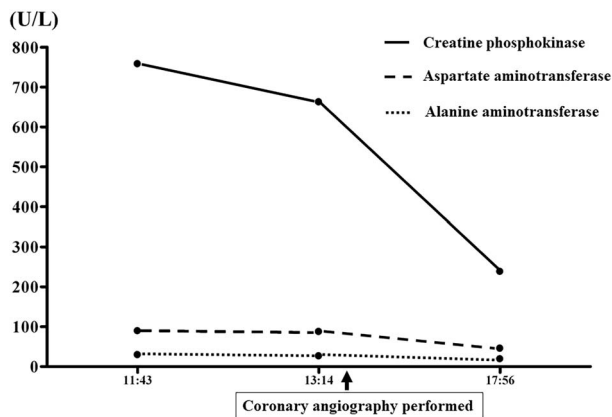**Figure 1.** Serial changes in 12-lead ECG. Days 1–87, days from the onset of the first visit to outpatient clinic.

Figure 2. Serial changes in serum aspartate aminotransferase, alanine aminotransferase and creatine phosphokinase.

Figure 3. Coronary angiography (CAG) findings. 2a, right coronary artery finding by CAG in the control contrast dye injection. 2b, left coronary artery finding by CAG in the control contrast dye injection. 2c, left coronary artery finding by CAG after intra-coronary injection of 100 μg of acetylcholine (ACh) into the left coronary descending artery. Arrow indicates ACh-induced vasospasm. 2d, left coronary artery finding by CAG after intra-coronary injection of 0.2 mg of nitroglycerin into left coronary descending artery. The ACh-induced vasospasm was relieved.

and myocarditis were excluded. Emergency coronary angiography showed no significant stenotic lesions. Before angiography, aspirin 100 mg and clopidogrel sulphate 300 mg were orally administered as standard treatment for STEMI. However, a bolus injection of 100-μg acetylcholine into the left coronary descending artery revealed 90% occlusion of the proximal portion of the artery, which was relieved by intra-coronary nitroglycerin injection. Acute myocardial infarction (MI) was diagnosed due to coronary spasm (Fig. 3). The clinical course was stable with administration of a calcium antagonist (benidipine hydrochloride 4 mg b.i.d) and aspirin (100 mg, q.d.). About 3 months after MI episode, flow-mediated vasodilatation (FMD, measured by EF18G; UNEX, Nagoya, Japan) and peripheral tonometry of
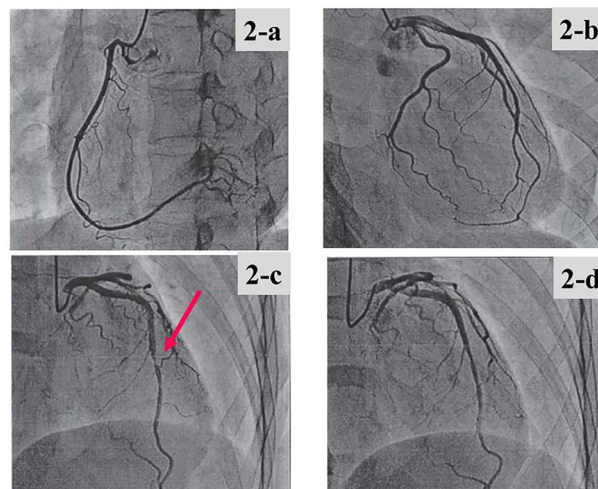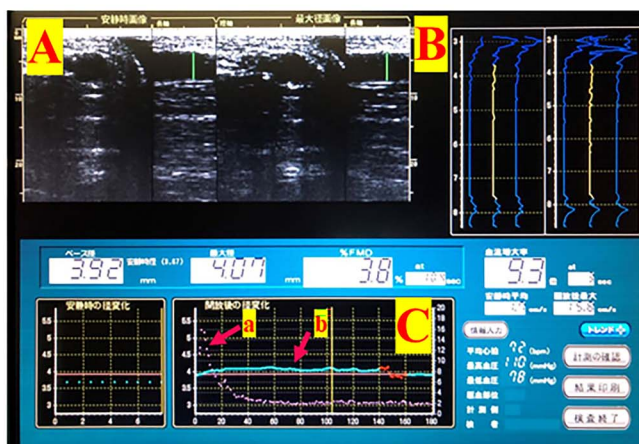
EndPAT tests were performed (reactive hyperaemia index [RHI], measured by EndPAT2000 system [Itamar Medical, Caesarea, Israel]) after washing out of medication around 2 p.m. As a result, the FMD and RHI were 3.8% and 1.23, respectively (Fig. 4). Endothelial dysfunction was observed. Written informed consent was obtained from the patient.
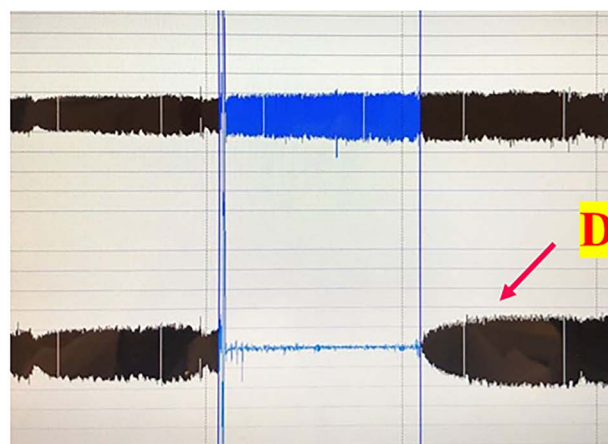
1) Brachial artery FMD

UNEX EF18G

FMD=3.8%

2) Peripheral tonometry;

EndPAT2000

RHI=1.23

Figure 4. Systemic endothelial function tests. (**A**) From the left, short and long axis images of brachial artery before reactive hyperaemia, and maximally dilated short and long axis images of brachial artery after reactive hyperaemia, are shown. (**B**) A-mode ultrasound images of brachial artery diameter are shown. The flat lines indicate the longitudinal diameters of the brachial artery, which are identical to the values obtained from the images in (A). (**C**) The changes in blood flow velocity (arrow labelled 'a') and the changes of longitudinal diameters of brachial artery from rest to after the reactive hyperaemia (arrow named 'b') are continuously plotted along the time course and the maximal percent changes of brachial diameters in response to reactive hyperaemia are determined. These changes are endothelial cell dependent. (**D**) EndPAT2000 measurement is another method of assessing endothelial function. It is a reactive hyperaemia-peripheral tonometry test. It mainly reflects not only nitric oxide but also endothelium-dependent hyperpolarising factor and prostacyclin. This method measures blood flow changes by reactive hyperaemia and endothelial function, and is similar to FMD. After the upper arm occlusion by cuff with a pressure above either systolic pressure of 60 or 200 mmHg for 5 min, the cuff was released. The measurement of both index fingers' blood flow by tonometry throughout the study was performed. Reactive hyperaemia-related endothelial-dependent blood flow increase was measured. Based on the measurement of the flow of both fingers, suspected artefacts are cancelled and real blood flow increase can be detected, as shown in (D; indicated by arrows). A comparison between before and after reactive hyperaemia is conducted in hyperaemia-induced finger and is adjusted by comparing the flow changes of the other fingers. The ratio after/before (RHI) was then determined. If RHI was < 1.67, endothelial dysfunction was diagnosed. In this case, endothelial dysfunction was observed. Same as RHI method, hyperaemia-related endothelial-dependent brachial artery diameter vasodilatation was measured by ultrasound in FMD. This vasodilatation is mainly caused by endothelial-dependent nitric oxide release. FMD, flow-mediated vasodilatation; RHI, reactive hyperaemia index. FMD < 4.0% and RHI < 1.67 are significantly abnormal.

DISCUSSION

The main features of this patient were as follows: first, VSA-induced STEMI in MINOCA in a premenopausal young adult woman without gynaecological problems; second, no significant coronary risk factors or organic comorbidity; third, complaint of atypical chest pain; and finally, impaired endothelial function revealed by FMD and RHI.

In this case, VSA-induced STEMI due to VSA was diagnosed, and abnormal endothelial function tests were performed. In young premenopausal women complaining of chest pain, VSA, coronary artery microvascular dysfunction, coronary artery dissection, Takotubo cardiomyopathy and myocarditis are important disorders to consider in the differential diagnosis and these were excluded in this case. Coronary endothelial dysfunction has been well investigated for the possible pathophysiology of VSA [5]. FMD and RHI were measured in the afternoon and in the fasting phase as well as the appropriate menstrual phase. In the settings where the confounding factors influencing endothelial function and the diurnal variation of endothelial function in VSA were taken into account [6]; her endothelial function was the most likely aetiological factor. In the chronic phase of her clinical course, when STEMI did not influence the endothelial function test, FMD and RHI showed significant endothelial dysfunction. FMD was < 4.0%, while RHI was < 1.67, respectively [7].

A previous study showed that decreased FMD and RHI reflect adverse outcomes in coronary artery disease, and FMD could possibly be a significant modality for diagnosing coronary artery disease [8]. However, reports on the prognostic and diagnostic values of FMD and RHI in VSA are limited [9]. In this case, where significantly lower FMD and RHI values were observed, the important role of systemic endothelial function in VSA-induced STEMI in MINOCA might be significant. In addition, among the calcium antagonists that are first-line medications for VSA, we chose benidipine hydrochloride according to a previous report, and the patient's condition was stable under this medication. If benidipine is not available, either nifedipine of 40 mg or diltiazem of 200 mg daily

is acceptable therapy, and no further treatments except aspirin were necessary because any risk factors did not exist.

Since this case showed relatively atypical chest symptoms and most patients with VSA have been reported to be asymptomatic or have an atypical presentation [10], the supplemental use of either FMD or RHI in already diagnosed VSA for predicting subsequently developing STEMI could be indicated. In addition, according to the findings of this case, the prognostic value of either FDM or RHI in VSA-induced STEMI in MINOCA should be prospectively investigated. This kind of study would be worth conducting in the near future. This case provides a clue to the above-mentioned concept.

CONFLICT OF INTEREST

There are no conflicts of interest pertaining to any authors.

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None declared.

ETHICAL APPROVAL

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

CONSENT

Written informed consent was obtained from the patient for this publication.

GUARANTOR

None declared.

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