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*Case Report*

# Perioperative care of the pediatric patient for pial synangiosis surgery

Matthew DiGiusto[1], Tarun Bhalla[2], Ronald Grondin[3], Joseph D Tobias[2]

*[1]The Ohio State School of Medicine, Columbus, Ohio; [2]Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital and the Ohio State University, Columbus, Ohio; [3]Department of Neurosurgery, Nationwide Children's Hospital, Columbus, Ohio*

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**Abstract:** Moyamoya disease (MMD) is a cerebrovascular occlusive disorder which causes recurrent strokes and transient ischemic attacks in children. The arteriopathy of MMD targets the internal carotid arteries (ICA) and their branches resulting in ischemia of the ICA circulation. Small perforator branches of the ICA dilate to provide collateral perfusion to ischemic areas. This small vessel dilatation creates the characteristic angiographic appearance that gives the disease its name ("moyamoya" after the Japanese expression for "something hazy just like a puff of cigarette smoke drifting in the air"). Best medical management involves the prevention of thromboembolic events with antiplatelet agents, maintaining adequate hydration, and avoidance of hyperventilation which can contribute to cerebral vasoconstriction. Presently there are no definitive medical options to halt or correct the process of MMD. Surgical procedures include both direct and indirect revascularization. Direct revascularization involves anastomosis of a branch of the external carotid artery to a branch of the internal carotid artery (STA-MCA bipass). However, indirect procedures are often chosen in the pediatric population due to the technical difficulty of direct procedures related to small diameter blood vessels. Indirect procedures rely on neovascularization, so the increase in cerebral blood flow is delayed beyond the immediate postoperative period. One such indirect procedure is pial synangiosis, which involves suturing the adventitia of the superficial temporal artery to the pial surface of the cerebral cortex after opening of the arachnoid. The authors present two pediatric patients who required anesthetic care for pial synangiosis surgery. The perioperative care of such patients is reviewed and suggestions presented for the intraoperative anesthetic management.

**Keywords:** Perioperative care, pediatric patient, pial synangiosis surgery, Moyamoya disease

## Introduction

Moyamoya disease (MMD) is an arteriopathy of the cerebrovasculature that predisposes patients to thrombotic strokes and transient ischemic attacks (TIAs). It is characterized by a progressive narrowing or stenosis of the intracranial component of the internal carotid arteries as well as the proximal branches of the anterior and middle cerebral arteries [1]. Small perforator branches of the intracranial carotid artery, which supply the optic nerves, pituitary gland, dura, and other skull base structures, dilate to provide collateral perfusion of the ischemic brain distal to the occlusion [2]. These dilated blood vessels create the characteristic angiographic appearance that gives the disease its name. Suzuki and Takaku were the first to coin the term "moyamoya" after the Japanese expression for "something hazy just like a puff of cigarette smoke drifting in the air" to describe the angiographic appearance of these collateral vessels [3]. Although once believed to be specific to the Japanese population, it has more recently been reported in patients of various other ethnic groups.

Although, there are currently no known medical options to halt or correct the process of MMD, antithrombotic agents, such as salicylates, may be used to prevent microthrombi at areas of stenosis [2]. When there are recurrent cerebral ischemic events or reduced perfusion, surgical intervention may be needed. One such surgical option is pial synangiosis, which involves affixing the superficial temporal artery (STA) to the

brain surface after opening of the dura and arachnoid to expose the surface of the cerebral cortex [2]. We present two pediatric patients undergoing pial synangiosis for the treatment of MMD. The perioperative care of such patients is reviewed and suggestions presented for the intraoperative anesthetic management.

## Case reports

Institutional Review Board approval for case reports involving one or two patients is not required by Nationwide Children's Hospital (Columbus, Ohio).

*Patient #1*

The patient was a 7-year old, 22 kg boy with a past medical history significant for trisomy 21, surgical repair of an atrioventricular septal defect (AVSD), and hypothyroidism. MMD was discovered while being treated for multiple episodes of weakness and gait changes that were determined to be related to cerebrovascular events. Radiologic imaging studies revealed MMD bilaterally with occlusion of the internal carotid arteries and tenuous anterior and middle cerebral arteries (Suzuki stage IV). Further evaluation demonstrated the need for operative intervention. Preoperative medications included salicylates, acetaminophen, and levothyroxine. The patient was originally admitted for a right craniotomy for pial synangiosis with possible left craniotomy for pial synangiosis under the same anesthetic; however, the left sided revascularization was postponed due to EEG slowing intraoperatively during the right sided procedure. During the initial procedure, the patient was held *nil per os* for 6 hours and was transported to the operating room where routine American Society of Anesthesiologists' (ASA) monitors were placed. Anesthesia was induced with intravenous propofol (2 mg/kg) and fentanyl (2 μg/kg). Tracheal intubation was facilitated with vecuronium (0.15 mg/kg). Following anesthetic induction and endotracheal intubation, an arterial catheter was placed. Continuous electroencephalograph (EEG) monitoring was performed. Maintenance anesthesia consisted of a sufentanil infusion in doses varying from 0.05 to 0.6 μg/kg/hour and inhaled isoflurane with an exhaled concentration of 0.5-0.7%. Ongoing neuromuscular blockade was achieved with intermittent doses of vecuronium titrated according to train-of-four monitoring. Approximately 90 minutes after the start of the procedure, EEG slowing was noted. This correlated with a low mean arterial blood pressure (MAP) into the 50-55 mmHg range. This was treated with the administration of 5% albumin (5 mL/kg) and intermittent doses of phenylephrine (1-2 μg/kg). This resulted in improvement in the MAP to 65-75 mmHg with a subsequent improvement in the EEG findings. Although a bilateral procedure had been planned, given the intraoperative EEG slowing, it was decided to perform the left-sided pial synangiosis at a later date. Residual neuromuscular blockade was reversed with neostigmine and the patient's trachea was extubated. The patient was transported to the postoperative anesthesia care unit (PACU). Postoperatively, analgesia was provided with oral oxycodone (0.05 mg/kg every 4 hours as needed) and intravenous morphine (1.2 mg every 3 hours as needed). The patient was admitted to the Pediatric ICU for monitoring of his mean arterial pressure (MAP) and neurologic status. His postoperative course was unremarkable and he was discharged home on postoperative day 5.

The patient was readmitted the following month for a left-sided craniotomy for pial synangiosis. The patient was held *nil per os* for 6 hours and was transported to the operating room where routine ASA monitors were placed. Anesthesia was induced with intravenous propofol (3 mg/kg) and fentanyl (2 μg/kg). Tracheal intubation was facilitated with rocuronium (1 mg/kg). Following anesthetic induction, an arterial catheter and a left internal jugular central venous catheter were placed. Maintenance anesthesia consisted of a remifentanil infusion in doses varying from 0.05 to 0.3 μg/kg/min and inhaled isoflurane with an exhaled concentration of 0.4-0.8%. Ongoing neuromuscular blockade was achieved with intermittent doses of rocuronium titrated according to train-of-four monitoring. Continuous EEG monitoring was performed and although some minor fluctuations in the EEG were noted, no treatment was required and the EEG remained stable throughout the procedure. The surgical procedure lasted 187 minutes. Estimated blood loss was minimal (less than 30 mL) and intraoperative fluids included 400 mL of lactated Ringer's and 400 mL of normal saline. Following completion of the surgical procedure, residual neuromuscular blockade was reversed with neostigmine

and the patient's trachea was extubated. The patient was transported to the postoperative anesthesia care unit (PACU). As before, analgesia was provided by intermittent, as needed doses of oral oxycodone and intravenous morphine. This was supplemented with fixed interval ketorolac on postoperative day 1. The patient was admitted to the Pediatric ICU for MAP monitoring with a goal of maintaining the MAP ≥ 65 mmHg to maintain the cerebral perfusion pressure (CPP). At one point while the patient was sleeping after a dose of intravenous morphine, the MAP fell to 57 mmHg. The patient was awoken and the MAP increased to 75 mmHg. The remainder of his postoperative course was unremarkable and he was discharged home on postoperative day 5. The patient's first postoperative follow-up was approximately one month later in the stroke clinic. The patient's mother reported that the patient had returned to baseline level of cognitive and motor function. No ischemic events have been reported since the surgery.

*Patient #2*

The patient was a 15-year old, 55 kg male with a past medical history positive for pituitary carcinoma, panhypopituitarism, diabetes insipidus, and multiple TIAs linked to stenosis of the right carotid artery and right middle cerebral artery. Past medical history was pertinent for a history of pituitary carcinoma treated with gamma knife radiation therapy. The patient presented with increasing frequency of TIA's which included the inability to speak, left arm numbness, facial numbness, and hearing loss. Angiography showed a decrease in caliber of the right supraclinoid internal carotid artery consistent with MMD. Initial attempts at medical therapy included acetylsalicylic acid (162 mg by mouth every day) and clopidogrel (75 mg every day). However, no relief of his symptoms was noted and surgical intervention was planned.

The patient was held *nil per os* for 6 hours and was transported to the operating room where routine ASA monitors were placed. Inhalation induction was achieved with increasing concentrations of sevoflurane in nitrous oxide and oxygen. Following anesthetic induction, an 18 gauge intravenous cannula was placed in the right hand. Propofol (2 mg/kg) and fentanyl (2 μg/kg) were administered. Neuromuscular blockade was achieved with rocuronium (1 mg/kg) followed by endotracheal intubation. An arterial catheter and an internal jugular central venous catheter were placed. Maintenance anesthesia consisted of a remifentanil infusion in doses varying from 0.05 to 0.25 μg/kg/min and inhaled isoflurane with an exhaled concentration of 0.5-0.8%. Continuous electroencephalograph (EEG) monitoring was performed. Two hours into the surgical procedure, the neurologist noted EEG slowing. The remifentanil was decreased to 0.05 μg/kg/min to allow the MAP to increase to 65-70 mmHg which resulted in return of the EEG to baseline. At two subsequent points during the surgical procedure, EEG slowing was treated with incremental doses of phenylephrine (1-2 μg/kg) to increase the cerebral perfusion pressure (CPP). Improvement in the EEG signal was noted once the MAP increased above 70 mmHg. Rocuronium was administered in intermittent doses according to train-of-four monitoring. The surgical procedure lasted 285 minutes. Estimated blood loss was minimal (less than 30 mL) and intraoperative fluids included 100 mL of lactated Ringer's and 200 mL of normal saline. Following completion of the surgical procedure, residual neuromuscular blockade was reversed with neostigmine and the patient's trachea was extubated. The patient was transported to the PACU and then admitted to the Pediatric ICU for postoperative blood pressure monitoring and ongoing assessment of neurologic function. Postoperative analgesia was provided by intravenous morphine (2 mg every 2 hours as needed) for the first 2 postoperative days. This was transitioned to fixed interval ketorolac (15 mg every 6 hours) with as needed doses of oral oxycodone. The patient experienced several episodes of speech difficulties within the first two postoperative days, but they were unrelated to changes in the MAP. The remainder of his postoperative course was unremarkable and he was discharged home on postoperative day 8. He was readmitted two days later to the Pediatric ICU with left facial numbness, facial droop, and slurred speech. Symptoms were consistent with a TIA and confirmed with an MRI that showed increased stenosis of the supraclinoid ICA. The symptoms resolved without intervention. Laboratory evaluation was unremarkable except for a low serum sodium (130 mEq/L) which was treated

by holding his usual dose of intranasal antidiuretic hormone (desmopressin). In addition to his usual daily dose of clopidogrel, low dose acetyl salicylic acid was started. The patient was again readmitted one month later with a chief complaint of difficulty speaking. At that time, the patient's TIA's were attributed to a low hemoglobin value (8.8 gm/dL) related to bone marrow suppression from his cancer treatment course. The patient was subsequently transfused to maintain a hemoglobin value ≥ 12 g/dL and no additional TIA's have been reported since that time.

## Discussion

MMD is a specific arteriopathy that affects the ICA while sparing the external carotid artery (ECA) [1]. MMD takes on a natural progression through stages that includes worsening stenosis of the ICA and an increase in the formation collateral vessels. Despite the formation of collateral blood flow, ischemia occurs distal to the area of involvement of the ICA. As first described by Suzuki, there are 6 stages of MMD, based on angiographic findings [3]. Stage I of MMD is a narrowing of the carotid fork with no other abnormalities. Stage II includes dilation and enlargement of the intracerebral main arteries at the base of the brain. Stage III includes the development of the classic angiographic pattern. The anterior and middle cerebral arteries begin to disappear from the angiogram and are instead replaced by moyamoya vessels or tiny collateral vessels that cause the angiogram to look like a puff of smoke. Stage IV includes occlusion of the ICA as far as the posterior communicating artery, causing the disappearance of the posterior cerebral artery. In this stage, the moyamoya vessels begin to minimize and collateral vessels from the scalp begin to form. Stage V includes significant occlusion of the ICA, minimization of moyamoya vessels and increased growth of collateral vessels from the ECA. Stage VI, the terminal stage in MMD, includes marked complete occlusion of the ICA and the disappearance of moyamoya vessel. Perfusion of the brain is provided only by collaterals from the ECA or vertebral arteries.

Various surgical procedures have been adopted for the treatment of MMD including direct and indirect revascularization. In direct revascularization, a branch of the ECA is directly anastomosed to a branch of the ICA. The most common direct surgical option is the superficial temporal artery-to-middle cerebral artery bypass (STA-MCA). In the event that the STA artery diameter is too small for anastomosis, the occipital artery can be used [4]. A major benefit of direct procedures is the immediate increase in blood flow to the ischemic regions of the brain. However, indirect procedures are not generally chosen in the pediatric population due to the technical difficulty of direct procedures related to the small diameter of the extracranial blood vessels [1].

Indirect procedures rely on neovascularization, so the increase in cerebral blood flow (CBF) is delayed beyond the immediate postoperative period. An advantage of the indirect procedures is that increased blood flow is not restricted to the MCA distribution. Some of the more common indirect procedures include encephalomyosynangiosis (EMS), encephaloduroarteriosynangiosis (EDAS), encephaloduroarteriomyosynangiosis (EDAMS), and the drilling of cranial burr holes. EMS involves removing the arachnoid layer, placing a portion of the temporalis muscle directly over the cerebral cortex followed by the approximation of the dura mater over the muscle [5]. Revascularization occurs following the EMS via angiogenesis of the deep temporal artery. EDAS involves opening the dura, laying the STA onto the exposed cortical surface, and suturing a galeal cuff with the STA to the dura [5]. EDAMS entails placing the temporalis muscle, a portion of the STA, and a segment of the galeal flap over the cortex. Dural inversion is another indirect procedure that involves rotating a large flap of dura so that the periosteal surface of the dura is in direct contact with the cortical surface of the brain [6]. The dural flap is pedicled based on the middle meningeal artery, thereby recruiting the middle meningeal artery circulation for revascularization.

Multiple cranial burr holes may be used as an adjunct to these revascularization procedures. After the burr hole is placed, the underlying meninges are opened, and a pericranial flap is placed in contact with the cortex. Cranial burr holes are helpful as an adjunct because they can revascularize areas supplied by the anterior and posterior cerebral arteries, territories of perfusion often missed by both indirect and direct revascularization methods [5]. More recently, pial synangiosis, a modification of the

indirect EDAS procedure, has been introduced. The technical modification in this procedure is removal of the arachnoid in the region of the dural opening. The arachnoid is removed as it has been theorized that it may serve as a barrier to the ingrowth of vessels [7]. After opening of the arachnoid layer, the adventitia of the STA can be sutured directly to the pial surface.

The specific perioperative concerns of such patients includes co-morbidities related to the disease itself, the basic tenets of anesthetic care for a craniotomy, as well as the specific issues presented by the surgical procedure including continuous EEG monitoring (see below) [8]. In general, patients with MMD will have areas with decreased cerebral perfusion related to the disease process. As such, the anesthetic regimen should maintain the appropriate depth of anesthesia while minimizing hemodynamic effects and hence decreases in CPP and CBF. Hemodynamic depression may occur throughout the anesthetic care, but is most likely to occur during anesthetic induction. Given that our patients were free of co-morbid cardiovascular disease, we chose to use a combination of propofol and fentanyl in our first patient while an inhalation induction with sevoflurane was used in our second patient. This was supplemented with propofol and fentanyl once intravenous access was achieved. Although propofol may decrease blood pressure [8], it also decreases the cerebral metabolic rate for oxygen ($CMRO_2$) thereby providing some degree of cerebral protection [9, 10]. In the event that hypotension occurs following anesthetic induction propofol, the administration of the direct acting α-adrenergic agonist, phenylephrine (1-2 μg/kg), is generally effective in quickly increasing the MAP and restoring the CPP. Alternatively, especially in patients with co-morbid cardiovascular disease, etomidate may be used for anesthetic induction. While etomidate effects on $CMRO_2$ and intracranial pressure (ICP) are similar to those of propofol, it generally has minimal effects on cardiac function and MAP thereby maintaining or increasing CPP [11-14].

Choice of neuromuscular blocking agent for anesthetic induction and maintenance is important to ensure limited effects on cerebral dynamics. Succinylcholine has been shown to increase ICP and cause histamine release, which may decrease MAP and further decrease MAP [15, 16]. A neuromuscular blocking agent with minimal hemodynamic effects and limited histamine release is recommended for neuromuscular blockade during surgery. Both rocuronium and vecuronium have been shown to have minimal effects on ICP, MAP and CPP as well as limited histamine release [16, 17]. Given the need for prompt postoperative neurologic evaluation, the anesthetic should be planned to allow for early tracheal extubation including the use of train-of-four monitoring. Likewise, the agents for maintenance anesthesia should allow for easy titration, have limited effects on MAP, ICP and CPP while providing rapid recovery. Short acting agents such as remifentanil which can be rapidly titrated by intravenous infusion to provide a stable plane of anesthesia with a rapid dissipation of effects once the procedure is completed and the infusion is discontinued appear to offer advantages over longer acting opioids. The intense analgesia provided by remifentanil also decreases the requirements for inhaled volatile agents (approximately 1 minimum alveolar concentration of isoflurane in our patients) thereby limiting the effects on ICP, limiting the possibility of intracerebral steal, and allowing for rapid awakening. Cerebral vasodilators may result in intracerebral steal in patients with moyamoya disease as vasodilatation occurs only in the normal vasculature resulting in shunting of blood away from the ischemic area [18]. Although we chose to use isoflurane in a concentration ≤ 1 MAC, others have suggested that a total intravenous anesthetic technique is preferred [19].

Although a time-honored therapy for neurosurgical anesthesia includes mild hypocarbia to decrease ICP, potential adverse effects related to intraoperative hypocarbia including decreases in CBF have led to changes in practice both intraoperatively and in the ICU [20-22]. These may be of more clinical significance in patients with decreased CBF related to ischemic disease processes. Hyperventilation and the resultant hypocarbia alter the EEG in patients with MMD due to cerebral vessel constriction and decrease in CBF [23]. A decrease in CBF is also seen with hypercarbia as MMD patients lose the normal CBF response to hypercarbia [24]. Given these concerns, the close control of intraoperative $PaCO_2$ is suggested with adjustment of minute ventilation according to the

end-tidal $CO_2$ as well as intermittent arterial blood gas analysis. In addition to intraoperative $PaCO_2$ control, pre- and postoperative control of $PaCO_2$ may also impact the incidence of TIA's and decreases the postoperative hospital stay [24]. Hyperventilation, which may occur due to crying, can lower $PaCO_2$ and cause cerebral vasoconstriction potentially precipitating an ischemic event. Techniques to reduce postoperative pain and agitation should be implemented to present such issues. However, the benefits of such techniques should be weighed against the risks of respiratory depression. As the latter may be more common when the analgesic technique relies solely on opioids, adjunctive agents such as acetaminophen or non-steroidal anti-inflammatory agents should be considered. In our patients, ketorolac was started during the postoperative period once concerns of bleeding had ceased.

In addition to maintaining normocarbia, it is likewise import to maintain normothermia. Although hypothermia reduces $CMRO_2$ and imparts some degree of neuroprotection, a decrease in body temperature may result in cerebral vasospasm in a patient with MMD resulting in ischemia [26, 27]. Conversely, an increase in body temperature may increase CMRO2 and likewise induce ischemia [28].

In addition to routine ASA monitoring, given the association of hypotension with perioperative ischemic events, invasive arterial pressure monitoring is generally indicated. Placement of a central venous catheter is suggested to allow for central venous pressure monitoring as an indicator of intravascular status. Isotonic fluids are administered for maintenance fluids, to expand intravascular volume, and to replace 3$^{rd}$ space and blood losses. Although we chose to use a combination of crystalloid and colloid in our patients, there is no evidence based medicine to support this practice. Excessive blood loss during surgery along with intraoperative hypovolemia and hypotension are associated with perioperative ischemic events [29].

Both of our patients had intraoperative EEG monitoring to provide early detection of intraoperative decreases in cerebral blood flow and ischemia. Although somewhat non-specific, EEG slowing may be indicative of ischemia thereby alerting the clinician to intervene with strategies to alert either CBF to $CMRO_2$. EEG slowing is a common finding during pial synangiosis, being reported in 45.5% and 66% of cases in two studies [2, 8]. To increase the specificity of EEG slowing, the anesthetic regiment should be tailored to maintain a constant depth of anesthesia as well as a stable $PaCO_2$ as an increased depth of anesthesia or alterations in $PaCO_2$ may also impact the EEG. During the pial synangiosis procedure, slowing is most common when the STA is being sutured to the brain surface. Despite its general acceptance as part of intraoperative monitoring for such procedures, there is no evidence based medicine to demonstrate an improvement in patient outcomes [8].

As previously discussed, there are particular times during pial synangiosis surgery that have been noted as causing transient EEG slowing. It is important to react only when EEG slowing becomes persistent. In the event of EEG slowing, checks should be made to ensure that oxygenation and ventilation are adequate and that there have been no acute changes in intravascular volume related to blood loss. Intraoperative EEG slowing was noted and treated by increasing the MAP with phenylephrine in both of our patients.

Although uncommon, MMD can be seen in patients of various ethnic origins throughout the world. As the disease generally manifests during the first decade of life, pediatric anesthesiologists may be called upon to provide perioperative care for these patients. One of the primary focuses of such care is controlling the balance between cerebral oxygen delivery and requirements by regulating CPP, ICP and $CMRO_2$. During perioperative care normal homeostatic parameters of $PaCO_2$, body temperature, MAP, and intravascular volume should be maintained. Intraoperative hypocarbia, hypercarbia, hypotension, hypovolemia, hyperthermia, and hypothermia have all been identified as potential risk factors for ischemic complications. In particular, hypotension may be particularly harmful [30]. No specific recommendations can be made for specific choices of anesthetic agents, but in general, short-acting and easily titrated agents with limited effects on hemodynamic function are preferable. The tenets of this intraoperative strategy should be carried over into the postoperative period.

**Address correspondence to:** Dr. Joseph D Tobias, Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital, 700 Children's Drive, Columbus, Ohio 43205. Phone: 614-722-4200; Fax: 614-722-4203; E-mail: Joseph.Tobias@Nationwidechildrens.org

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