

Moyamoya, Dystonia During Hyperventilation, and Antiphospholipid Antibodies

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A 5-year-old Asian male presented with episodes of dystonia involving the right upper extremity during vigorous crying. He was diagnosed with moyamoya disease. Initial laboratory evaluation revealed positive anticardiolipin and antinuclear antibodies. © 2002 by Elsevier Science Inc. All rights reserved.

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Introduction

Moyamoya disease is a progressive vascular stenosis and blockage involving mostly the supraclinoid segment of the internal carotid arteries and the first part of the middle or anterior cerebral arteries and, to a lesser extent, the posterior cerebral arteries. Extensive collateral circulation appears angiographically like a “puff of smoke,” which is the Japanese term for moyamoya disease. Most of the patients are under 10 years of age. Symptoms include seizures, stroke-like events, or transient ischemic attacks during hyperventilation. Moyamoya disease may cause

mental retardation and epilepsy. Neurofibromatosis type I, sickle cell disease, homocystinuria, Down syndrome, meningitis, and radiation have been noted with moyamoya syndrome. A review of the literature from 1966 to 2000 does not reveal a previously described case of childhood moyamoya disease associated with dystonia during hyperventilation.

Case Report

A 5-year-old Asian male born to a 28-year-old gravida 1 para 1 at 36 weeks gestation after a normal pregnancy. He weighed 2330 gm after a normal vaginal delivery. The patient achieved all of his milestones at the appropriate times, and he was in kindergarten doing well. His immunizations were current. He had no cardiovascular, respiratory, gastrointestinal, genitourinary, or skin-related disorders.

In February of 1999 the patient began having episodes while crying, during which his right hand became stiff. The fingers curled and he was unable to move them in any direction actively or passively. His right lower extremity was also stiff. These episodes would last for a few minutes, and they were noticed initially by his grandmother and then his parents. During these events the patient had no alteration of consciousness and no activities to indicate seizures, such as tonic-clonic, myoclonic, or atonic-related events. In between these episodes the patient seemed normal. He was evaluated in the pediatric neurology clinic at Rainbow Babies and Children's Hospital. Physical examination disclosed three small café-au-lait spots. Family history was unremarkable for any neuromuscular-related disorders and no history of stroke, congenital heart disease, juvenile diabetes, short stature, deafness, or movement disorders. The patient was hospitalized to evaluate the possibility of decreased blood supply to the left hemisphere during hyperventilation that would explain the above-mentioned dystonia while crying. Cranial magnetic resonance imaging and magnetic resonance angiography of the head and neck were obtained. Magnetic resonance imaging revealed a deep left centrum semiovale infarct and magnetic resonance angiography revealed severe stenosis of the intracranial carotid arteries bilaterally (Fig 1). A cerebral angiogram confirmed the diagnosis of moyamoya disease (Figs 2 and 3). The electroencephalographic result without hyperventilation was normal. Laboratory evaluation revealed findings suggestive of connective tissue disease and the presence of antiphospholipid antibodies (Tables 1 and 2).

The patient underwent bilateral cerebral revascularization procedures under general anesthetic. The right side was performed first. A frontotemporoparietal craniotomy was performed to permit a pial synangiosis. In effect, this is a nonanastomotic bypass in which a branch of the superficial temporal artery is swung in continuity onto the surface of the brain. Additionally, an occipital burr hole was placed and the dura opened to encourage extracranial to intracranial revascularization. The identical procedures were then performed on the left side.

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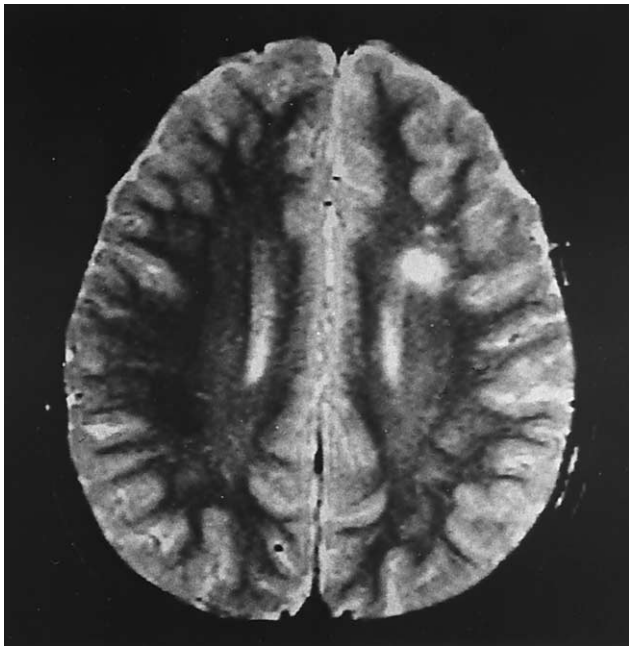


Figure 1. Deep left centrum semiovale infarct.

The patient awoke from surgery with a dense left hemiparesis. This improved rapidly and by 6 weeks his strength was normal except for mild weakness of left ankle dorsiflexion. Follow-up computed tomography and magnetic resonance imaging revealed bilateral frontal lobe encephalomalacia. There was a small left epidural hematoma without mass effect, and this resolved spontaneously. The patient was maintained on aspirin and phenytoin.

Discussion

Children with moyamoya disease can have marginal cerebral perfusion. It is recognized that they can present with seizures, transient ischemic attacks, or strokes. Activities associated with hyperventilation, such as crying, can precipitate symptoms. This patient is unique in that transient dystonia caused by hyperventilation has not previously been reported in moyamoya disease, although there has been a case report of recurrent torticollis in an 8-month-old female with the disease [1]. It is known that patients with this disease may have a "rebuild-up phenomenon" [slow activity] on recorded electroencephalograms several minutes after hyperventilation [2,3]. In an attempt to explain the above phenomenon, studies have been performed using near infrared spectroscopy. It was found that during hyperventilation there is a decrease in the concentration of oxyhemoglobin and total hemoglobin. Termination of hyperventilation was followed by partial recovery of these values, although they dropped subsequently. It was found that cytochrome oxidase was also reduced. The above disturbances were closely correlated to the rebuild-up phenomenon and with transient ischemic attacks [4]. The same results were reached by Lin et al. [5]. In another study ^{99m}Tc -HmPAO single-photon electron spectroscopy (SPECT) revealed a critical decrease of regional blood flow during the rebuild-up phenomenon in the parietal and occipital regions bilaterally. Acetazolamide testing indicated a severe deficit of perfusion reserve. This finding was also related to the rebuild-up phenomenon observed in the entire hemisphere 30 seconds later, includ-

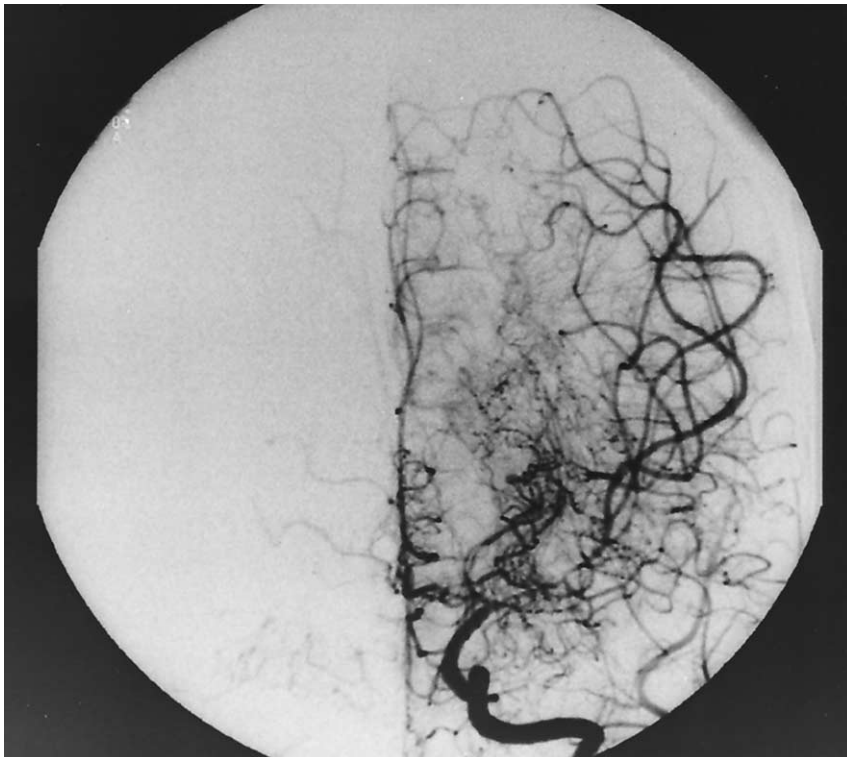


Figure 2. Left side of cerebral angiogram confirms the diagnosis of moyamoya disease.

Figure 3. Right side of cerebral angiogram also confirms the diagnosis of moyamoya disease.



ing the areas where ischemic changes were not noted [6]. Fujiwara et al. [7] administered oxygen to children with moyamoya disease and found that it eliminated the re-build-up phenomenon.

In a study measuring intraoperative cortical blood flow and CO₂ response during hyperventilation in children with moyamoya disease, it was demonstrated that basal moyamoya vessels were constricted by hyperventilation. This may explain the ischemic symptomatology observed during hyperventilation [8]. Togawa et al. concluded that in young children even a moderate decrease in blood flow could cause metabolic impairment. This impairment is caused by high cerebral metabolic demands, which may explain why we see transient ischemic attacks in children with moyamoya disease during hyperventilation [9]. From

the above literature, we can speculate on the mechanism of the above presentation of our patient with dystonia during hyperventilation. The weakness and numbness observed could be caused by decreased blood supply with decreased oxygen and vasoconstriction of the basal ganglia regions. An asymmetric blood supply may explain why he presented with unilateral transient dystonia during hyperventilation.

The laboratory findings suggest that his presentation might be secondary to autoimmune phenomena. This presentation has been reported in pediatric patients with moyamoya disease who had antiphospholipid antibodies [10-12]. Elevation of antinuclear, anti-DNA, anti-SM, and anti SS-A antibodies are observed in children with systemic lupus erythematosus but may be temporarily

Table 1. Laboratory results

	Patient's Values	Normal Range
Von Willebrand's factor	159	50-150%
C3 complement	254	77-168 mg/dL
C4 complement	60	13-36 mg/dL
CH 50-complement total	20	100-300 CH50 units
C-reactive protein	3.38	0-1 mg/dL
Westergren erythrocyte sedimentation rate	76	0-13 mm/h
Immunoglobulin M	279	25-136 mg/dL
Immunoglobulin A	271	23-116 mg/dL
Immunoglobulin G	1157	429-1131 mg/dL
Activated partial thromboplastin time	36	25-33 sec
Platelets	503	150-400 × 10 ⁹ /L
Epstein-Barr virus viral capsid antigen IgG	2.5	<1-Negative
Epstein-Barr virus early antigen IgG	>5	<1-Negative
Epstein-Barr virus nuclear antigen IgG	>5	<1-Negative

Table 2. Laboratory results

Laboratory Tests	Abnormal Values	Normal Values/Reference
Antinuclear antibody screen	Positive	Negative
Antinuclear antibody titer	1:80	<1:80
Anti-Sm	1.9	<1-Negative
Anti-SS-A (Anti-Ro)	2.1	<1-Negative
Anti-DNA	35	<25 Negative IU/mL 25-30 Borderline positive 30-60 Low positive 60-200 Positive >200 Strong positive
Anti-Scl-70	1.1	<1-Negative
Anticardiolipin IgG immunoglobulin G	75	Negative 0-12 GPL units Equivocal 13-18 Positive >18
Anticardiolipin IGA immunoglobulin A	85	Negative 0-10 APL units Equivocal 11-15 Positive >15
Antinuclear antibody screen	Positive	Negative

increased after infection with the Epstein-Barr virus, although active lupus usually results in decreased levels of complement C3 and C4. In this patient, they are increased, although the functional level of CH50 is decreased. This decrease may occur if the functional assay is not performed promptly after phlebotomy or if another constituent of the complement cascade is decreased or absent. Prolongation of the activated partial thromboplastin time may be due to the presence of a lupus anticoagulant or deficiency of other clotting factors. The elevated anticardiolipin antibody does not cause prolongation of the activated partial thromboplastin time. The high sedimentation rate C-reactive protein platelet count and Von Willebrand factor could be observed in patients with vasculitis. Could moyamoya disease be the cerebral equivalent of Takayasu disease? Further studies are required.

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