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Letter to the Editor

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Cerebrovascular Events Secondary to Pulmonary Arteriovenous Malformation Based on Genetic Heterogeneity

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Dear Editor,

Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant systemic disorder of angiogenesis characterized by vascular malformations in mucocutaneous tissues, visceral organs, and the central nervous system (1). HHT-related neurological deficits and stroke are observed in 15% of patients and generally occur as a result of a right-to-left shunt induced by pulmonary arteriovenous malformation (PAVM). In patients in whom PAVM and patent foramen ovale (PFO) coexist, both conditions may be responsible for paradoxical embolism. Furthermore, the coexistence of HHT and/or PFO with inherited hypercoagulable states may identify subjects at higher risk for paradoxical embolism. The coexistence of the three disorders leading to stroke via paradoxical embolism is quite rare and gives important information regarding hereditary predisposition.

A 19-year-old female patient who had experienced two previous attacks within the last 3 years was admitted to the neurology department with complaints of double vision, right-sided numbness, and gait disturbance. Cranial magnetic resonance imaging showed an acute ischemic lesion in the left thalamus. Transesophageal echocardiography showed a Chiari network and PFO. Coagulation test revealed antithrombin III (AT III) deficiency [repeated twice at different times, result: 68 (80–120)]. After treatment with acetylsalicylic acid, the patient experienced an episode of epistaxis. Her nasal examination revealed nasal telangiectasias. Her history revealed that her mother and grandfather also had frequent episodes of epistaxis and telangiectasia on the lips. Thoracic and USAominal computed tomography demonstrated multiple pulmonary and hepatic arteriovenous malformations. On genetic investigation, an unknown heterozygous mutation from T to C at the c.88T>C position of the ENG gene was detected. We performed no genetic examination related to AT III deficiency. HHT and thrombophilia are rarely seen concomitantly as two genetic disorders that exhibit theoretically opposite actions on hemostasis (2,3,4). The genetic heterogeneity of HHT may lead to its coexistence with different genetic disorders. Recent studies suggested that prothrombotic mutations are genetic risk factors for cryptogenic ischemic stroke in young adults (5,6), and a relationship between prothrombotic mutations and a risk for cerebral ischemia is present in younger PFO patients (7,8,9). Other reports also state an association between PFO-related cerebral infarction and inherited thrombophilia (7,10,11,12). In fact, genetic thrombophilic defects may affect the potential risks and reduce the expected benefits of percutaneous PFO closure (10). Data by Botto indicate that the coexistence of PFO and inherited hypercoagulable states may identify individuals at higher risk for paradoxical embolism (10). Such conditions give rise to a difficult management problem when they occur concomitantly in one patient. On the other hand, for the clinical management of these patients, performing genetic testing and counseling for inherited thrombophilia may be useful to prevent vascular complications and use better pharmacological modalities, in consideration of the possible presence of both genetic conditions (13). Informed consent was obtained from patients and we consider that the coexistence of these three disorders may not be a coincidence, but may have arisen from a novel ENG mutation.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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