Moyamoya disease is a chronic progressive vasculopathy that leads to stenosis and occlusion of the intracranial internal carotid arteries and their proximal branches. Compensatory collateral vessels develop in response to poor cerebral perfusion. By definition, the primary form, or moyamoya disease, is idiopathic with bilateral involvement. The secondary form is termed moyamoya syndrome (MMS) and refers to patients with associated risk factors and bilateral arterial involvement or arteriographic findings that are only unilateral. Some of these risk factors include sickle cell disease (SCD), Down syndrome (DS), and neurofibromatosis type 1. The term moyamoya thus describes the characteristic “puff of smoke” pattern of these collateral vessels on angiography, without regard to the etiology. In a US study, the incidence of MMS was 0.086 per 100,000 persons, which is lower than the reported rates in Japan.

The initial presentation of moyamoya syndrome as stroke in the perioperative period of an otolaryngologic procedure has not been reported.

Methods

The retrospective medical record review was approved by the institutional review board of Vanderbilt University. Inpatient and outpatient records were searched for the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 437.5 diagnosis of moyamoya from 2000 to 2012. Variables such as age, sex, date of MMS diagnosis, date of initial stroke, signs and symptoms of MMS, imaging modalities, and types and dates of any otolaryngologic procedures were recorded. An in-depth medical record analysis and a systematic review of the literature were performed.

Results

The ICD-9-CM search identified 157 patients with code 437.5 for MMS, of which 137 patients were ultimately diagnosed as having moyamoya syndrome. Of these, 19 patients underwent otolaryngologic procedures; 3 children had strokes 2 to 4 days after adenotonsillectomy, including 2 children with Down syndrome. Intraoperative carotid artery injury was considered but was proven not to be the cause of stroke. Bilateral moyamoya disease was diagnosed in all 3 patients via vascular imaging studies; all subsequently underwent revascularization procedures.

CONCLUSIONS AND RELEVANCE

Clinicians should be aware of an elevated prevalence of moyamoya syndrome in Down syndrome and sickle cell disease populations and should consider moyamoya syndrome in the differential diagnosis of postoperative stroke. Stroke risk is magnified in the perioperative setting related to perioperative dehydration and hypotension. Awareness and screening for cerebral vasculopathy in high-risk populations could prompt measures to decrease the occurrence of postoperative strokes after adenotonsillectomies.
ing this disease. Of the 19 patients with documented otolaryngologic procedures at some time in the past prior to MMS diagnosis (eTable in the Supplement), 3 patients younger than 18 years had strokes after adenotonsillectomies (Table). These strokes occurred within 2 to 4 days of the procedures. In addition, 1 adult had a stroke 3 days after bronchoscopy and was subsequently diagnosed as having MMS. In 2 of the 3 cases of strokes after adenotonsillectomies, the strokes were initially attributed to possible intraoperative injury to the carotid arteries by the admitting services. Vascular imaging studies subsequently revealed bilateral MMS in all 3 patients. Staged bilateral cerebral revascularization procedures were subsequently performed to reduce additional stroke risks. Down syndrome was present in 2 children, and 1 child had developmental delay related to prematurity with no other genetic or congenital syndromes.

Table. Comparison Between Patients Who Had Strokes After Adenotonsillectomies Because of Undiagnosed Moyamoya

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Age at moyamoya diagnosis, y</td>
<td>8</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>Syndromic comorbidity</td>
<td>None</td>
<td>Down syndrome</td>
<td>Down syndrome</td>
</tr>
<tr>
<td>ENT diagnoses</td>
<td>OSAS</td>
<td>OSAS, recurrent tonsilitis, chronic sinusitis, serous otitis media</td>
<td>OSAS</td>
</tr>
<tr>
<td>ENT operation performed</td>
<td>T+A</td>
<td>T+A, tympanostomy tube insertion</td>
<td>T+A</td>
</tr>
<tr>
<td>Known stroke prior to T+A</td>
<td>No</td>
<td>No</td>
<td>Yes; 2 prior strokes</td>
</tr>
<tr>
<td>Date of postoperative stroke</td>
<td>POD 2</td>
<td>POD 4</td>
<td>POD 2</td>
</tr>
<tr>
<td>Initial symptoms of stroke</td>
<td>Altered mental status, hemiparesis</td>
<td>Somnolence, hemiparesis</td>
<td>Apraxia, hemiparesis</td>
</tr>
<tr>
<td>Time from initial stroke to moyamoya diagnosis</td>
<td>2 d</td>
<td>4 d</td>
<td>11 y</td>
</tr>
<tr>
<td>Diagnostic imaging</td>
<td>CT, MRI, CTA, DSA</td>
<td>CT, CTA, DSA</td>
<td>CTA, MRA, DSA</td>
</tr>
</tbody>
</table>

Abbreviations: CT, computed tomography; CTA, computed tomographic angiography; DSA, digital subtraction angiography; ENT, ear, nose, and throat; MRA, magnetic resonance angiography; OSAS, obstructive sleep apnea syndrome; POD, postoperative day; T+A, adenotonsillectomy.

Figure. Example of Cerebral Infarcts and Moyamoya Syndrome

A, Bilateral watershed and borderzone infarcts (arrowheads) seen on magnetic resonance imaging in a child with moyamoya. B and C, Digital subtraction angiogram shows stenosis of the internal carotid artery (lateral view [B] and anterior-posterior view [C]) and resulting moyamoya-type vessels in the same child.

Report of Cases

Case 1
An 8-year-old boy with a history of mild speech and motor delays presented with symptoms of severe obstructive sleep apnea syndrome (OSAS) and was treated with adenotonsillectomy (Table). His intraoperative and postoperative course was complicated by severe hypertension believed to be secondary to clonidine withdrawal and postoperative bleeding a few hours after surgery. He returned to the operating room for control of the bleeding and was admitted to the hospital for observation. A hematologist was consulted for an elevated prothrombin time of 16.1 seconds. It corrected without treatment, and a primary coagulopathy was believed to be unlikely. On postoperative day 2, the patient developed an altered mental status and right-sided weakness. Computed tomography (CT) of the head without contrast followed by magnetic resonance imaging (MRI) of the brain showed bilateral acute and chronic areas of watershed infarction (Figure, A). A computed tomographic angiogram (CTA) of the brain was consistent with a moyamoya-type pattern. The patient’s neurologic status improved, coagulation studies returned to normal levels, and hypertension was controlled, prompting a safe discharge to home. After discharge, digital subtraction angiography confirmed bilateral internal carotid artery (ICA) and middle cerebral ar-
tory stenoses and formation of collateral vessels (Figure, B and C). The patient was started on a daily aspirin regimen. Revascularization surgery for MMS, termed encephaloduroarterio- synthangiosis (EDAS), was performed in a staged fashion by a neurosurgeon.

Case 2
A 5-year-old boy with DS and no stroke history was found to have adenotonsilllar hypertrophy, obstructive sleep-disordered breathing, recurrent tonsillitis, chronic rhinitis, and otitis media (Table). He was treated medically for 3 months with no significant improvement of symptoms. A polysomnogram revealed mild obstructive sleep apnea with a central component, and he underwent adenotonsillectomy and bilateral tympanostomy tube insertion with no apparent intraoperative complications. He was observed in hospital and was placed on intravenous fluid therapy until his oral intake was optimized. He was discharged on postoperative day 3, ambulatory and interactive. At home, he refused all oral intake. On postoperative day 4, he returned to the emergency department because of acute somnolence and new right-sided weakness. Head CT showed bilateral infarcts, and digital subtraction angiography confirmed MMS. He was discharged on postoperative day 11 on an aspirin regimen. Subsequently, he underwent staged EDAS.

Case 3
A 15-year-old girl with a medical history notable for DS, OSAS, and multiple strokes presented as an outpatient for a second opinion evaluation for possible MMS (Table). At age 3 years, she had scarlet fever and presented with acute onset left-sided weakness that was found to have been caused by a right middle cerebral artery watershed stroke. She recovered with no neurological deficits. At age 4 years, she underwent adenotonsillectomy for OSAS at an outside institution. Despite intravenous hydration after the surgery, she had an ischemic stroke on postoperative day 2. She was started on a daily aspirin regimen. At age 15 years, she developed apraxia with right facial droop and arm weakness. An MRI of the brain demonstrated a new infarct. Subsequent CTA revealed collateral vessels and bilateral occlusion of ICAs. She presented to our center at this time, and digital subtraction angiography confirmed the diagnosis of MMS. The patient underwent revascularization by a neurosurgeon.

Discussion
Stroke after adenotonsillectomy is rare and should prompt consideration of cerebral vasculopathy because such a diagnosis has important implications for clinical management. Moyamoya syndrome is associated with a number of genetic conditions including DS, SCD, and neurofibromatosis type 1, in which otolaryngology procedures are commonly performed. In a study by Jea et al, 16 of 181 patients (9%) with MMS had DS. Patients most commonly presented with symptoms of cerebral ischemia at a mean age of 9.3 years. Although none of these patients were reported to have had strokes after an otolaryngologic procedure, 1 patient had a stroke after a cardiac surgery. Kainth et al 3 observed that 3.8% (3760 per 100 000) of patients admitted with MMS had coexisting DS, and this prevalence was 2-fold higher (10.6%) among patients younger than 15 years.

A majority of patients with DS undergo adenotonsillectomy as a first-line treatment for OSAS. Common postoperative complications include acute upper airway obstruction, oxygen desaturation, postextubation stridor, and bleeding from the surgical site. Emesis and poor oral intake are also common and can be prolonged in patients with DS. Although stroke is not a commonly considered complication, cases of stroke from ICA dissection after tonsillectomy have been reported. In an article published in 2003, a pediatric patient with no reported intraoperative complications developed hemiplegia after a tonsillectomy. The clinical and radiographic findings were most consistent with ICA dissection that led to cerebral infarction. It has been suggested the tonsillar bed is in closer proximity to the ICA in children younger than 12 years, which may pose a risk for an inadvertent ICA injury. Chronic tonsillar infection was also suggested to contribute to the stroke by causing vasospasm and thrombosis.

The presence of DS in 2 of the 3 children with moyamoya disease or syndrome who had strokes within the perioperative period of adenotonsillectomies in our study is important (Table). In both cases, the patients were not diagnosed preoperatively as having MMS, and therefore their families and physicians were unaware of their predisposition for ischemic brain injury. Patients with moyamoya disease or syndrome have tenuous cerebral perfusion related to ICA occlusions that may increase stroke risk associated with surgical procedures. Both surgery and anesthesia may be associated with risk factors for stroke in MMS including hypotension due to anesthetic agents and dehydration due to refusal of oral intake postoperatively, as well as hypovolemia, anemia, hyperventilation, and hypocapnea. Preoperative knowledge of MMS might have an impact on perioperative anesthesia and fluid management in these patients.

Currently, widespread screening for MMS is not recommended by American Heart Association guidelines. However, noninvasive screening by imaging modalities in select populations with known predisposed conditions such as DS, SCD, and neurofibromatosis type 1 is supported. Trancranial Doppler (TCD) sonography is a widely available modality, and its use has evolved in the recent years with the Stroke Prevention Trial in Sickle Cell Anemia (STOP) protocol for the primary prevention of strokes in children with SCD. Trancranial Doppler screens for intracranial vessel narrowing by evaluating cerebrovascular flow velocities. Children with SCD and significantly elevated TCD velocities receive aggressive and highly effective stroke prevention therapy. Also, TCD is used for diagnosis and follow-up of vasculopathies, evaluation of acute cerebrovascular disorders in intensive care unit patients after a traumatic brain injury, and confirmation of brain death.

Owing to a small population of children with MMS, the utility of TCD as a screening tool for MMS has not been investigated. Trancranial Doppler has been studied for diagnosis of
MMS with equivocal results, and digital subtraction angiography remains the gold standard for diagnosis. However, studies have determined that TCD has a high reliability for noninvasive detection of disease manifested by high blood flow velocity (>200 cm/s) in stenotic intracranial vessels. Given its effectiveness as a screening tool for increased stroke risk in patients with SCD, TCD may also be a reasonable screening tool for MMS in high-risk populations like DS with a prevalence of MMS up to 10.6%, especially prior to operations such as adenotonsillectomies. Screening for cervical instability in patients with DS is a similar example, in which a prevalence of 10% to 20% has led to routine radiographic screening prior to otolaryngologic surgery. Further studies may be considered to assess the cost-effectiveness of preoperative screening of predisposed populations with TCD.

Moreover, in our series, an adult patient underwent a bronchoscopy by pulmonology prior to surgery. There were no periprocedural complications. The patient presented with stroke 3 days after the procedure and moyamoya was diagnosed. Clinicians should be aware that procedures other than adenotonsillectomies, particularly those that require anesthesia and fluid management, could also be associated with a postoperative stroke with undiagnosed MMS. Lastly, while 15 patients in our series with undiagnosed MMS underwent otolaryngologic procedures without acute neurologic events, it is important to note that these procedures could also have precipitated strokes.

Conclusions

In the unusual event of a stroke after adenotonsillectomy, the clinical entity of MMS should be considered as a possible cause. Given the rare but serious potential for strokes in patients with DS and SCD with undiagnosed MMS, this cerebral vasculopathy should be considered prior to these patients undergoing surgery. Patients with DS and SCD frequently undergo adenotonsillectomies, and increased awareness and screening could prompt measures to decrease the occurrence of postoperative strokes in these patients. Trancranial Doppler is a screening tool widely used for primary stroke prevention in SCD and can be considered for MMS screening in patients with DS and SCD. Research into the cost-effectiveness of this modality may be considered for future study. Suggestions for perioperative management include careful anesthetic management to avoid hyperventilation and hypotension; postoperative attention to adequate hydration and pain control; and avoidance of hypercapnia, hypocapnia, and hyperthermia.

REFERENCES


