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Anesthesia in a Moyamoya and myasthenic patientundergoing encephalodural arteriosynangosis

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We report a case of patient with Moyamoya disease and myasthenia gravis who underwent general anesthesia for encephalodural arteriosynangosis (EDAS), designed to promote formation of collateral blood flow to the brain. We are aware of the effects of anesthetics, surgery and perioperative stress response on cerebral hemodynamics and the risk of postoperative respiratory failure. Our patient emerged from general anesthesia without any neurologic deficit. This report may help the clinician on anesthetic consideration for these patients. However, there is patient's variability in each specific clinical setting; thus the decision should based on individual judgement.

Keywords : *Moyamoya, Myasthenia gravis, Encephalodural arteriosynangosis, Anesthesia.*

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กรณีศึกษาผู้ป่วยโรคกล้ามเนื้ออ่อนแรง myasthenia gravis ร่วมกับพบมีภาวะ ผิดปกติในสมองจากความผิดปกติของเส้นเลือดอุดตันของเส้นเลือดแดงใหญ่บริเวณคอทั้งสองข้างส่งผลให้เกิดการสร้างเส้นเลือด collateral ในสมองที่ผิดปกติ เปราะบางและแตกง่ายในสมอง ซึ่งต้องมารับการผ่าตัดทางสมองเพื่อต่อเส้นเลือดไปเลี้ยงสมองส่วนที่ขาดเลือด ในการดมยาสลบในผู้ป่วยรายนี้พบว่ามีความเสี่ยงต่อการเกิดภาวะแทรกซ้อนจากการดมยาสลบ ทั้งจากการดมยาสลบที่ทำให้เกิดภาวะเลือดไปเลี้ยงสมองน้อยลง อาจเป็นเหตุให้เกิดสมองขาดเลือดเพิ่มขึ้น มีภาวะผิดปกติทางระบบประสาทมากขึ้นหลังผ่าตัด รวมทั้งผลจากยาหย่อนกล้ามเนื้อจะมีผลให้เกิดกล้ามเนื้ออ่อนแรงได้นานกว่าคนปกติในโรค myasthenia gravis ทำให้มีปัญหาในการพิจารณาถอดท่อช่วยหายใจหลังผ่าตัด และอาจจำเป็นต้องได้รับการช่วยหายใจต่อหลังผ่าตัดจากผลของยาหย่อนกล้ามเนื้อที่ออกฤทธิ์นานขึ้น อย่างไรก็ตามการดมยาสลบขึ้นกับความรุนแรงของโรคนี้ในผู้ป่วยแต่ละรายต่างกัน การดมยาสลบในผู้ป่วยรายนี้หวังว่าอาจเป็นแนวทางในการพิจารณาดมยาสลบในผู้ป่วยที่มีภาวะเดียวกันนี้

คำสำคัญ : *โมยาโมยา, ระงับความรู้สึก, ต่อเส้นเลือดสมอง*

Moyamoya is a progressive cerebrovascular occlusive disease of the internal carotid arteries and the anterior and middle cerebral arteries that affects children and young adults. Affected patients are pathophysiologically analogous to the patients who have bilateral internal carotid artery stenosis who are at very high risk of neurological complications. [1] Pathologically, the disease causes gradual narrowing of distal internal carotid and basilar arteries, leading to proliferation of penetrating arteries, primarily at the base of the brain. These abnormal dilated vessels are sources of collateral flow to the ischemic brain distal to the stenotic process and produce net-like images on cerebral angiograms. Suzuki and Takaku[2] named the disease moyamoya, which in Japanese means "something hazy, like a puff of cigarette smoke drifting in the air."

This disease occurs primarily in the japanese populations, the chinese and korean populations rank second in the number of case. It is more common in females and there is some evidence of a familial predisposition. Classifically, two distinct age groups are affected; children between 5 and 7 years and young adults in their mid-thirties. The clinical presentation is variable, proximal hemiplegia is common in children, whilst in adult. A sudden loss of consciousness associated with subarachnoid hemorrhage is a more common finding.

The etiology of this disease remains unknown, and so far there is no definitive medical treatment.[3-4] Hence, a number of surgical procedures have been developed since the late 1970s to improve compromised cerebral circulation [5-7] which can be direct – anastomosis (superficial temporal artery-middle cerebral artery bypass; STA-MCA bypass) or indirect anastomosis (encephalo-duralarterio-synangosis ;EDAS). Their effectiveness has been commonly recognized. [8] A surgical procedure called encephalodural arteriosynangosis (EDAS) was first developed and described by Matsushima *et al.*[6] in 1981. It is designed to promote a formation of collateral blood flow to the brain surface by utilizing the propensity of the ischemic brain to attract the in-growth of new blood vessels.

However, variable perioperative complications have been reported in association with the marked advancement in surgical treatment.[9-10]Among these complications perioperative stroke is most detrimental. Since then, preventing stroke has become a major anesthetic challenge in the treatment of patients with the disease, and successful anesthetic management has been reported.[11-14]

Myasthenia gravis is an autoimmune disorder caused by production of autoantibodies against acetylcholine receptors of the muscle endplate. In the process of the disease, the number of activated receptors become insufficient to cause a normal response and with repeated stimulation, hence results in fatigueness. Problems for the anesthetist include: 1. respiratory muscle weakness with the risk of respiratory failure; 2 .bulbar muscle weakness with the risk of pulmonary aspiration; 3. interaction with relaxant drugs, resistance to depolarizing agents, sensitivity to non-depolarizing relaxants.[15] Following surgery, although planned extubation is usually possible, postoperative care in a high-dependency area has been recommended where rapid respiratory support can be instituted if necessary.[16]

Case report

A 51-year-old Thai woman who had been given a diagnosis of myasthenia gravis and diabetes mellitus, three years ago presented with intraventricular hemorrhage from moyamoya disease. Her medication consisted of anticholinesterase agent, pyridostigmine (Mestinon) 60 mg every 3 hour, prednisolone 5 mg daily dose, Azathioprine (Imuran) 50mg daily and diabetic drugs. Because of her first diagnosis of myasthenia gravis, her symptom was weakness of her hands after frequent use of them, mild bilateral ptosis and ophthamoplegia, but without respiratory weakness. After receiving medical treatment, without surgical thymectomy, marked improvement was observed and she could lead normal life. Her blood glucose was also within control.

Two days before admission, she had a severe headache and her left arm was weakened. Her conscious became worse and she developed symptom of nausea and vomiting. However, she made no complains on fatigueness, diplopia or dysphagia. The neurological exam was normal, except motor weakness grade 4 of her arms. There was no bulbar palsy or facial weakness. The angiography showed a narrowing of cavernous, para and supraclinoid portion of bilateral internal carotid arteries with subsequent near total occlusion at C1 segment. There were numerous neovascular collateral vessels of supraclinoid internal carotid arteries. She was listed for elective STA-MCA anastomosis with EDAS.

On the day of operation she received her usual morning mestinon dose and she arrived at the operative theatre in the afternoon. Her muscle power decreased slightly before the start of anesthesia but the respiratory strength was quite good. Anesthesia was induced with thiopental 5 mg/kg and sevoflurane, and fentanyl 2 mcg/kg to blunt hemodynamic response to intubation. The intubation was performed without difficulty at the first attempt with endotracheal tube 7.5 mm and her conditions were evaluated as unacceptable (jaw relaxation complete, laryngoscopy easy, vocal cords open, but coughing, no movement). Anesthesia was maintained with 1-2 % isoflurane in 66 % nitrous oixide and 33 % oxygen to maintain normocarbia and intermittent dose of intravenous fentanyl. Controlled ventilation was adjusted. Neuromuscular blockade was monitored train-of-four (TOF). Her electrocardiogram, oxygen saturation, esophageal stethoscopy, body temperature, ETCO2 noninvasive and invasive arterial blood pressure, central venous pressure were monitored throughout the anesthesia with no abnormality. Spontaneous breathing resumed after induction. TOF was 4/4, atracurium was titrated and continuously infused 0.3 mg/kg/hr to maintain a TOF response of 1/4 -2/4. Fluid deficits were partially replaced by an IV administration of non-glucose containing crystalloid after induction. The depth of anesthesia was controlled to maintain normotension. Ventilation was adjusted to maintain normocarbia by closely measuring arterial CO2 tensions and end-tidal CO2. During intraoperative period, arterial blood was collected at least twice to measure blood gas tensions, serum electrolytes, blood glucose concentration, hematocrit.

After 4 hours of anesthesia atracurium infusion was stopped. According to surgical techniques, the neurosurgeon could perform only right EDAS. Above all, after considering the conflicting risks of prolonged

neuromuscular blockade and the potential risk of aspiration, muscle relaxant was not antagonized, the endotracheal tube was not extubated. The patient was transferred to the intensive care unit.

The patient received her second operation for elective left EDAS 20 days later. We decided not to give pyridostigmine in the morning of the surgery cause last time in the first operation showing her muscle power being full all over the time of surgery and in postoperative period. Neuromuscular transmission was monitored after thiopental 5 mg/kg and fentanyl 2mcg/kg induction by electromyography. The ulnar nerve was stimulated supromaximally at the wrist and the resulting EMG response of the adductor pollicis muscle was displayed. The monitor used the train-of-four (TOF). The EMG monitor showed a 20 % decrease of T1/C ratio when 0.02 mg/kg cisatracurium was injected intravenously. The trachea was intubated with a 7.5 mm endotracheal tube. Anesthesia was maintained by isoflurane 1.5 % in 2 L 70 % N2O:O2. Titrated administration of cisatracurium was carried on until it produced complete neuromuscular block, and no twitching response was recorded during the following 45 min. Complete recovery of neuromuscular transmission, as evidenced by a T4/T1 ratio of 1.0 which appeared before isoflurane was turned off. The operation was complete. Following the recovery of neuromuscular function, all anesthetics was discontinued a mixture of 0.025mg/kg neostigmine and 0.01mg/kg atropine was then administered. The patient became conscious, resumed adequate spontaneous respiration and the trachea was extubated. The postoperative course showed a marked improvement in muscle power.

Discussion

Several aspects of anesthetic management of patients with moyamoya disease are controversial. Anesthetic techniques reported to be suitable for patients with this disease vary. Soriano *et al.*[11] advocated nitrous/fentanyl-based anesthesia with supplement isoflurane, and we also prefer this method at present, because the combination provides a stable hemodynamic state. Furthermore, isoflurane has cerebral protective effects during transient cerebral ischemia in adults undergoing carotid endarterectomy.[16]

Anesthetic management of moyamoya should focus on the maintenance of adequate cerebral blood flow. This can be accomplished by minimal interference with cerebrovascular resistance and maintaining the cerebral perfusion pressure to ensure adequate cerebral oxygenation.

Carbon dioxide is a potent modulator of cerebrovascular tone, and its intraoperative management has been considered an essential part of anesthesia practice for moyamoya disease.
Several studies have recently suggested that either hypo- or hyper-capnia causes harmful response in patients with the disease.

While hypocapnia cause vasoconstriction leading to cerebral hypoperfusion, hypercapnia can result in" intracerebral steal" effect. Cerebral vasodilatation in the region with relatively preserved carbondioxide reactivity could diurt blood away from regions with impaired carbondioxide reactivity.

Given the pathophysiologic processes inherent in moyamoya syndrome, there are several factors that can minimize neurological morbidity

during intraoperative management. The optimal management of cerebrovascular disease is dependent on balancing CMRO2 and CBF. Therefore, a level of anesthesia should decrease the relatively high CMRO2 while maintaining adequate CBF. Factors that increase CMRO2, such as painful stimuli (laryngoscopy, tracheal intubation, and surgical incision), should be minimized by the adequate levels of anesthesia. To ensure adequate CBF, we avoided intraoperative hypotension during the early part of the surgical procedure and by utilizing a balanced anesthesia. Halogenated anesthetics produce a dose dependent decrease in peripheral vascular resistance and cerebral vascular tone.

During her preoperative visit, her MG was well controlled. The premedication consisted of her usual dose of pyridostigmine; and her time to the operation room was set in the afternoon. A recent report found sevoflurane was suitable as a sole anesthetic agent for a myasthenid undergoing sternal-split thymectomy. This implies that sevoflurane alone provides adequate muscle relaxation.[17] Sevoflurane appears to suppress neuromuscular transmission to the same degree as isoflurane, although in one myasthenic patient the sensitivity was much greater (>85 % T1 suppression). Anesthetic managements consisting of barbiturates and propofol for myasthenic patients without untoward effects have been described. [18-19]

Opioid analgesics in therapeutic concentrations did not appear to suppress the neuromuscular transmission in myasthenic muscle. [20] However, central respiratory depression may be a problem with opioids. The introduction of a short-acting opioid makes these drugs more titratable in myasthenic patients.

On the first operation intubation was done successfully by deep sevoflurane anesthesia, and fentanyl was used to blunt the reflex to laryngoscope and intubate. Neuromuscular blocking drugs act by interrupting neuromuscular transmission at the level of the nicotinic acetylcholine receptors at the motor end plate. Their modes of action were classified as antagonist (non-depolarzing) or agonist (depolarizing), both produce blockade.[21] Myasthenic patients are typically sensitive to non-depolarizing neuromuscular blockers. The use of a small dose for priming or defasciculation was therefore not appropriate, because it might result in the loss of airway protection or respiratory distress. Sensitivity to non-depolarizing agents was described in patients with minimal disease (i.e., ocular symptoms only)[22], in those in apparent remission[23], or those with sub-clinical undiagnosed myasthenia.[24] Long-acting muscle relaxants should be best avoided in these patients. Intermediate and short-acting non-depolarizing agents could be used with careful monitoring of neuromuscular transmission. Wide variability in requirements was also noted for atracurium.[25] The ED95 was 58 % (0.14mg/kg *vs.* 0.24mg/kg) of the value for normal patients.[26] Similarly, myasthenic patients are sensitive to cisatracurium, evidenced by a more rapid onset and more marked neuromuscular block compared to control patients. Recovery was prolonged in a patient receiving pyridostigmine.[27] It should therefore be used with caution in patients receiving pyridostigmine in the morning of surgery. Several general anesthetic techniques have been proposed, although none has been proven to be superior to the others. Some prefer to avoid muscle relaxants altogether and use potent

inhaled agents both for facilitating tracheal intubation and providing relaxation for surgery. These agents allow neuromuscular transmission to recover, with rapid elimination of these agents at the end of surgery. The marked sensitivity of this myasthenic patient to small dose of atracurium and cisatracurium compared to normal patients may be a normal variation response of myasthenic patients to muscle relaxants.

Many commonly use drugs that affect neuromuscular transmission to a small degree. In normal patients, this is usually of no clinical significance. In myasthenic patients, upon emergence from anesthesia and surgery, the interaction of these drugs with residual anesthetic effect and the disease state of MG may be more significant. Corticosteroids, although used in the treatment of MG, may also exacerbate MG.[28] Corticosteroids have not been shown to affect the dose-response to succinylcholine, but they have been shown to decrease the dose requirements for non-depolarizing relaxants in myasthenics.[29]

There have been several attempts to predict the need for postoperative ventilation.[30-32] Based on the preoperative condition of the patient, the surgical procedure, and the residual anesthetic effects, a carefully planned extubation may be carried out in most patients. Adequate postoperative pain control, pulmonary toilet, and the avoidance of drugs that interfere with neuromuscular transmission will facilitate tracheal extubation. All patients with MG should be closely monitored postoperatively in the postanesthetic care unit or surgical intensive care unit, where respiratory support can be immediately reinstituted. Weakness after surgery presents a special problem. The diagnosis includes myasthenic crisis, residual effects of anesthetics, non-anesthetics interfering with neuromuscular transmission and cholinergic crisis.

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