

Moyamoya Syndrome in an Adolescent With Essential Thrombocythemia

Successful Intracranial Carotid Stent Placement

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Background—Essential thrombocythemia (ET) is a chronic myeloproliferative disorder with increased frequency of thrombotic events, including transient ischemic attacks (TIAs) and stroke. Moyamoya syndrome is a rare cerebrovascular disease characterized by progressive occlusion of intracerebral arteries with a typical “puff of smoke” angiographic pattern. We report the development of moyamoya syndrome in a patient with ET.

Case Description—The patient is an 18-year-old female who presented at age 13 with recurrent TIAs. Persistent thrombocytosis was found, a diagnosis of ET was made, and treatment with anagrelide was started. Despite normal platelet counts, she experienced recurrent TIAs and stroke. Severe stenosis of the supraclinoid segment of the left internal carotid artery (LICA) and abnormal collateral vessels were found, and moyamoya syndrome was diagnosed on the basis of the characteristic angiographic appearance. An intracranial stent was placed in the LICA, and since then, she has had an uneventful outcome after a 46-month follow-up.

Conclusion—To our knowledge, the development of moyamoya phenomenon has not been reported in ET, and the relationship between these 2 disorders remains unclear. Besides, this is the first intracranial carotid stent implanted successfully in a patient with moyamoya. (*Stroke*. 2005;36:e71-e73.)

Key Words: moyamoya disease ■ stents ■ ultrasonography, Doppler, transcranial

Essential thrombocythemia (ET) is a chronic myeloproliferative disorder characterized by an increased frequency of arterial and venous thrombosis and microvascular disturbances caused by intravascular platelet aggregates such as erythromelalgia and transient nonlocalizing neurologic symptoms.¹

Moyamoya syndrome is a rare cerebrovascular disease characterized by progressive occlusion of the major trunks of intracerebral arteries. Typical angiographic findings include bilateral occlusive lesions at the distal portion of the internal carotid artery (ICA) or middle and anterior cerebral arteries and an abnormal vascular network at the cerebral base with a “puff of smoke” appearance.² In children, usual manifestations include ischemic cerebrovascular events and seizures, whereas in adults, hemorrhagic stroke is more frequent. At autopsy, thickening and fibrocellular hyperplasia of the intima are typical findings, without evidence of inflammation.³

We report an ET patient with recurrent transient ischemic attacks (TIAs) and stroke, in whom a diagnosis of moyamoya was made.

Case Reports

A 13-year-old caucasian girl presented with transient episodes of recurrent right hemiparesia, and MRI revealed small T2

hyperintense areas in left frontal brain and middle and posterior left semioval center. Six months after the onset of symptoms, persistently elevated platelet counts, up to $1480 \times 10^9/L$, were detected. No cause of reactive thrombocytosis was found. Bone marrow showed hypercellularity with increased number of megakaryocytes and a normal karyotype. A diagnosis of ET was made according to the Polycythemia Vera Study Group criteria,¹ anagrelide was administered, and platelet counts returned to normal until present. One year later, she presented with a new episode of dysarthria and right faciobrachial paresia, which lasted >24 hours. Subsequently, despite treatment with aspirin, she had other episodes of right hemiparesia, and neurologic examination revealed a mild motor sequelae in the right arm. No source for cardioembolism was detected by echocardiography, and screening for inherited and acquired thrombophilia yielded negative results. A transcranial Doppler examination disclosed acceleration in blood flow in the left ICA (LICA; Figure 1). Magnetic resonance angiography of cerebral and neck arteries and cerebral digital angiography (DA) revealed severe stenosis of the supraclinoid segment of the LICA and irregular vessel wall of the supraclinoid segment of the right

Received April 29, 2005; accepted May 10, 2005.

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Stroke is available at <http://www.strokeaha.org>

DOI: 10.1161/01.STR.0000174193.89864.55

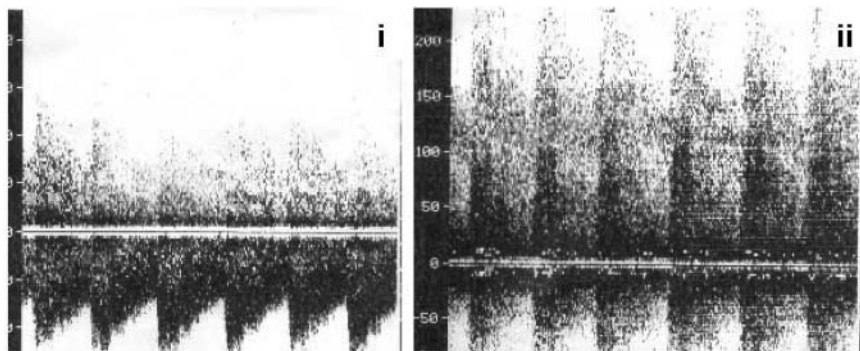


Figure 1. Transcranial Doppler examination of right (i) and left (ii) supraclinoid ICA, revealing an acceleration of blood flow in the LICA.

ICA (Figure 2A). An abnormal collateral network with a “puff of smoke” appearance characteristic of moyamoya is evident on the left side, whereas enlarged collateral vessels are seen in the right pericallosal area (angiographic stage 2, according to Susuki²; Figure 2A). After premedication with aspirin and clopidogrel and under heparinization, an AVE INX 3×12 mm stent (Medtronic) with a cerebrovascular protection device was implanted in the LICA without complications (Figure 2B, i–ii). Control DA, performed 46 months after the procedure, revealed stent patency, without evidence of restenosis and residual collateral vessels through the basal ganglia (Figure 2B, iii). No new abnormalities were found by MRI. She has a normal lifestyle without stroke recurrence under treatment with anagrelide.

Discussion

Overall, one third of ET patients present neurologic symptoms such as headaches, visual disturbances, TIAs, and, less frequently, stroke.^{4,5} At disease onset, neurologic events in our patient were attributed to ET. However, the recurrence of ischemic episodes once platelet counts returned to normal led us to consider other diagnostic possibilities, and the angiographic pattern allowed the diagnosis of moyamoya.

Although the pathogenesis of moyamoya is still unclear, primary and secondary forms have been recognized. The primary idiopathic form is more frequent in Japan and Korea and is characterized by bilateral angiographic lesions.³ Secondary forms, which may be unilateral or bilateral, occur in association with other potential etiologies, including neurofibromatosis, pseudoxanthoma elasticum, cranial irradiation and Down syndrome.^{2,6} In addition, prothrombotic conditions such as protein S deficiency or antiphospholipid antibodies have been found in 40% of children.⁷ This rare case could be classified as a secondary form of moyamoya, with predominantly unilateral involvement, associated with ET.

To our knowledge, the development of moyamoya in ET has not been described previously. Whether this association is casual or causal remains a matter of speculation. Interestingly, other hematologic disorders leading to occlusion of the vasa vasorum have been linked to moyamoya, such as sickle cell anemia⁸ and paroxysmal nocturnal hemoglobinuria. Small vessel occlusion and fibromuscular intimal proliferation is a frequent finding in ET.⁹ Platelet-mediated occlusion of vasa vasorum could be related to the pathogenesis of moyamoya in the patient reported. Several platelet-derived growth factors, such as fibroblast growth factor and trans-

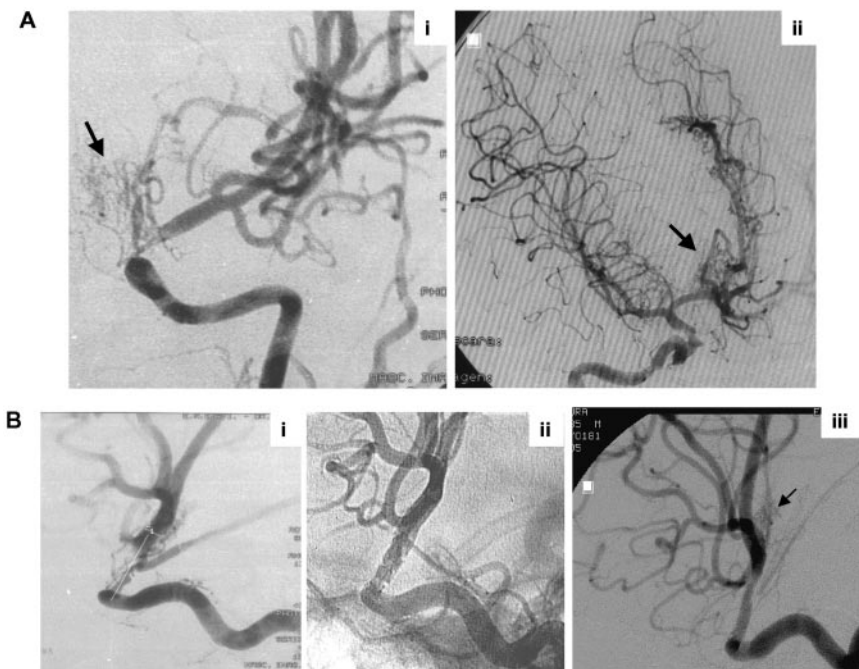


Figure 2. Ai, Intracerebral DA showing severe stenosis of the supraclinoid segment of the LICA and a “puff of smoke” appearance characteristic of moyamoya (arrow); Aii, irregular vessel wall of the supraclinoid segment of the right ICA, together with collateral vessels in the pericallosal area (arrow). B, Angiography performed before (i), during (ii), and 46 months after (iii) stent placement in the LICA. Residual collateral vessels through the basal ganglia are indicated by the arrow.

forming growth factor- β (TGF β), have been proposed to play a role in the pathogenesis of moyamoya.⁶ Of interest, our patient had elevated plasma levels of TGF β 1, as described by us in a cohort of ET patients.¹⁰

Besides, intracranial carotid artery thrombosis has been reported in rare patients with ET^{11,12} and could potentially result in the formation of local collateral vessels. However, this possibility seems unlikely in this case because large vessel thrombosis is rare in young ET patients without additional thrombotic risk factors, and the moyamoya pattern found is not limited to the area surrounding the stenosis.

Surgical direct and indirect revascularization techniques can ameliorate the progression of moyamoya but are associated with significant morbidity and mortality.³ Stent-assisted angioplasty has proven to be technically feasible and safe for treating selected patients with intracranial carotid atherosclerotic stenosis.¹³ To relieve the severe stenosis in the LICA found in this patient, an intracranial stent was placed. As far as we know, this is the first intracranial carotid stent implanted in a patient with moyamoya, with a favorable outcome.

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