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Moyamoya Disease and Coronary Artery Disease

—Case Report—

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Abstract

A 26-year-old female with idiopathic moyamoya disease developed chest pain with concomitant ST depression on electrocardiography. Coronary angiography detected no stenotic lesions in the epicardial coronary arteries. The clinical diagnosis was vasospastic angina pectoris. She was medicated with calcium antagonists, which reduced the frequency of chest pain episodes. Angina pectoris is a rare occurrence in young patients with moyamoya disease. Coronary artery disease and moyamoya disease may have common etiological factors.

Key words: angina pectoris, coronary artery disease, moyamoya disease

Introduction

Moyamoya disease is characterized by progressive steno-occlusive changes at the terminal portions of the intracranial internal carotid arteries and development of so-called 'moyamoya' vessels at the base of the brain, both occurring bilaterally.[10,14] The clinical manifestation of moyamoya disease is typically brain ischemia in the pediatric population and brain hemorrhage in adults. The steno-occlusive changes in moyamoya disease are believed to be confined to the intracranial arteries and rarely occur in the extracranial arteries, including the coronary arteries. Patients with moyamoya disease rarely develop ischemic heart disease. We treated a patient with moyamoya disease who presented with angina pectoris.

Case Presentation

A 26-year-old female first presented at the age of 6 years when she suddenly developed left hemiparesis. Cerebral angiography identified idiopathic moyamoya disease. She underwent bilateral extracranial-intracranial bypass surgery 2 months after the ictus at another hospital. She did not experience another brain ischemic event for 19 years. She underwent follow-up cerebral angiography at our hospital at the age of 21 years, which again confirmed moyamoya disease. At that time she was alert and well oriented. Neurological examination was normal except for minimal left leg monoparesis and hypalgesia, and left lower quadrantanopsia. Magnetic resonance imaging of the brain showed the old infarction as cerebral atrophy in the right frontal and parieto-occipital regions (Fig. 1 *left*). Digital subtraction angiography revealed steno-occlusive changes at the terminal portions of the bilateral internal carotid arteries with sufficient collaterals from the external carotid system through the surgically established bypass (Fig. 1 *center*, *right*). The moyamoya vessels at the base of the brain were poorly developed. The angioarchitecture for this patient was stage 5 bilaterally according to Suzuki and Takaku.[14] She was followed up as an outpatient without medication for moyamoya disease.

The patient began to experience moderate left anterior chest pain when she climbed stairs at the age of 25 years. This chest pain resolved after 2–3 minutes' rest. However, chest pain began to appear even at rest within 2 weeks, and the frequency increased up to 10 episodes per day. She was then referred to the Department of Cardiology with suspected angina pectoris. Except for the pre-existing neurological deficits described above, the patient was neurologically normal. She was of moderate stature with blood pressure of 120/80 mmHg and heart rate of 70 beats/min. She did not smoke or drink. Hypertension, diabetes mellitus, hyperlipidemia,

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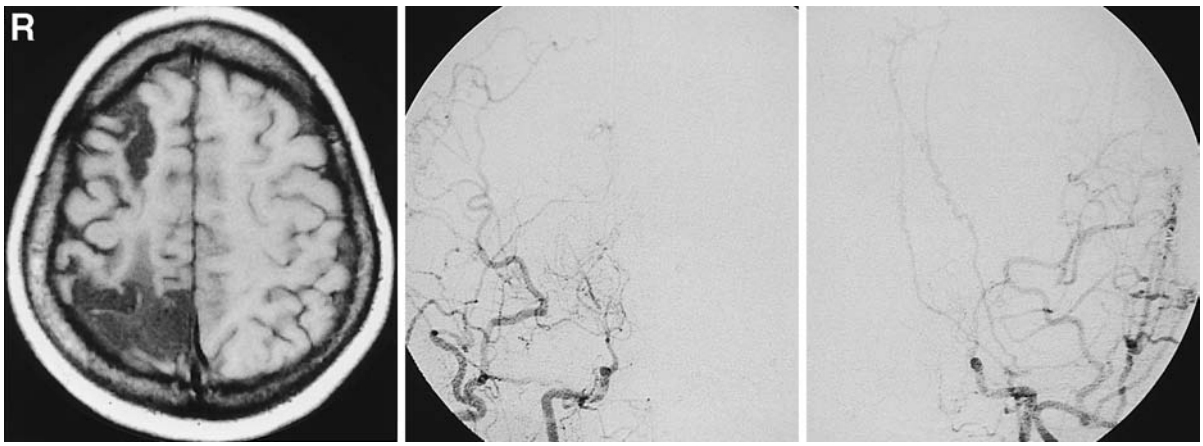

Fig. 1 **T_1-weighted spin-echo magnetic resonance image (*left*) showing the old infarction as atrophy in the right frontal and parieto-occipital regions. Cerebral angiograms, right (*center*) and left carotid injection (*right*), frontal views, revealing steno-occlusive changes at the terminal portions of the bilateral internal carotid arteries with sufficient collaterals from the external carotid system through the surgically established bypass**

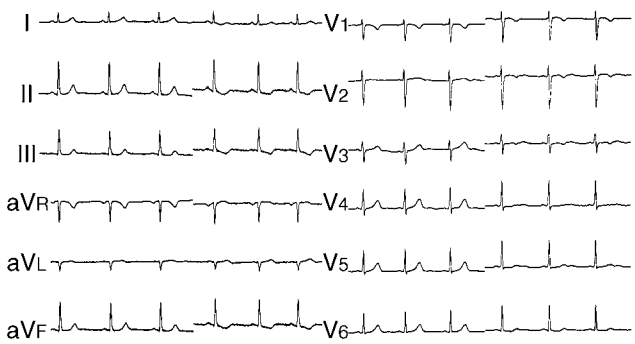

Fig. 2 **Electrocardiograms on admission (*left column*) and during chest pain (*right column*). An ST depression of about 0.5 mm in the II, III, and aVF leads is observed during chest pain.**

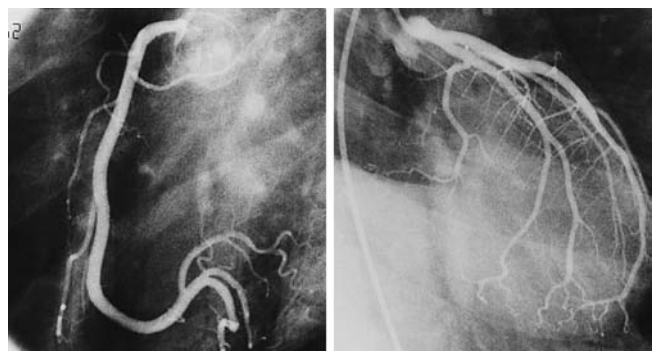

Fig. 3 **Right (*left*) and left coronary angiograms (*right*) showing absence of stenotic changes.**

Kawasaki disease, and autoimmune disease were excluded. Family history was not contributory. Laboratory data, including anti-nuclear antibody and anti-phospholipid antibodies, were normal. Electrocardiography at admission showed no abnormalities, with regular sinus rhythm, normal axis, and no ST deviation. Echocardiography also showed no abnormalities with a left ventricular ejection fraction of 70%.

Electrocardiography showed an ST depression of about 0.5 mm in the II, III, and aVF leads when the patient developed chest pain after dinner during the admission (Fig. 2). This ST depression returned to the baseline within 5 minutes after sublingual administration of nitrates. Coronary angiography failed to show stenotic lesions in the epicardial coronary arteries (Fig. 3), and left ventricular angiography showed no abnormalities. Provocation test with intracoronary injection of acetylcholine was not performed for fear of inducing vasospasm resulting in bradycardia and/or hypotension, followed by brain ischemia. She was medicated with calcium antagonists, which reduced the frequency of chest pain episodes. Vasospastic angina pectoris was strongly suspected because of the typical clinical picture, ST depression, and positive response to nitrates and calcium antagonists.

Table 1 Cases of moyamoya disease associated with coronary artery disease

Case No.	Author (Year)	Age at presentation of coronary disease	Sex	Ethnicity	Coronary manifestation	Coronary angiography	Moyamoya disease manifestation	Age at presentation of moyamoya disease	Cerebral angiography (Suzuki's staging)	Treatment for coronary disease	Treatment for moyamoya disease	Associated diseases	Remarks
1	Furuta et al. (1985)[3]	14	M	Japanese	none	stenosis of rt CA	ischemia	6	?	none	bypass surgery	sick sinus syndrome, hypertrophic cardiomyopathy	
2	Shiratori et al. (1985)[13]	29	F	Japanese	angina pectoris	stenosis at ostium of lt CA MT, irregular wall at bil CAs	ischemia?	28	rt ICA stenosis, lt ICA occlusion	?	bypass surgery (lt side)		ejection fraction 49%
3	Sakamoto et al. (1987)[12]	31	M	Japanese	angina pectoris	stenoses of rt CA and lt ADA	ischemia?	29	rt MCA occlusion	?	bypass surgery		atypical moyamoya disease
4	Saito et al. (1987)[11]	36	M	Japanese	angina pectoris	stenosis of lt ADA	ICH	41	?	CABG	?		younger sister: moyamoya disease
5	Tateno et al. (1988)[16]	30	F	Japanese	angina pectoris	stenosis of lt ADA	ischemia?	24	?	?	?		lt hemiparesis and sensory disturbance at moyamoya disease presentation
6	Suzuki et al. (1989)[15]	40	F	Japanese	heart failure	stenosis at ostium of lt CA MT, atherosclerosis of lt ADA	ischemia	28	rt MCA, bil PCA, and rt ACA occlusion	none	?		dead on arrival
7	Tokunaga et al. (1996)[17]	34	M	Japanese	silent myocardial ischemia	hypoplastic lt CxA, diffuse scleroses of rt CA and lt ADA	ischemia	15 (or at least 28)	rt 5, lt 4	medication	none	diabetes mellitus, hypertension	normal renal arteries, atherosclerosis origin?
8	Akasaki et al. (1998)[2]	23	M	Japanese	angina pectoris	stenosis of lt ADA	asymptomatic	—	rt 4, lt 4	medication	none	renovascular hypertension	lt renal artery stenosis
9	Ikeda et al. (1998)[8]	48	M	Japanese	angina pectoris	normal, positive to Ach provocation	ischemia	47	?	calcium antagonists, nitrates medication	?		
10	Ahn et al. (1999)[1]	19	F	Korean	myocardial infarction	stenosis of middle lt ADA	ischemia	5	rt 6, lt 6	stenting	none	pituitary gigantism	ejection fraction 20%
11	Goar et al. (1999)[4]	38	M	Indian	angina pectoris	stenoses at ostiums of lt CA MT and rt CA	SAH	34	?	CABG, rotational atherectomy and stenting, rotational atherectomy and balloon angioplasty	none		repeated angina pectoris
12	Present case	25	F	Japanese	angina pectoris	normal, provocation not performed	ischemia	6	rt 5, lt 5	calcium antagonist medication	bypass surgery	none	normal renal arteries

ACA: anterior cerebral artery, Ach: acetylcholine, ADA: anterior descending artery, CA: coronary artery, CABG: coronary artery bypass grafting, CxA: circumflex artery, ICA: internal carotid artery, ICH: intracerebral hematoma, MCA: middle cerebral artery, MT: main trunk, PCA: posterior cerebral artery, SAH: subarachnoid hemorrhage.

Discussion

Only 12 cases, including our case, of moyamoya disease associated with coronary artery disease have been reported.[1–4,8,11–13,15–17] (Table 1). The patients were one Korean, one Indian, and 10 Japanese, five females and seven males aged from 14 to 48 years (mean 30.6 years). Two patients were asymptomatic, but the remaining 10 patients had cardiac symptoms: myocardial infarction in one patient, fatal heart failure in one, and angina pectoris in eight. Coronary angiography was normal in two patients, one of whom had a positive response to the acetylcholine provocation test, and demonstrated stenosis of a coronary artery in nine patients: stenosis of the right coronary artery in three, the left anterior descending artery in five, and the ostium of the left coronary artery main trunk in three. Treatment of the coronary artery disease included percutaneous transluminal coronary angioplasty (PTCA) in one patient, coronary artery bypass grafting (CABG) in one, both PTCA and CABG in one, medication in four, none in two, and not specified in three.

Ischemic symptoms of moyamoya disease developed in six patients at ages ranging from 5 to 47 years (mean 17.8 years). One patient suffered subarachnoid hemorrhage at the age of 34 years, another had intracerebral hematoma at 41 years, and one patient was asymptomatic. Staging of moyamoya disease was not less than 4 bilaterally in four patients. Extracranial to intracranial bypass surgery was performed in four patients and no surgery was performed in four. Renal angiography performed in three patients showed renovascular hypertension due to renal artery stenosis in one and normal renal arteries in two. Interestingly, the symptoms of moyamoya disease always progressed to cardiac symptoms except in Case 4, who developed an intracerebral hematoma after angina pectoris. The interval between the initial symptoms of moyamoya disease and the subsequent cardiac symptoms ranged from 1 to 19 years (mean 8.6 years).

The steno-occlusive changes in moyamoya disease are believed to be confined to the intracranial arteries. However, the pulmonary, renal, pancreatic, and coronary arteries in patients with moyamoya disease may manifest histopathologic changes similar to the stenotic changes of the intracranial internal carotid arteries.[5,7,15,18,19] Angiographic studies of the external carotid system are contradictory, as stenotic lesions were found in about 20% of patients studied (13 of 66 patients)[6] whereas no steno-occlusive changes were identified in 39 patients.[9]

Stenosis of the extracranial arteries in patients with moyamoya disease rarely becomes clinically symptomatic except in the renal arteries.[9] Like the steno-occlusive changes in the internal carotid arteries, stenosis of the renal and coronary arteries does not occur in entire segments, but in limited areas within the segment.[18] This suggests that moyamoya disease involves both systemic and focal etiologic factors affecting the intracranial as well as extracranial vessels.

Coronary artery disease associated with moyamoya disease may be attributable to stenosis of the coronary arteries caused by fibrous intimal thickening, vasospastic angina, or a microvascular coronary perfusion disorder. The stenosis of coronary arteries is similar to the histopathological changes of the intracranial internal carotid arteries in patients with moyamoya disease. There was no apparent stenosis in the epicardial coronary arteries of three patients (Cases 7, 9, and 12), suggesting that an abnormal coronary artery response such as vasospasm and/or abnormal coronary microcirculation are possible etiologies of the myocardial ischemia in these patients.

Ten Japanese patients with moyamoya disease have developed coronary artery disease clinically. The estimated total of patients with moyamoya disease in Japan is 4000, so the incidence of cardiac ischemia in association with moyamoya disease is extremely low. The combination could be a chance occurrence, but we believe that there is some unknown common pathogenesis because the presentation of cardiac ischemia occurs in younger patients with moyamoya disease. Atherosclerosis is usually not contributory at such ages. The three main characteristics of the 12 reported patients including our patient are relatively early onset of coronary artery disease (mean 30.6 years), relatively late onset of moyamoya disease (mean 23.9 years), and male predominance (males/females = 1.4).

The etiology of moyamoya disease is still unknown, but the disease can be regarded as a systemic arterial disease. Physicians who follow up patients with moyamoya disease should be aware of the possibility of cardiac ischemia as well as neurological manifestations. We believe that educating the patients about possible cardiac symptoms is also important so that these patients will seek medical attention if cardiac symptoms manifest.

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