

Corticosteroid Therapy was Effective in Controlling Refractory Coronary Vasospasms Complicated by Hypereosinophilia

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Abstract

A 48-year-old man suffered from uncontrollable coronary vasospasms, even when taking the maximum dose of vasodilators. The patient had a history of hypereosinophilia, and as the eosinophilia worsened, more frequent and intense coronary spastic angina (CSA) attacks occurred. He was treated with 20 mg/day of oral prednisolone, and the chest symptoms of CSA completely resolved thereafter. We encountered a refractory CSA patient with an allergic predisposition for which the oral administration of corticosteroids was markedly effective. Although the priority of corticosteroid therapy is not clinically high in patients with CSA, it can be effective especially in patients with an allergic background.

Key words: coronary spastic angina, hypereosinophilia, corticosteroid

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Introduction

It is widely recognized that coronary spastic angina (CSA) is a significant pathophysiology associated with acute myocardial infarction, fatal arrhythmia and sudden death. It is more frequently observed in Japanese than in Caucasian patients (1). In most cases, the coronary vasospasms are well controlled with vasodilator drugs such as calcium antagonists and/or nitrates. On the other hand, approximately 20% of patients with variant angina are reported to be refractory to optimal medical treatment (2). Patients with refractory CSA are generally younger, more frequently smokers and have more normal blood pressure values than ordinary CSA patients.

Case Report

A 48-year-old man who had been receiving medication including multiple vasodilators for CSA visited the emergency room (ER) complaining of intensive anterior chest pain that suddenly developed while he was driving a car.

The chest symptoms had mostly resolved upon arrival to the ER. The patient had no coronary risk factors, although he exhibited bronchial asthma and an irritable colon. He had quit smoking two years previously. His blood pressure was 130/72 mmHg and his pulse was 64/min and regular. A 12-lead electrocardiogram (ECG) demonstrated slight ST-segment depression in a down-sloping manner in V2 and V3 of the anterior chest leads (Fig. 1A), and ultrasound cardiography (UCG) showed no asynergy of the left ventricle. A laboratory study revealed eosinophilia and an increased level of immunoglobulin E and high-sensitivity C-reactive protein. No cardiac enzyme release was observed (Table). The patient was suspected of having had an attack of CSA and was therefore hospitalized.

At midnight on day 2 of hospitalization, the patient complained of the sudden onset of anterior chest pain at rest. A 12-lead ECG demonstrated ST-segment elevation in the II, III and aVF limb leads and V5,6 chest leads accompanied by reciprocal changes (Fig. 1B). The intravenous administration of isosorbide dinitrate (ISDN) and nicorandil relieved his symptoms, and the ECG findings normalized within a few minutes.

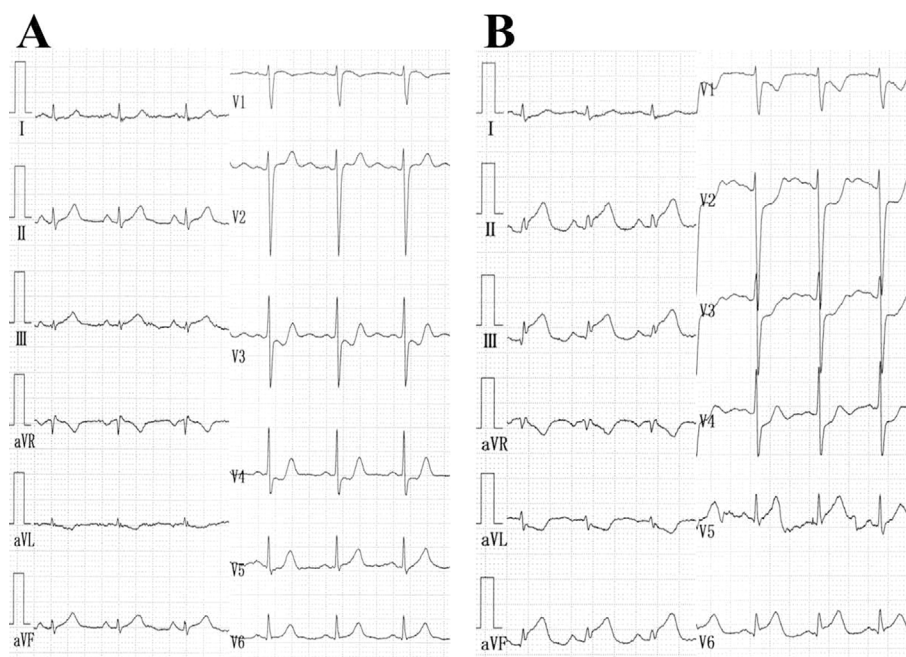


Figure 1. A 12-lead ECG obtained on admission demonstrated slight ST-segment depression in a down-sloping manner in V2 and V3 of the anterior chest leads (A). An ECG obtained on a chest attack demonstrated an ST-segment elevation in the II, III and aVF limb leads and the V5, 6 chest leads accompanying reciprocal changes (B).

Table. Laboratory Data on Admission

Na	141 mmol/dL	WBC	7,990 / μ L
K	3.4 mmol/dL	neutr.	44.7 %
Cl	109 mmol/dL	eos.	14.3 %
BUN	9.9 mg/dL	bas.	0.3 %
Cre	0.74 mg/dL	mon.	6.0 %
S-AMY	56 IU/L	lymp.	34.7 %
CPK	96 IU/L	RBC	459 $\times 10^4$ / μ L
AST	12 IU/L	Hgb	14.8 g/dL
ALT	13 IU/L	Hct	40.5 %
LDH	133 IU/L	Plt	21.6 $\times 10^4$ / μ L
ALP	113 IU/L		
T-Bil	0.7 mg/dL	IgE	2,440 IU/ml
CRP	0.0 mg/dL	hs-CRP	2,210 ng/ml
BS	99 mg/dL	T4	8.13 μ g/dL
Trop T	(-)	FT3	2.76 pg/mL
		TSH	1.72 μ IU/mL

We performed a coronary angiogram (CAG) to examine organic coronary lesions, no significant organic stenosis was observed. We then provoked coronary vasospasms with acetylcholine (ACh) under the oral administration of multiple vasodilators in order to evaluate the effects of the drugs. The intracoronary injection of 50 μ g of ACh provoked the right coronary artery to exhibit diffuse intensive spasms and the left coronary artery to demonstrate segmental total occlusion (Fig. 2). Both of the spasms were resolved with the intracoronary injection of ISDN. At that time, the patient had already taken multiple vasodilators, as follows: benidipine 8 mg/day, nifedipine 60 mg/day, isosorbide mononitrate (ISMN) 80 mg/day, ISDN patch 40 mg/day and nicorandil 15 mg/day (Fig. 3). Taking into account the patient's back-

ground, the coronary vasospasms observed in this case could not be controlled with ordinary medications for CSA.

The patient had suffered from mild eosinophilia for many years. In addition, there was a tendency in which the more severe the eosinophilia, the more frequent the CSA attacks (Fig. 3). He was treated with 20 mg of prednisolone (PSL) every day, after which the eosinophilia improved and the CSA attacks completely resolved. We are now gradually decreasing the doses of PSL and vasodilators, and no adverse events requiring hospitalization have been observed for almost two years.

Discussion

We encountered a refractory CSA patient with an allergic predisposition. A provocative study using ACh provoked severe coronary vasospasms even under treatment with multiple vasodilators. There are several strategies for managing this situation however, no treatment protocols have been established and the condition must be controlled on a case-by-case basis.

Several previous reports have demonstrated that stent deployment is effective for treating refractory CSA patients with discrete and proximal fixed obstructive coronary artery lesions as well as multiple and diffuse spastic lesions (3, 4). However, because there are significant risks of stent restenosis and recurrent vasospasms at different coronary sites with some frequency, providing appropriate medical treatment remains the gold standard for managing coronary vasospasms.

Multiple factors, such as hereditary and acquired factors, are associated with functional changes in the coronary arter-

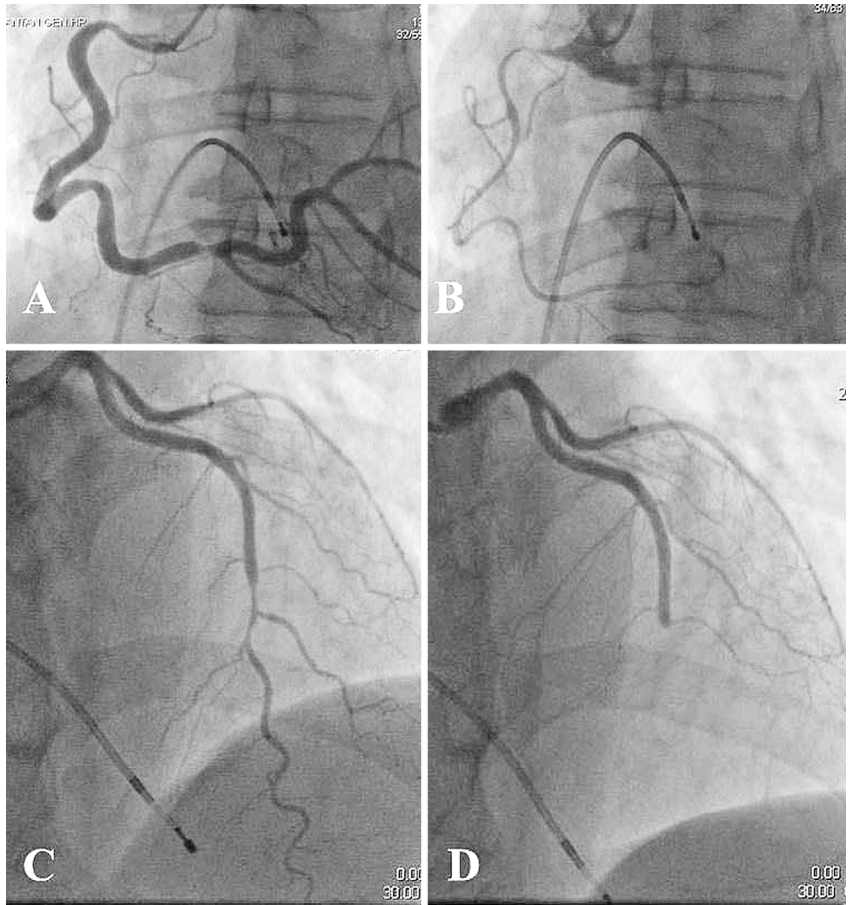


Figure 2. CAG demonstrated no significant organic stenosis. (A, C) The intracoronary injection of 50 µg of ACh provoked the right coronary artery to exhibit diffuse intensive spasms (B) and the left coronary artery to demonstrate total segmental occlusion (D).

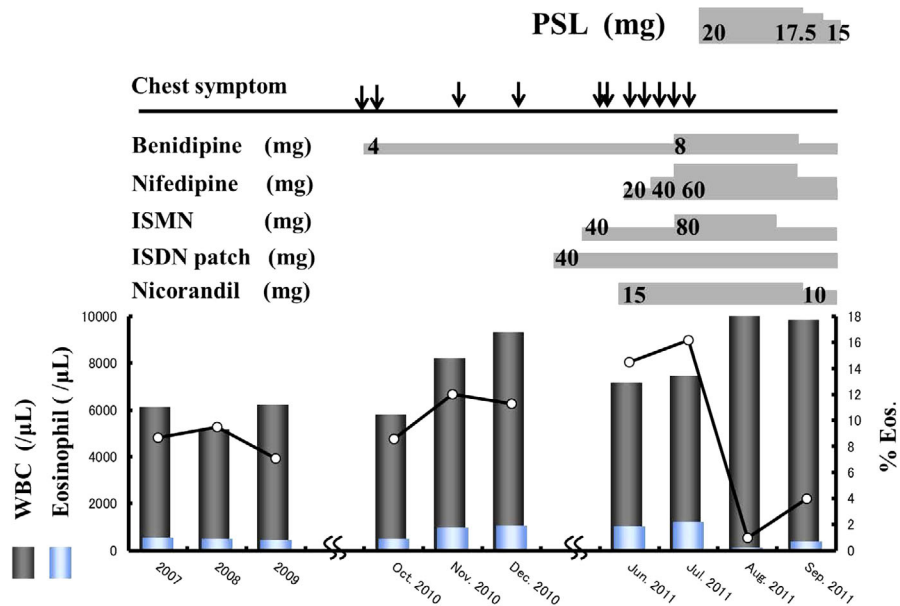


Figure 3. Time course of the patient's clinical background.

ies. Inflammatory mechanisms, in particular, are a significant factor in the development of coronary vasospasms, and there are many reports regarding the association between va-

sospasms and inflammation both *in vitro* (5) and *in vivo* (6). Furthermore, there is one report that the administration of anti-inflammatory corticosteroids is effective for treating re-

fractory coronary vasospasms, similarly to that observed in our case (7). A multi-center study examining the effects of statins on CSA was recently published. The addition of fluvastatin to conventional calcium channel blocker (CCB) therapy for six months significantly reduced the number of patients with ACh-induced coronary vasospasms as compared with the conventional CCB therapy (8). Statins have been shown to exert anti-inflammatory effects and improve the endothelial function.

Moreover, there is a clinical case report of coronary vasospasms associated with hypereosinophilia (9). In this setting, from the point of experimental studies, intimal injury of the coronary artery is thought to be caused by major basic proteins or eosinophil cationic proteins in the vesicles of eosinophils, and autacoids, such as histamine or serotonin are released from eosinophils and can induce vasospasms (10, 11). The cause of hypereosinophilia in this case was not thoroughly investigated. Eosinophilic leukemia, malignant tumors, vermination and drug allergies were ruled out based on the patient's complications. The patient's clinical history involved comorbidities of bronchial asthma in addition to hypereosinophilia for many years, suggesting the possibility of allergic granulomatous angiitis involvement. However, because no findings of angiitis were observed in multiple organs in this case, we cannot conclude that the definitive diagnosis is allergic granulomatous angiitis. We plan to carefully continue to investigate whether any findings derived from angiitis and/or dermatopolymyositis that often complicate allergic granulomatous angiitis appear upon decreasing the dose of corticosteroids.

We herein encountered a case of refractory coronary vasospasms in which corticosteroid therapy was markedly effective. However, it taken into account that inflammation is merely one of the mechanisms of coronary vasospasms. Although the administration of steroids in this case resulted in anti-inflammatory effects, fully suppressed the eosinophilia and resulted in a good prognosis, corticosteroids are not specific medicines for CSA. In general, the priority of corticosteroid administration for CSA is not clinically high. We believe that treatment with corticosteroids can be effective in CSA cases, especially among patients with an allergic back-

ground.

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

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