Hemorrhagic stroke caused by moyamoya disease in a patient with obstructive hypertrophic cardiomyopathy

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To the Editor: Hypertrophic cardiomyopathy (HCM) has an increased risk of developing ischemic stroke (5%–10% in unselected HCM patients), whereas hemorrhagic stroke only accounts for no more than 0.6% of HCM patients.[1] We present a rare case of HCM complicated with hemorrhagic stroke that caused by underlying moyamoya disease.

A 42-year-old woman was admitted due to exertional dyspnea, chest pain, and dizziness. However, she denied a history of palpitation, headache, syncope, or seizure. She had been diagnosed as obstructive HCM and treated with metoprolol for 10 years. She was always found in sinus rhythm. Her mother was identified to have HCM due to mild exertional dyspnea at the age of 30 years, but she and other family members refused any further investigations. On admission, echocardiography showed asymmetrical left ventricular (LV) hypertrophy with a peak pressure gradient of 79 mmHg in the LV outflow tract (LVOT). Cardiac magnetic resonance imaging revealed remarkable hypertrophy of the interventricular septum with focal late gadolinium enhancement [Figure 1A] and a narrowed LVOT at mid-systole [Figure 1B]. The patient underwent a modified Morrow surgery and recovered successfully without symptoms during a regular follow up for 8 months. However, she was readmitted due to sudden onset of unconsciousness when computed tomography scan confirmed left parietal lobe and intraventricular hemorrhage in the brain. Transcatheter angiography demonstrated the typical feature of "moyamoya" as steno-occlusion of the distal part of bilateral internal carotid arteries and moyamoya-associated collateral networks at the base of brain [Figure 1C–F].

By whole-exome sequencing, we identified a single site mutation (p.G407C, c.1219G>T) in myosin heavy chain 7 gene, the most frequently tested pathogenetic gene for HCM. This mutation results in an amino acid change (glycine to cysteine) that destroys the second structure of the protein which is considered as likely pathogenic.[2] Another mutation (p.R2954H, c.8834G>A) in ring finger protein 213 gene (RNF213) was also detected, which is the first susceptibility gene of moyamoya. In the current patient, moyamoya disease was considered after moyamoya syndrome associated underlying conditions, such as Down syndrome, sickle cell disease, neurofibromatosis type 1, and hyperthyroidism were excluded.[3] However, it remains unclear how variants in RNF213 lead to moyamoya, and the p.R2954H variant identified in this patient has never been reported in moyamoya in any previous study.[4]

HCM is a monogenetic heart disease with a prevalence of 0.07% to 0.2% in general population. In addition to frequent occurrence of atrial fibrillation in HCM secondary to advanced diastolic dysfunction and left atrial remodeling, the disease entity *per se* is an independent risk factor of ischemic stroke.[1] However, hemorrhagic stroke is a rare complication in HCM where the mechanisms have not been suggested. Moyamoya is a rarer disease with more patients found in Asia (3.2–10.5/100,000 population in Asia, *vs*. 0.086/100,000 in US and 0.3/100,000 in Europe).[3] Chronic steno-occlusion of the distal part of bilateral internal carotid arteries and fragile collateral networks as typical moyamoya features make the patients susceptible to both ischemic and hemorrhagic stroke. In Asian adult patients, hemorrhagic stroke is the major presenting type.[3] Before this case, the very rare coexistence of HCM and moyamoya was only reported in a 14-year-old boy back to 1985.[5]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts

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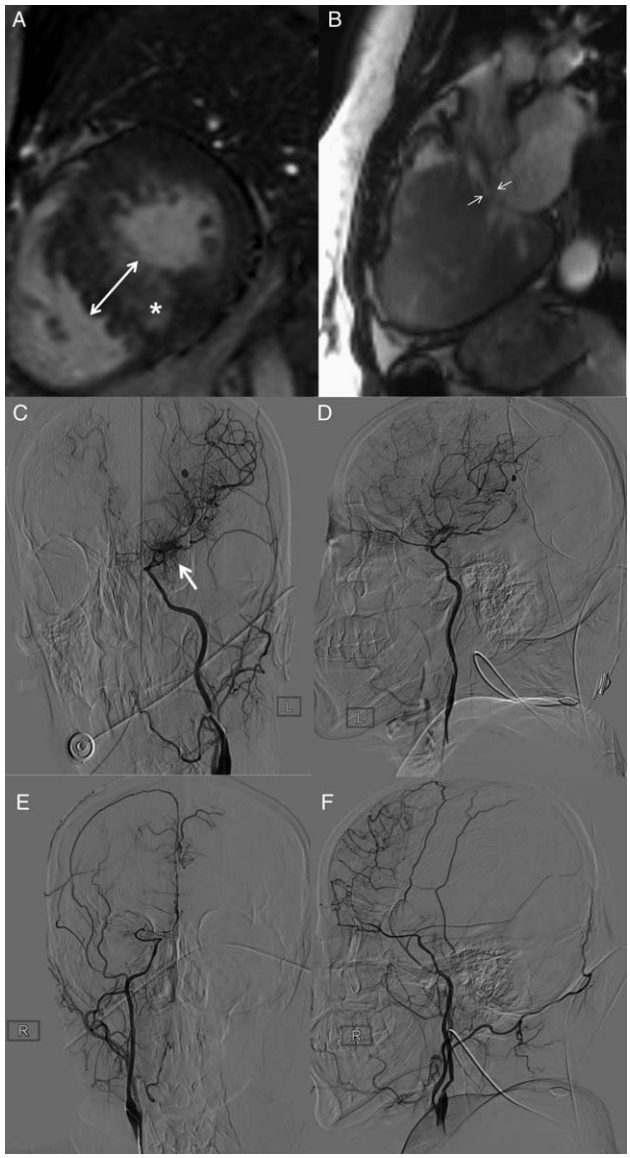

Figure 1: Obstructive hypertrophic cardiomyopathy and moyamoya disease coexist in a patient. Asymmetric hypertrophy involving the interventricular septum with a maximum thickness of 32 mm (A; double-headed arrow) and focal late gadolinium enhancement (A; asterisk), as well the left ventricular outflow obstruction at mid-systole (B; between thin arrows) by cardiac magnetic resonance imaging; and steno-occlusion of the distal left (C and D) and right (E and F) internal carotid arteries and typical moyamoya collaterals in the basal region of the left brain hemisphere (C; thick arrow) by transcatheter angiography.

will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

None.

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