A Case of Cardiac Arrest due to Multivessel, Diffuse Coronary Spasm in Moyamoya Disease

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Moyamoya disease is characterized by progressive stenosis of the distal portion of the internal carotid arteries and fragile collateral vessels in the brain. The precise pathogenesis is still not known. Although extracranial vessel involvement is very rare, coronary arterial involvement has recently been reported. Here, we report a case of diffuse, multivessel coronary spasm leading to cardiac arrest and myocardial infarction in a 47-year-old man with moyamoya disease with no underlying emotional or physical stress.

Key Words: Moyamoya disease, Stress-induced cardiomyopathy, Sudden cardiac death

Moyamoya disease is a rare cerebrovascular disease involving stenosis of the bilateral internal carotid arteries and the development of an abnormal vascular network (moyamoya vessel) in the vicinity of the arterial occlusions, which may lead to stroke.¹ There have been several reports of involvement of extracranial vessels, especially the renal and coronary arteries, in moyamoya disease. Whether ischemic heart disease in moyamoya disease is concomitant or simply coexistent remains a subject of debate. Recent reports considered moyamoya disease as a systemic arterial disease, because coronary plaque is pathologically similar to the cerebral arterial lesions, with soft intimal proliferation and minimum lipid deposition. Patients with coronary artery disease in moyamoya disease are younger and have few coronary risk factors, in contrast to those with atherosclerotic coronary artery disease.²³

Although a few cases of variant angina with focal spontaneous and pharmacologically induced spasm have been reported in moyamoya disease, multivessel, diffuse coronary spasm leading to cardiac arrest and myocardial infarction mimicking stress-induced cardiomyopathy (SIC) is rarely reported. Here, we report a case of diffuse, multivessel coronary spasm leading to cardiac arrest and myocardial infarction in a 47-year-old man with moyamoya disease, with no underlying emotional or physical stress.
CASE

A 47-year-old man was brought to the emergency room (ER) due to cardiac arrest. He had received cardiopulmonary resuscitation (CPR) by emergency technicians for 15 minutes in the ambulance. His wife reported that he had severe substernal chest pain for 3 hours before cardiac arrest. He had been diagnosed at a local tertiary hospital with both corona radiata infarction and moyamoya disease 6 years earlier (Fig. 1). Three years ago, he had severe resting chest pain after breakfast and visited the local hospital. The ECG at that time revealed ST elevation in leads II, III, aVF, and V2-V6 (Fig. 2A), and coronary angiography revealed normal vessels with elevated troponin I levels (data not shown). He had taken carvedilol, amlodipine, isosorbide dinitrate, and atorvastatin since then, but arbitrarily discontinued his regular medication for 3 days prior to admission. The patient had no coronary risk factors such as hypertension, smoking history, diabetes mellitus and family history of coronary disease. After cardiac defibrillation and resuscitation for a further 20 minutes, blood pressure was restored to 100/80 mmHg; the ECG showed ST elevation in leads I, II, III, and V2-V6, with frequent ventricular premature contractions, which was a pattern similar to that seen on the previous visit at a local tertiary hospital (Fig. 2B). Echocardiography showed an apical ballooning pattern as akinesis in the mid- to apical segments of the left ventricular (LV) wall, with severe LV dysfunction (ejection fraction 25%), which mimicked stress-induced cardiomyopathy (Fig. 3A, Fig 3B). Brain computed tomography (CT) showed no evidence of intracranial bleeding (not shown). Laboratory findings in the ER were as follows: glucose, 125.6 mmol/L; hemoglobin, 17.1 g/dl; white

![Fig. 1. Cerebral angiogram after injection of contrast demonstrates stenosis in both internal carotid arteries, with net-like collaterals (black arrow) typical for moyamoya disease.](image-url)
Cardiac Arrest due to Diffuse Coronary Spasm in Moyamoya Disease

blood cells, 4.86×10^9/L; platelets, 2.94×10^9/L; glycated hemoglobin, 5.1%; blood urea nitrogen, 6.9 mmol/L; creatinine, 71 μmol/L cholesterol, 7.66 mmol/L (< 200 mmol/L); creatine kinase-MB 18.9 ng/ml; troponin-I, 1.23 ng/ml; thyroid stimulating hormone, 5.43 mU/L (0.5-4.7 mU/L); and free thyroxine, 1.23 ng/dL (0.93-1.75 ng/dL). Immediate angiography revealed severe diffuse spasm of all

Fig. 2. Local hospital ECG 3 years ago for acute chest pain showed ST elevation in leads II, III, aVF, and V2-V6 (A). ECG after electro-cardioversion: the irregular rhythm converted to sinus rhythm with ST elevation in I, II, III, and V2-6, with frequent ventricular premature complexes (B). Follow-up ECG 5 days later showed ST resolution in I, II, III, and V2-6, and Q waves in V1-5 (C).
three major coronary arteries (Fig. 4A, Fig. 4B). After intracoronary nitroglycerin was injected, the coronary spasm was relieved, with no visible stenosis (Fig. 4C, Fig. 4D). Troponin I was elevated to the maximal level measurable with a laboratory kit for 3 days.

After 2 weeks, echocardiography still showed true apical akinesis, and the apical anterior septum and lateral wall of the left ventricle were hypokinetic. However, wall motion of apical segments was much improved; global LV systolic function was also much improved, with an ejection fraction of 45%, compared to 25% on admission (Fig. 3C, Fig. 3D). Follow-up ECG showed ST resolution in leads I, II, III, and V2-6, and an abnormal Q wave in V1-5 (Fig. 2C). Cardiac magnetic resonance imaging (MRI) showed subendocardial myocardial infarction in the territories of multiple coronary vessels, but mainly in the entire apical and septal regions (Fig. 5). Brain MRI showed multiple old ischemic lesions/infarction in the right basal ganglia, with involvement of cerebral white matter and complete occlusion of bilateral middle cerebral artery M1 segments. The treatment of this patient aimed

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**Fig. 3.** Echocardiography demonstrated akinesis in the entire mid- to apical segments of the left ventricular (LV) wall, with severe LV dysfunction (LV ejection fraction 25%) and mild apical dilatation (white arrow), which suggest stress induced cardiomyopathy (A: systolic phase, B: diastolic phase). Follow up echocardiography demonstrated true apical akinesis, and hypokinesis of the apical anterior septum and anterior LV wall, with improved LV function; LV ejection fraction 45% (C: systolic phase, D: diastolic phase).
to prevent coronary spasm with diltiazem and isosorbide. He was discharged without other cardiac or cerebral complications, and did not complain of any chest discomfort.

**DISCUSSION**

Moyamoya disease is most prevalent in East Asian populations such as Koreans and Japanese. It is an increasingly recognized cause of stroke in both children and adults.\(^1\) Numerous genetic factors and proteins have been studied to determine the precise pathogenesis, which is still not clearly understood. Pathological autopsy analysis has revealed that the involved intracranial vessels do not have associated arteriosclerotic or inflammatory changes, but rather show fibrocellular thickening of the intima, and hyperplasia of smooth-muscle cells.\(^2\) Other autopsy studies demonstrated that moyamoya disease involves not only intracranial arteries but also extracranial pulmonary, renal, and pancreatic arteries, suggesting that the disease is systemic. Lee et al. reported that the coronary artery plaque in moyamoya disease is mainly composed of a homogeneous, soft intimal proliferation with minimal

**Fig. 4.** Angiography reveals diffuse spasm of the right (A) and left (B) coronary arteries (black arrow). After intracoronary nitroglycerin injection, spasm was relieved in both coronary arteries (C, D).
lipid deposition, similar to the changes found in the involved intracranial vessels in moyamoya disease, suggesting a common pathogenesis.\(^3\) Choi et al. reported a case of focal coronary spasm confirmed by an ergonovine challenge test in women with moyamoya disease.\(^4\) They emphasized genetic and ethnic factors based on the high prevalence of variant angina and moyamoya disease in East Asian people. Severe diffuse spasm of all three major coronary arteries in this patient might be explained by the pathologic change and/or genetic predisposition to moyamoya disease.

Another possible explanation in this case is the association with SIC. The clinical presentation and findings in this patient mimicked SIC, except for persistent apical myocardial infarction, which regarded as an exclusion criterion in Mayo clinic diagnostic criteria of SIC.\(^5\) The pathophysiology of SIC is complex, but recent consensus suggests an “abnormal brain-heart response,” which includes the cardiovascular response to sudden surges in endogenous or exogenous catecholamines, often in the context of acute severe stress.\(^6\) Normally, in response to a given stress, the cognitive center of the brain activates the hypothalamic–pituitary–adrenal (HPA) axis, and this HPA gain induces the release of catecholamines. Patients susceptible to SIC may have high HPA gain and excessive catecholamine release. SIC is often related to acute injury to the brain such as subarachnoid hemorrhage. However, to our knowledge, the association with moyamoya disease and SIC has not
been reported. A case was reported suggesting that a cerebral ischemic lesion caused by moyamoya disease might trigger "paroxysmal sympathetic hyperactivity," manifested by fever, tachycardia, hypertension, tachypnea, hyperhidrosis, and dystonic posturing. Multiple, wide-area strokes might rarely trigger an effect on sympathetic tone, but this usually occurs during the acute stage. Although this patient had no evidence of new intracranial hemorrhage or cerebral infarction on follow-up brain CT and MRI, we could not exclude the possibility that an unrecognized transient ischemic event in preexisting old cerebral ischemic lesions might trigger a sympathetic surge and lead to an SIC response. If the pathophysiologic mechanism of "brain-heart response" is elucidated by intensive basic and clinical research in the future, we believe that the association with moyamoya disease and diffuse coronary spasm will be clarified, and cardiologists and neurologists will develop practical strategies for prevention and treatment of coronary spasm in patients with moyamoya disease.

REFERENCES