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Moyamoya Syndrome Associated With Down Syndrome: Outcome After Surgical Revascularization

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ABSTRACT. *Objectives.* This study was undertaken to describe the clinical, radiologic, and angiographic features of moyamoya syndrome in a surgical series of children and adults with Down syndrome. We wished to define the features of moyamoya syndrome associated with Down syndrome and to determine the results of surgical revascularization among these patients at early and late follow-up times.

Methods. We reviewed the clinical, radiologic, and angiographic records of all patients with moyamoya syndrome associated with Down syndrome, as a subset of a previously reported, consecutive series of patients who underwent cerebral revascularization surgery with a standardized surgical procedure, pial synangiosis, between January 1, 1985, and June 30, 2004.

Results. Of 181 patients with moyamoya syndrome from the initial series who were treated surgically during the study period, 16 patients had Down syndrome (10 female patients and 6 male patients). The average age at onset was 9.3 years (range: 1–29 years); the average age at the time of surgery was 9.8 years (range: 2–29 years). Although the presenting symptoms were transient ischemic attacks for 10 patients and strokes for 6 patients, computed tomographic and/or MRI scans demonstrated bilateral infarctions for 9 patients and unilateral infarctions for 6, with only 1 patient having no imaging evidence of a previous stroke. No cases presented with intracerebral hemorrhage. Preoperative angiography showed the presence of bilateral moyamoya syndrome changes for all patients, including posterior circulation involvement for 8 patients. Surgical treatment included pial synangiosis for all patients, although 1 patient underwent a superficial temporal artery-middle cerebral artery bypass in the contralateral hemisphere. Surgical complications included symptomatic subdural hematomas requiring evacuation, at 48 days and 54 days postoperatively (2 cases), seizures (2 cases), and strokes within 30 days after surgery, at 1 day and 7 days postoperatively (2 cases). Late clinical and radiologic follow-up data (average: 67.6 months; range: 6–146 months) demonstrated no worsening in neurologic status for any patient except for 1 patient who developed a seizure disorder with associated chronic hypocalcemia; she was totally dependent at the 10-year follow-up evaluation, despite no evidence of new infarction since her surgery. There was no clinical or radiologic evidence of new infarction for any patient in late follow-up evaluations. Postoperative angiography, conducted 1 year after surgery for 11 patients, revealed radiologic evidence of good to excellent cerebral revascularization in 85% of the surgically treated hemispheres. Patients were maintained on lifetime aspirin therapy.

Conclusions. The clinical, radiologic, and angiographic features of moyamoya syndrome associated with Down syndrome seem comparable to those of primary moyamoya disease. Cerebral revascularization surgery with the pial synangiosis technique seems to confer long-lasting protection against additional strokes in this patient population. The presence of moyamoya syndrome should be considered in the evaluation of patients with Down syndrome who present with transient ischemic attack-like symptoms. *Pediatrics* 2005;116:e694–e701. URL: www.pediatrics.org/cgi/doi/10.1542/peds.2005-0568; *moyamoya disease, moyamoya syndrome, Down syndrome, stroke, pial synangiosis, surgery.*

ABBREVIATIONS. ADL, activities of daily living; MRA, magnetic resonance angiography.

Moyamoya syndrome is a chronic, occlusive, cerebrovascular disorder of unknown pathogenesis that is characterized by progressive stenosis of the bilateral supraclinoid internal carotid arteries, with concomitant formation of tortuous arterial collateral vessels at the base of the brain, which reconstitute distal branches of the cerebral circulation. In this study, we sought to compare the clinical, radiologic, and angiographic features of the moyamoya phenomenon associated with Down syndrome with those of primary moyamoya disease and to explore possible reasons for the high frequency of moyamoya syndrome in the Down syndrome population. We wished to determine the efficacy of a specific revascularization technique, pial synangiosis, in preventing additional episodes of cerebral ischemia and progressive disability among these patients.

METHODS

We reviewed a previously reported, consecutive, surgical series of patients with moyamoya syndrome who underwent pial synangiosis between January 1, 1985, and June 30, 2004, to identify patients with Down syndrome.[1] The charts of these patients were reviewed retrospectively, to determine gender and age at presentation, symptoms, results of radiologic studies (including computed tomography, MRI/magnetic resonance angiography [MRA], and cerebral arteriography), perioperative and late complications, length of follow-up period, and long-term clinical and radiologic outcomes. The functional status of each patient was graded with a modified Rankin outcome scale (0 = no symptoms;

TABLE 1. Clinical and Radiologic Summary of 16 Patients With Moyamoya Syndrome and Associated Down Syndrome

Patient No.	Age at Presentation, y	Gender	Associated Abnormalities	Clinical Presentation	Treatment	Postoperative Follow-up Period, mo	Complications	Clinical Outcome	Modified Rankin Scale Score
1	5	M	Slipped R femoral head, VSD, B undescended testicles, repeated tonsillitis, repeated sinusitis	R hemiparesis and speech difficulties with some recovery	Staged B pial synangiosis with B frontal burr holes plus ASA	115	None	Mild persistent R hand weakness	2
2	19	F	Hirschsprung's disease, repeated conjunctivitis, repeated otitis externa	R UE paresis with speech disturbance 1 y ago; recent L hemiparesis	B pial synangiosis plus ASA	128	None	Improved L LE strength but now wheelchair bound and totally dependent for ADL	5
3	13	M	None	L hemiparesis with almost complete recovery	Staged B pial synangiosis with B frontal burr holes	104	None	Mild persistent L hemiparesis	2
4	6	F	Acute lymphocytic leukemia, AV canal, repeated pneumonia	L facial droop; 1 mo later, R facial droop, R hemiparesis, and decreased speech production	B pial synangiosis with B frontal burr holes plus infant ASA	113	L subacute SDH on POD 48	Persistent R hemiparesis and speech difficulties	3
5	14	F	Hypothyroidism, NIDDM, repeated pneumonia, repeated urinary tract infections	R hand weakness with speech disturbance; partial recovery	B pial synangiosis with B frontal burr holes plus infant ASA	78	None	Neurologically intact	0
6	2	F	AV canal, hydrocephalus, acute lymphocytic leukemia, tethered cord	L hemiplegia with partial recovery; 1 wk later, R hemiplegia and R visual field deficit	B pial synangiosis plus ASA	68	None	Persistent spastic quadriparesis; walks with gait trainer	3
7	4	F	PDA, hyperthyroidism, duodenal atresia	R UE tremors; gait instability	B pial synangiosis with L parietal burr hole plus ASA	78	L subacute SDH and seizure on POD 54	Neurologically intact	0
8	8	M	Intussusception, repeated otitis media, tonsillitis, and pneumonia	L hemiparesis with recovery; 1 y later, R hemiparesis	Staged B pial synangiosis with L frontal burr hole and R parietal burr hole plus infant ASA	146	None	Neurologically intact	0
9	29	F	Repeated upper respiratory infections	R hemiparesis and speech difficulties	Staged L STA-MCA bypass and then R pial synangiosis plus ASA	42	R hemiplegia with new L MCA territory infarction after direct bypass	Neurologically intact	0
10	5	F	ASD, patent foramen ovale	L hemiparesis with complete resolution; 3 mo later, R hemiparesis; 1 mo later, L hemiparesis	Staged B pial synangiosis plus ASA	25	None	Neurologically intact	0

TABLE 1. Continued

Patient No.	Age at Presentation, y	Gender	Associated Abnormalities	Clinical Presentation	Treatment	Postoperative Follow-up Period, mo	Complications	Clinical Outcome	Modified Rankin Scale Score
11	7	F	PDA, ADHD, celiac disease	R UE paresis	Staged B pial synangiosis plus infant ASA	23	New-onset seizures 1 y postoperatively	Neurologically intact	0
12	2	M	ASD, VSD	R hemiparesis with complete resolution	B pial synangiosis with B frontal burr holes plus infant ASA	112	None	Neurologically intact	0
13	13	M	AV canal	R focal seizures; 1 mo later, R hemiplegia, aphasia, and swallowing difficulties with gradual improvement	R pial synangiosis plus ASA	14	New-onset R hemispheric seizures 5 mo postoperatively	Mild persistent R hemiparesis and behavioral problems	3
14	12	F	AV canal, ureteral stenosis, repeated tonsillitis	L hemiparesis with almost complete recovery	B pial synangiosis plus ASA	21	None	Mild persistent L hemiparesis	2
15	3	M	Patent foramen ovale, repeated pneumonia and otitis media	L hemiplegia with almost complete recovery	R pial synangiosis; L temporalis muscle and deep temporal artery synangiosis plus infant ASA	9	None	Improved L-sided spasticity	1
16	15	F	Atlantoaxial instability, occipitocervical instability, hyperthyroidism, repeated otitis media	R hemiplegia and speech difficulties; 2 mo later, R UE paresis and speech difficulties; 1 mo later, L hand weakness	B pial synangiosis plus ASA	6	None	NA	NA

ASD indicates atrial septal defect; VSD, ventricular septal defect; ASA, aspirin; R, right; L, left; B, bilateral; UE, upper extremity; AV, arteriovenous; SDH, subdural hematoma; POD, postoperative day; NIDDM, non–insulin-dependent diabetes mellitus; STA, superficial temporal artery; MCA, middle cerebral artery; PDA, patent ductus arteriosus; ADHD, attention-deficit/hyperactivity disorder.

Fig 1. Preoperative angiogram, demonstrating an injection of the right external carotid artery. The long posterior branch of the superficial temporal artery (arrow) should be noted.

1 = minor symptoms not affecting lifestyle; 2 = minor handicap but independent in activities of daily living [ADL]; 3 = requiring some help with ADL; 4 = requiring substantial help with ADL; 5 = totally dependent).

RESULTS

Patients

Sixteen patients with moyamoya syndrome associated with Down syndrome were treated surgically during the study period. Their clinical features are listed in Table 1. The average age at presentation was 9.3 years (range: 1–29 years), with a median of 7.8 years; the average age at the time of surgical treatment was 9.8 years (range: 2–29 years), with a median of 8.0 years. There were 6 male patients and 10 female patients.

Associated Systemic Manifestations

The most common associated systemic abnormalities were congenital cardiac anomalies (11 cases), gastrointestinal anomalies (4 cases), and endocrine disturbances (3 cases). Other significant associated abnormalities included acute lymphocytic leukemia (2 cases) and atlantoaxial instability (1 cases).

Clinical Features

All patients presented with symptoms consistent with cerebral ischemia, with chief complaints of transient ischemic episodes for 10 patients (62.5%) and stroke for 6 patients (37.5%).

TABLE 2. Complications Related to Surgical Revascularization for 16 Patients With Moyamoya Syndrome and Down Syndrome

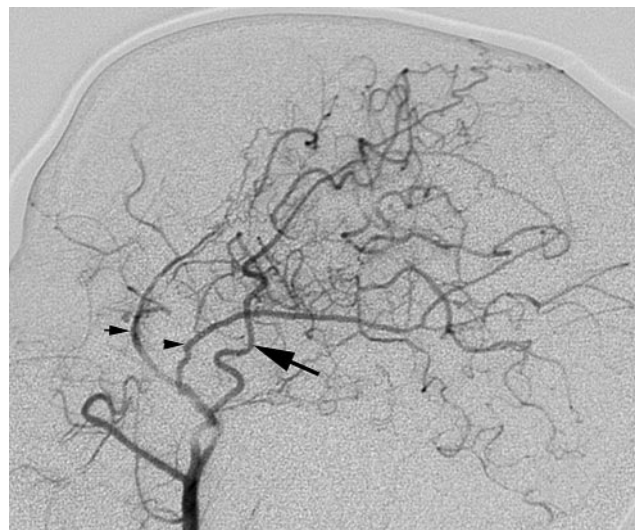| Complication	No. of Patients	Postoperative Time
Subacute SDH	2	48 d; 54 d
Medically controlled seizures	2	5 mo; 1 y
New infarction	2	Immediate; 7 d

SDH indicates subdural hematoma.

Fig 2. Postoperative angiogram, demonstrating an injection of the same right external carotid artery as seen in Fig 1, 1 year after surgery. The site of pial synangiosis, with a hypertrophied superficial temporal artery and abundant collateral vessel development (large arrow), should be noted. In addition, enlarged middle meningeal branches, also supplying collateral branches to the cortex (small arrows), can be seen.

Preoperative Radiologic and Angiographic Features

Despite the clinical presentations noted above, all except 1 patient demonstrated the presence of infarction on preoperative computed tomographic and/or MRI scans. Preoperative angiograms were available for review for 12 patients (24 hemispheres) and showed typical bilateral involvement of the supraclinoid internal carotid artery and its major branches for all patients; in addition, 8 patients demonstrated posterior circulation involvement (Fig 1). Because of severe behavioral disturbances, 1 patient was treated surgically on the basis of MRI/MRA findings only and did not undergo formal angiography.

Surgical Treatment

All patients in this series underwent pial synangiosis to revascularize the affected hemisphere, although 1 adult patient also underwent a superficial temporal artery-middle cerebral artery anastomosis in 1 of her surgically treated hemispheres. Pial synangiosis is a modification of the encephaloduroarteriosynangiosis described originally by Matsushima and Inaha.[2] A branch of the superficial temporal artery is dissected intact from the scalp, and this healthy vessel is then sutured to the pial surface of the brain after a craniotomy is performed. The vessel is left intact; once the bone is replaced, the vessel passes under the skull proximally to contact the brain and then comes back out to the scalp distally.

TABLE 3. Clinical Outcomes After Surgery for 15 Patients With Moyamoya Syndrome and Down Syndrome

Clinical Outcome	Modified Rankin Scale Score	No. of Patients
Intact or minimal deficit	0 or 1	8
Mild neurologic deficits	2 or 3	6
Dependent	4 or 5	1

Subsequent ingrowth of blood vessels from the donor vessel and dural margins occurs over several months after the operation and results in collateral blood flow to the ischemic brain tissue.[3] The average follow-up period was 67.6 months (range: 6–146 months).

Complications

Complications from surgical treatment in the series (Table 2) included delayed subdural hematoma formation that required evacuation for patients 4 and 7 (at 48 and 54 days after surgery, respectively), postoperative seizures for patients 11 and 13, and new infarctions within 30 days after surgery for patients 9 and 16.

Clinical Outcomes

Clinical outcomes were available for 15 patients (Table 3). Fourteen patients showed no worsening in neurologic function. Eight of these patients were thought to have demonstrated improvement in their neurologic examination results and/or recovery from preexisting deficits (Rankin scale scores of 0 or 1); 6 demonstrated no changes in their preexisting deficits and were graded in Rankin categories 2 or 3. One patient who developed a chronic seizure disorder in the setting of chronic hypocalcemia exhibited deterioration during the follow-up period, despite no evidence of new infarction on MRI scans, and was given a Rankin scale score of 4. All patients were maintained on chronic aspirin therapy (81 mg daily).

Radiologic and Angiographic Outcomes

One-year follow-up angiograms were available for 11 of 16 patients (21 hemispheres); 20 of the 21 hemispheres (95%) developed new collateral circulation via the synangiosis (Figs 1 and 2). Annual postoperative MRI/MRA scans were available for 10 patients; none of the patients demonstrated evidence of new infarction.

DISCUSSION

Reports of Moyamoya Syndrome

The moyamoya arteriopathy was first described in a case report from Japan by Takeuchi and Shimizu[4] in 1957. The typical angiographic appearance of the small, fragile, basal, collateral vessels prompted Suzuki and Takaku[5] to use the Japanese word "moyamoya," meaning "hazy, cloudy, or puff of smoke," to define the vasculopathy. The disease is usually bilateral, although unilateral presentations of the disorder have been described.[6,7] In much of the Japanese literature, the primary idiopathic form, "moyamoya disease," has been distinguished from an "associated" form, "moyamoya syndrome," in which the arterial changes are seen among patients with various syndromes or other disease processes.[8–46] However, the clinical and radiologic features of the associated and idiopathic forms seem identical.[1,32]

The pathogenesis of moyamoya syndrome is unknown. The age at onset of symptoms of moyamoya syndrome shows a bimodal distribution, peaking in the first decade at age 5 and in the fourth decade at age 34. The majority of children with moyamoya syndrome present with ischemic symptoms, whereas adults present with intraparenchymal, intraventricular, or subarachnoid hemorrhage, as well as stroke and transient ischemic attacks. A fixed, unilateral, neurologic deficit is the most common initial finding,[47] although alternating hemiplegia may be seen for some patients.[48] Seizures and involuntary movement disorders may also occur in the pediatric population.[49]

There are relatively few reports of the occurrence of moyamoya syndrome in association with Down syndrome, although moyamoya syndrome has been reported to occur with a higher frequency in Down syndrome than in the general pediatric population.[16] There have been 47 previous cases of moyamoya syndrome in association with Down syndrome reported in the world literature, including cases from Japan, the United States, Brazil, and Italy; there have been 26 cases reported in the English-language literature to date.

The prognosis of patients with moyamoya syndrome seems to depend on neurologic status at the time of diagnosis and surgical therapy.[49] It seems that untreated children experience continued, progressive, neurologic decline secondary to increasing stroke burden. Children with large unilateral or bilateral infarctions involving the dominant hemisphere, suffered at an early age, frequently are severely developmentally delayed and may have chronic seizure disorders. In contrast, patients with multiple small infarctions or a single large infarction in the nondominant hemisphere may have a satisfactory long-term prognosis if additional strokes can be prevented. For this reason, for our own patients we have recommended that revascularization surgery be performed early in the course of the disease, before the development of multiple infarctions.[50] Given the relentless progressive nature of moyamoya syndrome, we think that early intervention is justified.

Clinical Features of Our Patient Series

The usual peak of onset of moyamoya syndrome in childhood is during the first decade of life.[7] Our larger clinical series had an average age of onset of 7.1 years,[1] and the average age of onset of this series was 2 years older, ie, 9.3 years, with a range from 1 year to 29 years. The slightly older age of onset may reflect the greater difficulty of detecting symptoms in the Down syndrome population; in addition, transient neurologic symptoms among patients with Down syndrome may not be evaluated aggressively. We found that such symptoms were attributed frequently to sequelae of congenital cardiac anomalies or to a possible seizure disorder. Unilateral weakness has been reported as the most common clinical presentation for moyamoya disease,[5,51] and 13 of our 16 patients presented with hemiparesis or hemiplegia, with 6 of those 13 patients presenting with alternating hemiparesis or hemiplegia. The youngest patient in our series with moyamoya syndrome and Down syndrome was 2.5 years; the age at onset of his first ischemic episode, which was thought at the time to be secondary to complications from previous surgery

for a congenital cardiac anomaly, was 1 year. The youngest reported patient with moyamoya syndrome and Down syndrome was 20 months of age.[14] The preponderance of female patients (10 patients) over male patients (6 patients) in this Down syndrome series, with a ratio of 1.7:1, is comparable to a reported incidence ratio in the general moyamoya syndrome population of 1.4:1.[51] The overall long-term mortality rate for moyamoya disease has been reported variably as 4.3% to 13%.[7,52] The surgical mortality rate in our series was 0%, and no patients died during the follow-up period, which ranged from 6 months to 12 years.

Surgical Treatment

The most widely used procedure for the surgical treatment of moyamoya syndrome among children is probably encephaloduroarteriosynangiosis,[41] which was first described by Matsushima et al.[53] Every patient in our series underwent pial synangiosis (described above), but one 29-year-old patient had sufficiently large superficial temporal artery and middle cerebral artery branches that an anastomosis between the 2 could be conducted in one of the surgically treated hemispheres. The postoperative arteriograms obtained after the 2 procedures indicated excellent hemispheric collateral vessels on each side, which suggests that the observable collateral vessels resulting from the procedures are comparable.

Complications

Throughout the follow-up period, ranging from 6 months to 12 years, no strokes occurred outside a 30-day perioperative period for any of our patients. Two patients experienced early postoperative infarctions, with significant neurologic deficits; however, at the time of the most recent follow-up evaluations, the patients had recovered completely from their deficits. Other complications included formation of subdural hematomas for 2 patients (1 spontaneous and 1 posttraumatic) and new seizures for 2 patients. Both subdural hematomas required surgical evacuation, but neither patient experienced long-term sequelae from the hematomas. This patient population is particularly susceptible to this complication, because of the prior craniotomy, preexisting cortical atrophy, and chronic aspirin therapy.

Clinical Outcomes

Motor recovery in moyamoya syndrome associated with Down syndrome was good despite multiple and/or bilateral infarctions, consistent with the prognosis reported for primary moyamoya disease after surgical revascularization. Recovery among patients with primary moyamoya disease treated surgically was found to be good for 57%, fair for 22%, and poor for 20%.[54] In our previously reported series of 143 patients treated surgically with pial synangiosis,[1] nearly 75% of patients were leading independent and normal lives. In this Down syndrome series, good recovery was seen for 53%, fair recovery with persistent neurologic deficits was seen for 40%, and poor recovery with worsening neurologic status was seen for 7%. The good recovery from stroke among patients with moyamoya syndrome associated with Down syndrome is remarkable. Stroke recovery mechanisms seem to rely on neuronal adaptation, including synaptogenesis, axonal and dendritic growth, and changes in neurotransmitters; the neuronal abnormalities found in Down syndrome, including atrophy of cortical dendrites and reduced synaptogenesis,[13] would be anticipated to inhibit such recovery.

Radiologic and Angiographic Outcomes

Striking development of collateral circulation from synangiosis was seen in 95% of surgically treated hemispheres on 1-year postoperative angiograms. All patients remained clinically and radiologically stroke-free during long-term follow-up monitoring, despite evidence of angiographic progression of moyamoya syndrome in 42% of surgically treated hemispheres. The revascularization surgery for these patients seemed to be the major factor in preventing cerebral infarctions in the presence of worsening stenosis of major cerebral arteries.

Mechanisms of Pathogenesis

The association of Down syndrome with moyamoya syndrome is still not understood. The fact that so many children with Down syndrome have cardiac structural anomalies suggests that the genetic defect in Down syndrome may also lead to disturbances in the formation or growth of vascular structures elsewhere the body. Patients with Down syndrome have been noted to have an increased number of retinal vessels, compared with gender- and age-matched normal control subjects. These vessel are said to have a "spoke-like" pattern, with frequent early branching, and this observation lends support to the postulate that there is a general vascular dysplasia in Down syndrome.[55] Other vascular abnormalities described in Down syndrome include abnormal nail-bed capillary loops and renovascular hypertension.[56] Neuropathologic investigation of a child with Down syndrome who did not have moyamoya syndrome revealed significant structural abnormalities in vessels of the circle of Willis, ie, irregular internal elastic membrane surrounding regions of marked endothelial hyperplasia, which again suggests a possible underlying structural change in the cerebral arteries of children with moyamoya syndrome and Down syndrome.[30]

One report suggests that protein C deficiency among children with Down syndrome leads to thromboembolism and recurrent strokes.[57] Protein C deficiencies were not investigated systematically in our patient series, however. One patient in our series (patient 16) became symptomatic after starting treatment with an oral contraceptive, a known risk factor for stroke in many patient populations and a medication specifically contraindicated for patients with moyamoya syndrome.

The presence of autoimmune processes and autoantibodies among patients with trisomy 21 suggests the postulate that the presence of moyamoya syndrome in Down syndrome might result from an immunologic disturbance of some type. Idiopathic

moyamoya syndrome has been associated with antiphospholipid antibodies,[29] and our series included 3 patients with endocrine abnormalities, including 1 patient with both autoimmune hypothyroidism (Hashimoto's thyroiditis) and non–insulin-dependent (type 2) diabetes mellitus and 2 patients with hyperthyroidism (Graves' disease).

Down syndrome may, through its constellation of associated systemic manifestations, expose patients to the cumulative effects of other associated risk factors for moyamoya syndrome and thereby increase the patients' susceptibility to the disease. It has already been noted that certain clinical conditions are associated with moyamoya syndrome independent of Down syndrome, including congenital heart defects,[21] autoimmune disorders of the thyroid,[23,27,28,46] and head and neck irradiation.[11,25,33,37] Two of our patients with Down syndrome developed acute lymphocytic leukemia before the onset of clinical symptoms attributable to moyamoya syndrome; the incidence of leukemia in Down syndrome is 10- to 20-fold that in the general population.[58,59] Both patients received systemic and intrathecal chemotherapy as part of their treatment protocol, and 1 patient received a course of cranial radiotherapy. How these clinical associations independently affect the risk for developing moyamoya syndrome among children with Down syndrome is unknown. However, given the risk of significant strokes among patients with moyamoya syndrome, coupled with the effectiveness of treatment if it is instituted before debilitating strokes occur, we suggest that prophylactic screening of patients with Down syndrome for moyamoya syndrome with MRI/MRA may be useful. A similar strategy to screen for moyamoya syndrome among patients with sickle cell disease has been advocated by some. Additional study of the cost-effectiveness of this strategy may be warranted.

Previous data from our institution[1] support the practice of treating patients with moyamoya syndrome as soon as possible. Timelines of patient strokes document that moyamoya syndrome is a progressive disease with cumulative morbidity and that this progression can be arrested with surgical treatment.[1] The patients do require long-term aspirin therapy postoperatively. Although information regarding the potential complications of long-term aspirin therapy in this patient population is limited, a recent study comparing the use of aspirin versus warfarin among adult patients with intracranial arterial stenosis suggests that the long-term use of aspirin is relatively safe.[60]

CONCLUSIONS

Moyamoya syndrome in association with Down syndrome causes progressive neurologic disability resulting from cerebral infarction. The presence of moyamoya syndrome should be considered in the evaluation of patients with Down syndrome who present with transient ischemic attack-like symptoms. The clinical course and radiologic features of the moyamoya syndrome seen among these patients seem to mirror those of idiopathic moyamoya disease, and the patients with Down syndrome respond well to cerebral revascularization procedures such as pial synangiosis, just as the general population with moyamoya syndrome does. After surgery, additional strokes do not occur, and good functional outcomes can be anticipated for >50% of surgically treated patients. Given the treatable nature of this disease and its potentially severe consequences, we support the prophylactic screening of patients with Down syndrome for moyamoya syndrome with MRI/MRA.

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