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

Rosette Jabbour, MD; Ali Taher, MD; Ali Shamseddine, MD; Samir F. Atweh, MD

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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FACtOR V LEIDEn MUTATION that is associated with resistance to activated protein C is a risk marker for venous and arterial thrombosis. Although individuals with factor V Leiden mutation showed a trend toward a higher frequency of central nervous system thrombosis in premature neonates, infants, and children as well as in young adults, this complication was not found in older age groups. Furthermore, factor V Leiden mutation may predispose to large brain infarcts. In addition, heterozygosity for factor V Leiden mutation seems to increase the risk of stroke in children by almost 5-fold.

Stenotic disease of large cerebral vessels due to atherothrombotic lesion may lead to the development of moyamoya-type collateral circulation and may present as intracerebral hemorrhage. Herein we report a case of large vessel occlusion associated with heterozygous factor V Leiden mutation and complicated by moyamoya appearance on cerebral angiographies, manifesting with intraventricular hemorrhage in a middle-age patient.

REPORT OF A CASE

A 36-year-old, Syrian, nonhypertensive man was referred to our facility at the 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.
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, 2-5 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, 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, 5-15 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). Test results for mutation C677T of the methylenetetrahydrofolate reductase gene and mutation G20210 of the prothrombin gene (factor II) were negative. The patient had positive test results for a heterozygous mutation of factor V Leiden. The chest x-ray and urinalysis results were normal.

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 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 that will rupture secondary to hemodynamic changes at a later stage. Few reported cases presented with intraventricular hemorrhage. In these cases and in ours, the intraventricular hemorrhage was assumed to be secondary to a heterozygous factor V Leiden mutation and appeared to be a carrier of the Eastern Mediterranean region who have cerebrovascular disease and moyamoya collateral vessels.

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Correspondence: Rosette Jabbour, MD, American University of Beirut Medical Center, PO Box 113-6044, Hamra 110 32090, Beirut, Lebanon (rj04@aub.edu.lb or drrjabbour@hotmail.com).

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REFERENCES