Moyamoya Syndrome With Intraventricular Hemorrhage in an Adult With Factor V Leiden Mutation

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Objective: To report a case of proximal occlusion of 2 major cerebral vessels associated with moyamoya network circulation that manifested by spontaneous intraventricular hemorrhage.

Design: Case report.

Patient and Results: A 36-year-old Syrian man presented with symptoms of sudden-onset headache, neck stiffness, and confusion. The computed tomography scan of his brain showed intraventricular bleeding, and the subsequent 4 vessel angiographies revealed occlusion of the left middle and anterior cerebral arteries with moyamoya appearance in the terminal branches. The coagulation profile showed the presence of heterozygous factor V Leiden mutation. The patient was treated conservatively until resolution of his blood clot, and later he was started on oral anticoagulation.

Conclusion: Factor V Leiden mutation may cause large cerebral vessel occlusion with moyamoya syndrome in adults.

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Department of Internal Medicine, American University of Beirut Medical Center (Beirut, Lebanon) for evaluation and further management of an intraventricular hemorrhage. In March 2002, the patient developed sudden onset of severe global headache associated with nausea and projectile vomiting. His past medical illness was negative except for smoking and a positive family history of coronary artery disease. The physical examination upon admission to our hospital 1 week later revealed a low-grade fever (38°C) and meningeal signs, with confusion and agitation; otherwise, the physical examination findings were normal. A computed tomography scan of the brain done prior to admission showed an intraventricular hemorrhage involving the lateral and third ventricles (Figure 1). Four vessel cerebral angiographies performed under fluoroscopic control and through a right femoral artery approach showed total occlusion of the anterior and middle cerebral arteries at their proximal portions on the left side. The terminal branches of the occluded vessels were filling from collaterals derived from the posterior circulation and thalamic branches, giving the angiographic appearance of moyamoya vessels (Figure 2B). The right anterior, middle, and posterior cerebral arteries were patent (Figure 2A). The aortic and extracranial vessels in the neck showed no other stenotic lesions.

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Laboratory tests revealed normal blood cell counts, blood urea nitrogen levels, creatinine levels, electrolyte levels, and liver function tests. The erythrocyte sedimentation rate was 16 mm/h. The fibrinogen level was 5.1 g/L (normal range, 2.0-5.0 g/L). The C3 level was 1.17 g/L (normal range, 0.9-1.8 g/L), and the C4 level was 0.21 g/L (normal range, 0.1-0.4 g/L). A test for antinuclear antibodies was negative. Serological tests for brucella, VDRL (syphilis), and hepatitis B surface antigen (HbsAg) were all negative. A test for purified protein derivative (PPD) was negative.

The coagulation profile showed the following values: partial thromboplastin time, 31 seconds (patient) and 30.5 seconds (control subject); international normalized ratio, 0.95; protein S level, 64% (normal range, 59%-187%); protein C level, 86.3% (normal range, 70%-130%); antithrombin III level, 100% (normal range, 73%-130%); homocysteine level, 8.8 µg/mL (normal range, 5.1-15 µg/mL). Hemoglobin electrophoresis was consistent with heterozygous thalassemia and no sickle hemoglobin. A test for lupus anticoagulant was negative; tests for anticardiolipin antibodies were weakly positive (immunoglobulin G, 18 g/L; immunoglobulin M test, negative).

The patient was treated conservatively with sedation and fluid hydration. His neurological status and mentation improved gradually, and he was discharged after full neurological recovery. After his condition was stabilized, the patient was started on oral anticoagulation treatment.

**COMMENT**

Resistance to activated protein C (APC) degradation is caused by a specific point mutation in the factor V gene in which arginine 506 is replaced by glutamine.

Factor V Leiden mutation has the highest prevalence rate in the Eastern Mediterranean in apparently healthy individuals, and it is estimated to be 13.6% in Syria.11-13
Our patient belongs to a population with prevalent factor V Leiden mutation and appeared to be a carrier of the heterozygous gene. He suffered from an intraventricular hemorrhage with a large cerebral vessel occlusion and abnormal moyamoya-type collateral circulation. Moyamoya is a Japanese term meaning “hazy puff of smoke,” and the syndrome is defined as a combination of an occlusion of the large cerebral vessels either intracranially or extracranially and the angiographic appearance of telangiectatic collateral vessels. Many sporadic case reports of the occurrence of spontaneous large cerebral artery occlusion and intracerebral bleeding with moyamoya appearance have been described in the literature. The initial presentation is caused either by cerebral ischemia or intracerebral hemorrhages. The etiology of the hemorrhage is thought to be aneurysmal formation or dilated collaterals in the territory of these telangiectatic vessels. Many sporadic case reports of the occurrence of spontaneous large cerebral artery occlusion and intracerebral hemorrhages with moyamoya-like vessels have been described in the literature.

Herein, we report a patient as being the first case, to our knowledge, of intraventricular hemorrhage due to moyamoya collateral circulation caused by an occlusion of the proximal portions of the anterior and middle cerebral arteries, assumed to be secondary to a heterozygous factor V Leiden mutation. It is recommended that physicians check for factor V Leiden in patients from the Eastern Mediterranean region who have cerebrovascular disease and moyamoya collateral vessels.

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