Anesthetic Management of a Patient with Argininosuccinate Lyase Deficiency

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INTRODUCTION

Argininosuccinate Lyase (ASL) Deficiency, also known as Argininosuccinic Aciduria (AA), is the result of a mutated or deficient argininosuccinate lyase enzyme. This defective or deficient enzyme leads to inadequate ureagenesis, accumulation of argininosuccinic acid, and deficient endogenous arginine production[1]. Like other urea cycle disorders, this disease is rare, with incidence of approximately 1/70,000. ASL deficiency is passed via autosomal recessive inheritance, and may manifest in one of two forms: neonatal onset disease or a less severe late-onset form[2].

The urea cycle is a hepatic pathway that converts excess nitrogen to urea. Urea is then excreted via renal pathways. Stressors such as sepsis, surgery, fasting, high-protein meal consumption and heavy exercise may all induce catabolic metabolism. If the urea cycle is impaired, nitrogen accumulates in the form of ammonia[2]. Hyperammonemia may be harmful to multiple organ systems, especially the neurocognitive system[3]. Significant hyperammonemia may lead to encephalopathy associated with vomiting, lethargy, seizure, central respiratory depression and death within hours.

Typical procedures needing anesthesia for these patients include ENT, general surgery, dental, CT or MRI. Some children may require liver transplant for recurrent hyperammonemia and/or liver failure.

FIGURES

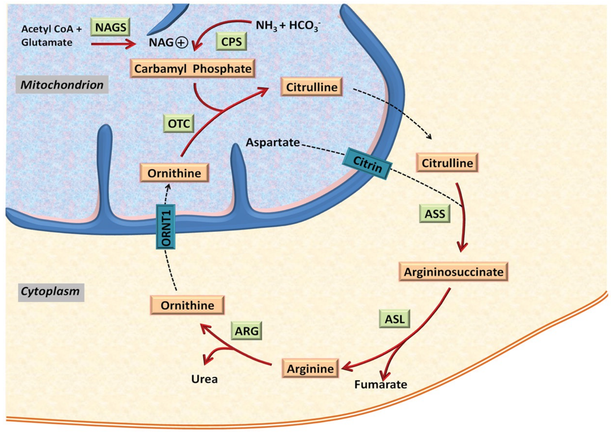

Figure 1. The Urea Cycle[4]

CASE DESCRIPTION

We present the case of a 7-month-old boy with Arginiosuccinate Lyase Deficiency. He was scheduled for bilateral myringotomy tube (BMT) placement to treat severe recurrent otitis media. The patient had been admitted to the hospital with fever and lethargy caused by acute otitis media. ENT evaluated the patient and determined that BMT placement was indicated. Preoperatively, ENT, Clinical Genetics and Anesthesiology coordinated to develop a plan of care for the patient. The patient was made NPO 6 hours prior to surgery. A 10% dextrose-1/2 normal saline solution was started at his maintenance rate. DOS labs were evaluated and demonstrated no signs of metabolic crisis. The patient was scheduled to be the first OR case of that day. The patient was brought to the operating room with his maintenance fluid running. Anesthesia was induced with sevoflurane and 1 mcg/kg IV fentanyl was administered. The patient was maintained with sevoflurane via face mask. Upon completion of the procedure, the patient was awakened in the OR and taken to PACU. PACU course was unremarkable and the patient was discharged to his inpatient unit after tolerating a clear liquid diet, with full feeds resumed that afternoon. The patient was observed for any signs of metabolic crisis and was discharged the following day.

RECOMMENDATIONS

If possible, involve a clinical geneticist in advance for preoperative planning. Surgery should only be carried out in centers prepared to manage acute hyperammonemic decompensations and should not be performed in the outpatient setting. Patients with ASL should be the first scheduled case of the day to minimize fasting for prolonged periods. Ammonia scavenging medication should be continued prior to surgery. The night before surgery, 10% glucose solution with electrolytes should be infused to ensure anabolic metabolism. Pre-op labs should include blood glucose, electrolytes, plasma ammonia, liver function tests, and coagulation studies.

There is insufficient data to support the superiority of any particular anesthetic agent or technique. Induction with sevoflurane, sodium thiopental, isoflurane, propofol and nitrous oxide have all been reported to be safe for induction of anesthesia in other urea cycle disorders. Maintenance with sevoflurane, isoflurane, and nitrous oxide have been safely used in other urea cycle disorders. Midazolam, s-ketamine, fentanyl and morphine in combination with surgical infiltration of ropivicaine have been reported as safe. Pancuronium, atracurium, cisatracurium and vecuronium have been used without prolongation of neuromuscular blockade in other urea cycle disorders. Drugs that induce catabolism such as dexamethasone and other steroids should be avoided[5-7].

RECOMMENDATIONS (CONTINUED)

ENT or dental procedures with potential bleeding into the GI tract should utilize OG tubes and/or throat packs to minimize the amount of blood ingested as this protein load may represent a metabolic stressor leading to decompensation. Hypothermia should be avoided intraoperatively.

Postoperatively, patients should be observed for signs of hyperammonemia in coordination with a clinical geneticist or metabolic physician. Arterial or venous blood gas, electrolytes, and serum ammonia should be evaluated post-operatively every 6 hours during the first 24 hours. These labs should also be checked if the patient experiences signs of metabolic decompensation such as vomiting, lethargy, tachypnea or seizures. Glucose containing IV fluids should be continued until the patient tolerates enteral nutrition. Oral feeds should be resumed as soon as possible to ensure optimal caloric intake and anabolic metabolism.

CONCLUSION

Performing anesthesia on a patient with ASL is a rare occurrence. For this reason, care was closely coordinated with the Genetics team to formulate a plan for pre-op, intra-op, and post-op care for this patient. Patient stressors were minimized by ensuring adequate hydration and lab values pre-op, maintaining normothermia, minimizing pain, and continuing a glucose infusion intra-op, starting enteral feeds soon after surgery, and checking serial labs and vitals post-op. These recommendations were then added to the OrphanAnesthesia online database to benefit other anesthesia providers, as well as their ASL patients[8].

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