Chapter

38 Moyamoya Disease

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A three-year-old boy presents for preoperative evaluation prior to pial synangiosis. A recent angiogram under general anesthesia to evaluate his cerebral circulation following recurrent transient ischemic attacks confirmed the diagnosis of Moyamoya disease. Current medications include aspirin. The nurse practitioner calls to determine what work-up and patient recommendations are appropriate prior to surgery.

What Are the Anatomic Changes and Pathophysiology Associated with Moyamoya Disease (MMD)?

Moyamoya is a Japanese word meaning "puff of smoke," which describes the web-like vascularity depicted when viewing the reticular anastomosis and collateral formations between the internal and external carotid arteries on cerebral angiography (Figure 38.1).

The disease involves a progressive stenosis of the internal carotid artery and its branches with gradual development of collaterals from the base of the brain and through the skull from the external carotid artery. Intimal thickening and hyperplasia result in vascular occlusion and consequent proliferation of collateral vessels at variant planes such as leptomeningeal, basal ganglia, and/or transdural. The result of this collateral vessel formation can be critically diminished blood flow in the cerebral vasculature which can lead to eventual ischemic crisis.

What Is the Epidemiology of MMD?

Moyamoya disease was originally reported by Takeuchi and Shimizui in 1957. In the United States, the ethnically specific breakdown of incidence ratio per 100,000 includes 4.6 in the Asian population, 2.2 for African Americans, and 0.5 for the Hispanic population. MMD is likely genetically inherited as there is a 9–12% incidence in those with a family history of the disease. There is a female predominance, with the female to male ratio being 1.8:1. Though the syndrome is thought to be genetically influenced, radiation and various infectious processes have been suggested as possible causes of pathogenicity.

What Disorders Are Associated with MMD?

Table 38.1 Disorders most commonly associated with Moyamoya development.

Congenital syndromes	Apert syndrome Hirschsprung disease Marfan syndrome Neurofibromatosis – type 1 Trisomy 21
Immunological disorders	Graves' disease
Hematological disorders	Aplastic anemia Fanconi anemia Sickle cell anemia Thalassemia
Neoplasia	Wilms tumor Craniopharyngiomas
Infectious	Tuberculous meningitis Leptospirosis
Vascular disorders	Atherosclerotic disease Cardiomyopathy Coarctation of the aorta Hypertension
Others	Radiation Pulmonary sarcoidosis Nephrotic syndrome

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What Is the Most Likely Age for Presentation?

Disease may be acquired as an autosomal dominant process and can even present in early infancy, while a chronic and progressive disease presentation occurs with the highest incidence within the first decade of life.

What Are the Signs and Symptoms of MMD?

In early childhood, MMD usually presents with ischemic symptoms, whereas adults may present with intracranial hemorrhage. In children, MMD often manifests with transient ischemic attacks or ischemic strokes. Symptoms may include headache, dizziness, and seizures, although some patients are asymptomatic. Decline in neurological function and/or cognition, choreiform movements, growth hormone deficiency, and visual impairment may occur as the disease progresses.

What Are the Disease Stages of MMD?

The dynamic and continual disease process is a slow progression ultimately leading to complete occlusion of the internal carotid artery. Early on, suprasellar carotid stenosis occurs followed by formation of basal collaterals. As stenosis worsens to include occlusion at the Circle of Willis vessels, extracranial collaterals form. With progressing stenosis, these extracranial collaterals enlarge and eventually provide nearly all flow.

What Factors Affect Prognosis?

A worse prognosis is associated with younger age at presentation (under six years), severe neurological deficits at presentation, and advanced angiographic changes.

How Is MMD Diagnosed?

If intracranial hemorrhage is suspected, then computed tomography (CT) of the head is indicated. Acute and chronic infarcts and areas of cortical ischemia will be revealed by magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) with roughly 90% sensitivity. Angiography is the gold standard for diagnosis, allowing for assessment of the internal and external carotid systems independently.

What Are the Angiographic Stages of MMD?

Table 38.2 Angiographic staging of Moyamoya disease.

Grade I	Carotid stenosis without collateral vessels
Grade II	Basal collateral vessels seen
Grade III	Prominent basal collateral vessels
Grade IV	Stenotic or occluded Circle of Willis and posterior cerebral arteries
Grade V	Extra cranial collateral network
Grade VI	Total carotid occlusion

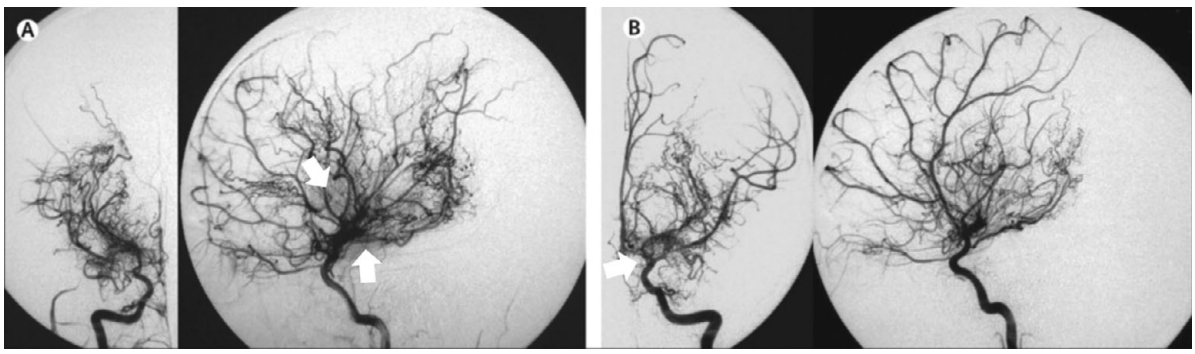

Figure 38.1 Cerebral angiogram of the right internal carotid artery (A) and left internal carotid artery (B) showing the classic Moyamoya vessels "puffs of smoke" (arrows). Reproduced from: *Lancet Neurol.* 2008 Nov;7(11):1056–66 with permission of Elsevier.

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What Are the Available Medical Therapies for MMD?

Most patients with MMD benefit from medical therapy for symptom relief. However, nearly all patients have disease progression and ultimately require surgical intervention. Medical management includes: calcium channel blockers (nimodipine or nicardipine), antiplatelet agents (aspirin or ticlopidine), and coagulation modifiers such as pentoxifylline. Patients experiencing seizures can be placed on anticonvulsant therapy.

What Are the Available Surgical Therapies for MMD?

There are many variations of surgical interventions aimed to revascularize areas of decreased cerebral perfusion that have shown subsequent ischemia and recurrent cerebral ischemic events. These procedures are generally focused on increasing collateral blood flow, or directly or indirectly bypassing the occluded areas. Up to 87% of surgical patients can obtain systemic benefits and relief from surgical intervention.

Access to the surgical field is obtained through the removal of dural flaps, craniotomy, or via burr holes. Variables in surgical procedure choice can be patient age, comorbidities, signs and symptoms, and surgeon preference and experience.

What Are the Major Anesthetic Considerations for Patients with MMD?

Preoperatively, detailed examination should be performed with attention to neurological deficits including frequency of ischemic attacks that may alert the provider to the extent of compromise of the cerebral vasculature. A reliable baseline blood pressure reading should be assessed. Routine laboratory examinations including CBC, electrolytes, coagulation studies, and type-and-screen should follow the same protocol as for craniotomies. Calcium-channel blockers or antiseizure medications should be continued until the day of surgery. Low dose aspirin may be continued perioperatively or stopped according to hospital or surgical guidelines, whereby then some facilities replace aspirin therapy with low molecular weight heparin.

Table 38.3 Common surgical procedures for Moyamoya disease

Direct bypass techniques	Most commonly done with a superficial temporal artery (STA) to middle cerebral artery (MCA) bypass. This procedure provides immediate increase in blood flow to ischemic brain, usually done in adults, and is technically difficult to conduct in children.
Encephaloduroarteriosynangiosis (EDAS)	Preferred indirect revascularization procedure in which the STA is mobilized and anastomosed to the edges of the opened dura. This is usually done in children but in adults is combined with STA-MCA bypass technique
Pial synangiosis	A modification of EDAS in which the surface of the dura is exposed and the pial surface is increased by opening it into multiple flaps to increase collateral vessel development from the dural vessels. A branch of the STA is sutured directly into the pial surface. Results from studies indicate majority of pediatric patients have significant halting of disease progression
Encephalomyosynangiosis (EMS)	An indirect revascularization procedure in which temporalis muscle is attached to the surface of the brain to promote collateral vessel formation
Encephaloduroarteriomyosynangiosis (EDAMS)	Combination of EDAS and EMS. Dural flaps created are folded into the dural/epi-arachnoid space with middle meningeal artery promoting angiogenesis. Neovascularization reported in 50–90% cases in different studies. Incidence of postoperative strokes is reduced when combined with STA–MCA bypass
Combination procedures	Encephalomyoarteriosynangiosis (EMAS), a combination of EDAS and EMS; encephaloduromyoarteriopericranial synangiosis
Other surgical procedures	Craniotomy with dural inversion, cervical sympathectomy, and omental transposition

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Preoperative intravenous access should be obtained when possible, avoiding pain and anxiety with the use of topical local anesthetic spray or creams, along with adequate oral premed to reduce anxiety. Prehydration with at least 20 cc/kg of crystalloid should be administered.

Premedication for sedation to decrease stress or crying is a consideration, as both can cause hyperventilation, decreasing cerebral blood flow due to hypocapnia, and can subsequently increase ischemic risk. The premedication should be adequate, but not excessive, as hypoventilation and hypercarbia will increase ischemic risk.

Anesthetic management must focus on maintaining cerebral perfusion and oxygen delivery throughout the perioperative period. The anesthesia goals for patients with MMD include:

- Maintaining a balance between cerebral oxygen supply and demand
- Maintaining normotension/avoiding hypotension (MAP at or above patient's baseline)
- Maintaining normocarbia or mild hypocarbia
- Maintaining normovolemia
- Avoiding hyperviscosity
- Avoiding anemia (Hct below 30%)
- Maintaining normothermia or mild hypothermia
- Avoidance of preoperative anxiety/stress
- Avoidance of postoperative pain (without causing hypoventilation)

What Are the Effects of Commonly Used Anesthetics on Cerebral Blood Flow (CBF) and Metabolic Rate ($CMRO_2$)?

While most agents have been used successfully in patients with MMD, it is most critical to avoid uncontrolled swings of blood pressure while being mindful of the various effects of agents on CBF and $CMRO_2$ as stated in Table 38.4.

Table 38.4 Effects of anesthetics on cerebral blood flow and metabolic rate; NC=no change

Anesthetic agent	Cerebral blood flow (CBF)	Cerebral metabolic rate ($CMRO_2$)
Volatile agents	⇧	⇩
Nitrous oxide	⇧	⇧/NC
IV anesthetics (propofol)	⇩	⇩
Ketamine	⇧	⇧
Dexmedetomidine	⇩	⇩
Opioids	NC	NC

Monitoring includes standard ASA monitors in addition to arterial blood pressure, urinary catheter and central body temperature. Transcranial EEG, near-infrared spectroscopy (NIRS), somatosensory evoked potentials (SEP), and transcranial Doppler (TCD) are useful for monitoring cerebral ischemia and are institution specific.

Mild hypothermia can offer some degree of neuroprotection by reducing the cerebral metabolic rate; however, there is not sufficient evidence to secure this as an evidence-based practice. Conversely, hyperthermia increases oxygen consumption and demand and can increase risk for ischemia. Normothermia is most often the goal for body temperature to avoid any cerebral vascular spasm that could occur from a hypothermic state, which could decrease flow in the brain. Heating blankets, underbody fluid mat systems, and fluid warmers can be used perioperatively to raise or lower body temperature.

Blood pressure should be maintained at or slightly above the baseline preoperative blood pressure perioperatively to avoid decrease in cerebral blood flow and cerebral perfusion pressure. Regional anesthesia in the form of a skull block may be considered with the theoretical risk of causing cerebral steal from regional vasodilation.

What Is the Risk of Cerebral Steal in MMD Surgery?

Collateral vessels in patients with MMD lack typical responses to CO_2. Thus, normal vessels with intact CO_2 activity will dilate with hypercarbia and potentially "steal" or shunt blood flow from collateral vessels. On the contrary, collateral vessels lack the ability to dilate with hypercarbia and are unable to increase blood flow to areas supplied by these vessels by altering CO_2. The baseline $PaCO_2/EtCO_2$ should be maintained to minimize steal or diversion away from the collaterals.

Complications during surgical interventions may include: blood pressure lability, seizures, and symptomatic postoperative hyper-perfusion injury (re-perfusion injury). Perioperative risks can involve varied ischemic

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neurological events, transient ischemic attacks (TIAs) or strokes, intracranial hemorrhage, or infection.

What Are the Important Postoperative Considerations in Patients with MMD?

Sedation and adequate pain control should be used to avoid crying, hyperventilation, and stress responses. In children, parental presence can be beneficial.

Pain control is crucial as pain is associated with an increase in cerebral metabolism as inadequate analgesia increases $CMRO_2$ and CBF. Patients are at high risk for postoperative cerebral infarction necessitating close monitoring, usually best accomplished by ICU admission. Postoperative opioid administration such as morphine can be titrated with keen observation to avoid hypoventilation. Neurological status must be assessed and intervened upon if abrupt changes occur. Appropriate nonopioid pain adjuncts should be considered.

After revascularization procedures, months are required to develop the necessary "bypass" collaterals and medical management should continue during this time to avoid complications, especially aspirin therapy.

Suggested Reading

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