A six year old girl with Trisomy 21, Moyamoya disease, and history of thyroid storm for total thyroidectomy

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Objectives

At the end of this PBLD, participants should be able to …

1. Discuss the anesthetic implications for a patient with Moyamoya disease.
2. Discuss the anesthetic implications for a patient with hyperthyroidism and thyrotoxicosis.
3. Demonstrate appropriate preoperative anesthesia assessment, intraoperative management, and post-operative care in a patient with Trisomy 21 and concurrent Moyamoya disease and hyperthyroidism.

Introduction

The patient is a six-year-old, 28 kg female with a past medical history significant for Trisomy 21 and Graves disease who presents with viral pneumonitis and thyroid storm. She develops a left sided simple partial seizure followed by residual left arm and leg weakness. Her clinical course deteriorates to respiratory failure requiring emergent intubation and ventilatory management. Evaluation of left sided hemiparesis includes CT angiogram and MRI. The studies confirm presence of bilateral frontal strokes and radiological evidence consistent with Moyamoya disease. Her acute episode of thyroid storm is successfully managed by Endocrinology but they feel a total thyroidectomy would be in her best interest as her Graves disease is very difficult to manage medically. Pediatric Surgery and Neurosurgery have been consulted regarding surgical options and surgical timing of their respective cases. Pediatric Anesthesia has been consulted to participate in the discussion of surgical timing. As the Pediatric Anesthesiologist, you need to prepare a safe anesthetic plan for a patient with Trisomy 21, Moyamoya disease, and post thyroid storm for total thyroidectomy.

Case Presentation

Upon her initial presentation for viral pneumonitis, the patient also has clinical evidence of hyperthyroidism. Prior to her admission, she has been clinically euthyroid on methimazole. Physical exam findings include: heart rate 150 BPM, temperature 40.2 ° Celsius, and a thyroid gland that is not enlarged. Her thyroid lab values are as follows: TSH = 0.05 (normal 0.50-4.50 mLU/L), free T4 = 4.9 (normal 0.8 – 2.0 ng/dL), thyroid stimulating Ig (TSI) = 306% (normal < 140% baseline). Shortly after admission, she develops a left sided simple partial seizure followed by left arm and leg weakness. Her clinical course quickly deteriorates to respiratory failure requiring emergent intubation and ventilatory management.

What is thyroid storm?

What is the treatment for thyroid storm?

Evaluation of left sided hemiparesis includes CT angiogram and MRI. The studies confirm presence of bilateral frontal strokes and radiological evidence consistent with Moyamoya disease.

What is Moyamoya disease?

What radiological findings do you expect to see in a patient with this diagnosis?

Why are children with Trisomy 21 more predisposed to Moyamoya disease?

How does the treatment of thyroid storm change with the diagnosis of Moyamoya disease?

What are the medical and surgical treatment options for Moyamoya disease?

The Endocrinology service has successfully managed her acute episode of thyroid storm and feels that her Graves disease is difficult to medically manage. Pediatric Surgery is consulted for total thyroidectomy. Neurosurgery is also consulted to evaluate the patient for revascularization for her Moyamoya disease. They recommend maintaining the patient's blood pressure in a systolic range of 120-140. Pediatric Anesthesia has been consulted to offer their opinion regarding the timing of these surgeries.

Is she a candidate for radioactive iodine therapy?

Which surgery do you think should be performed first, revascularization or total thyroidectomy, and why?

The consensus was to proceed with total thyroidectomy first.

What preoperative labs, studies would you like to see before anesthetizing this patient?

The patient has been medically optimized. After six weeks of rehabilitation, she has return of left leg function but some residual left arm weakness. Pre-operative vitals include: Temp 37.0 ° Celsius, Pulse 128, RR 20, BP 101/80, SpO_2 99%. Free T4 is within normal limits. Cervical extension and flexion films have been obtained.

How will you position the patient considering her diagnosis of Trisomy 21 for a total thyroidectomy?

What ASA monitors are imperative in this situation? Are there any other monitors that you would like to use in caring for this patient?

What are the intra-operative blood pressure goals for this patient? How will you manage her hemodynamics?

The patient cooperates with intravenous line placement. Cerebral oximetry is placed on the patient's forehead. Initial readings are L/R: 45/42. After an uneventful intravenous induction and intubation, a radial arterial line and second peripheral IV are placed. The surgeon says that central venous access is not necessary.

What are your arguments for and against central venous access? Would you do the case without an arterial line?

The central line is not placed and instead the neck is prepped and draped for possible subclavian central venous access.

Do the patient's cerebral oximetry saturations concern you? What are normal cerebral oximetry values? What values would you expect to see in a patient with Moyamoya disease?

How would you like to maintain the patient's anesthesia? What are the anesthetic implications of a patient with Moyamoya disease?

You decide to use an inhalational anesthetic that consists of Sevoflurane and Nitrous.

Is there an advantage of one technique over another anesthetic approach? How do the different agents affect CBF and $CMRO_2$?

In regards to ventilation, what can you do to maximize the patient's CBF? Where would you like to keep your $ETCO_2$?

You decide to keep the patient mildly hypercapnic with an $ETCO_2$ of 40-45. The surgeon wants to maintain systolic blood pressures from 120-140. Her blood pressure is currently 92/59.

What agent would you use to maintain blood pressure in this range? Are there benefits of one agent over another?

You decide to initiate a phenylephrine infusion. Cerebral oximetry now shows L/R: 60/65.

What do you attribute this increase in cerebral perfusion saturations to? Pressor support? Hypercarbia?

The total thyroidectomy proceeds uneventfully. Surgical time: 3 hr 30 min, IVF 1000, EBL 10 mL, UOP 300 mL. The patient is reversed and extubated successfully. She is taken to the PACU where her post-operative vitals are: BP 152/71, P 98, RR 24, Temp 36.8 ° Celsius, SpO_2 100%

Are you concerned about the patient's blood pressure? Is the patient at an increased risk of complications because of her hypertension and concurrent Moyamoya disease? Would you treat this blood pressure? If so, with what? Given the patient's intra-operative course, would you recommend that the patient go to the floor or a monitored unit?

Discussion

Trisomy 21, also known as Down's syndrome (DS), is a genetic disorder caused by the presence of all or part of a third copy of chromosome 21. It is one of the most common chromosomal abnormalities in humans and occurs in about 1 in 1000 births. It is characterized by physical growth delays, characteristic facial features, intellectual disabilities and an increased risk of a number of health problems, ranging from cardiac to endocrine to gastrointestinal to immunologic.

Patients with DS are more likely to have issues with their thyroid gland. It has been suggested that there is a lifetime prevalence of approximately 25-30% of thyroid dysfunction in these patients.[3] Hypothyroidism tends to be more common than hyperthyroidism, whether it is congenital or auto-immune in origin.[3] However, thyrotoxicosis, or thyroid storm, can also occur in these individuals.

Thyroid storm is a rare yet potentially life threatening complication of hyperthyroidism. Thyroid storm is also very rare in the pediatric population, with a frequency of 0.1–3.0 per 100,000.[9] It can occur in patients with partially treated hyperthyroidism that experience a precipitating event such as infection (viral pneumonia), surgery, trauma, or discontinuation anti-thyroid medications. It is characterized by high fever (above 40 ° Celsius), tachycardia and arrhythmias (atrial fibrillation), vomiting, diarrhea, tremulousness, and agitation. With late diagnosis, patients can present with hypotension in a stuporous or comatose state. Adult mortality rate for thyroid storm is 10-20%. Thyroid storm must be recognized immediately and treated on *clinical grounds* alone. Laboratory diagnosis cannot usually be obtained in a timely manner. The treatment of thyroid storm requires an intensive care unit setting for close monitoring of vital signs and access to invasive monitoring and inotropic support. Treatment often includes supplemental oxygen, ventilatory support, and intravenous fluids. Dextrose solutions are the preferred intravenous fluids to cope with continuously high metabolic demand. Aggressive fluid management, up to 3-5 L/day, may be indicated for profound GI and insensible losses. Electrolyte abnormalities need to be corrected and cardiac arrhythmias need to be treated. Atrial fibrillation may be refractory to rate control and conversion may not be possible until after anti-thyroid medication has been initiated. It is important to aggressively control hyperthermia by applying ice packs and cooling blankets and by administering acetaminophen (15 mg/kg orally or rectally every 4 h) to decrease the metabolic demand.

The goals of emergent medical therapy are:

- Inhibition of thyroid hormone synthesis
- Blocking hormone release
- Preventing peripheral conversion of T4 to T3
- Blockade of peripheral effects of overstimulation
- Aggressive treatment of the precipitating event

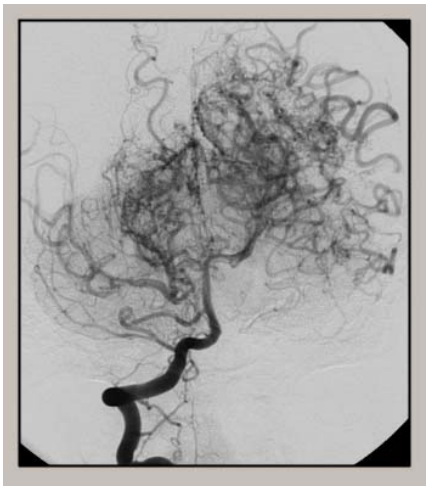
Anti-thyroid medication such as propylthiouracil (PTU) and methimazole (MMI) oppose synthesis of T4. Propylthiouracil (PTU) is preferred because of its early onset of action and capacity to inhibit peripheral conversion of T4 to T3. Clinical effects may be seen within an hour after oral administration. Both of these medications are ineffective in blocking the release of preformed thyroxine.

Iodine compounds (Lugol iodine or potassium iodide), either orally or via a nasogastric tube, are administered to block the release of thyroid hormones. Iodine administration is delayed one hour after the loading dose of PTU to prevent the utilization of iodine in the synthesis of new thyroid hormone. Lithium may be used in the iodine allergic patient.

Beta blockade remains the primary treatment for symptomatic thyrotoxicosis. Propranolol is most commonly used and has the added benefit of inhibition of peripheral conversion of T4-T3. Improvement of symptoms may occur within ten minutes. Administration of glucocorticoids can help decrease the peripheral conversion of T4 to T3 as well.

Iodine preparations should be discontinued once the acute phase resolves and the patient becomes afebrile with normalization of cardiac and neurological status. Glucocorticoids should be weaned then stopped and the dose of thioamides adjusted to maintain thyroid function in the normal range. Beta-blockers may be discontinued once thyroid function normalizes. If the patient is given PTU during treatment of thyroid storm, this should be switched to methimazole at the time of discharge unless methimazole is contraindicated. If there is a contraindication for the use of methimazole, alternative methods to treat hyperthyroidism should be considered after discharge, such as radioactive iodine or surgery. However, it is important to note, that radioactive iodine can trigger thyroid storm despite proper medical preparations.[10] Restoration of euthyroid state may take up to eight weeks.

Patients with DS have also been shown to be at an increased risk for concurrent Moyamoya disease.[4] Thyrotoxicosis has also been reported in association with Moyamoya disease.[11] Moyamoya disease is a chronic, occlusive, cerebrovascular disorder involving the circle of Willis of unknown pathogenesis with a prevalence of about 1: 100,000. Mortality rates from Moyamoya are approximately 10% in adults and 4.3% in children. It is characterized by progressive stenosis of the distal internal carotid arteries bilaterally with tortuous arterial collateral vessels. It is the extensive collateralization that gives the "puff of smoke" appearance on direct angiography, as seen in the image below.[13]



There is a bimodal distribution of age of onset, either the 1st decade of life in children or the 3rd or 4th decade of life in women. However, patients with DS tend to be diagnosed later in life. It has been suggested that autoimmune processes and auto-antibodies in Down's patients may be responsible for Moyamoya disease.[4] Unilateral weakness is the most common presentation. Children are more likely to have ischemic events whereas adults have hemorrhagic events more often. Medical treatment of the disease is often disappointing and includes therapies targeted at complications of disease: intracranial hypertension – manage hypertension, stroke – supportive, ischemic stroke – anticoagulation or antiplatelet agents.

Various surgical procedures are used in treatment[5,11,12]:

- Pial synangiosis is the most common operation in children which involves suturing a scalp artery (usually the superficial temporal artery) onto the pial surface of the brain to enhance revascularization
- Superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis
- Encephaloduroarteriosynangiosis (EDAS)
- Encephalodurarteriomyosynangiosis (EDAMS)

In patients with thyroid storm, the use of beta blockers (such as propranolol) as an anti-hypertensive agent is recommended because it blocks the conversion of T4 to T3, while controlling tachycardia and tremors. However, the concurrent reduction in blood pressure can decrease cerebral perfusion pressure, which may lead to ischemic events in a patient with pre-existing Moyamoya disease.

Anesthetic considerations in treating a patient with Moyamoya disease include[7]:

- Maintenance of cerebral blood flow (CBF)
- Normalization of intracranial pressure (ICP)
- Avoidance of cerebral vasoconstriction and vasodilatation
- Maintenance of stable hemodynamics
- Normocarbia (35-45)

Anesthetic agents affect CBF and cerebral metabolic rate of oxygenation ($CMRO_2$) differently. Inhalation agents will increase CBF and decrease $CMRO_2$ whereas propofol increases CBF secondary to vasodilatation of cerebral vasculature and decreases $CMRO_2$. Narcotics have little effect on CBF and $CMRO_2$. Usually a balanced anesthetic with careful hemodynamic monitoring is the best approach in patients with Moyamoya disease. As patients with Moyamoya disease have a propensity for altered cerebral auto-regulation, it has been suggested that cerebral oximetry trends, in addition to standard ASA monitors, can be useful in monitoring patients during revascularization procedures and post-operatively.[6,8] Normal values fall somewhere between 60-80% and depend on the monitor used.

Positioning of a Trisomy 21 patient's neck to avoid extreme extension and less head up position to improve cerebral blood flow should also be considered.

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