

Anesthetic Management of a Female Patient with Ornithine Transcarbamylase Deficiency

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Abstract: Ornithine transcarbamylase deficiency (OTCD) is an X-linked, inherited condition within the urea cycle characterized by failure of ammonia detoxification and urea formation. This may lead to hyperammonemic encephalopathy that, if uncontrolled, results in brain injury and death. Individuals susceptible to this disorder are at risk for hyperammonemic crises if a catabolic state is precipitated. We present an adult female patient with OTCD who underwent L5-S1 transforaminal lumbar interbody fusion. Since the NPO status and the stress of surgery predisposed the body to a catabolic state, the anesthetic management of this patient aimed at avoiding conditions that could stimulate protein catabolism.

Keywords: Ornithine transcarbamylase deficiency, urea cycle disorders, hyperammonemic encephalopathy, anesthetic management

INTRODUCTION

Ornithine transcarbamylase deficiency (OTCD) is an X-linked, inherited condition within the urea cycle characterized by failure of ammonia detoxification and urea formation. Individuals susceptible to this disorder are at risk for hyperammonemic encephalopathy that, if uncontrolled, results in brain injury and death [1]. The hyperammonemic crises can occur if a catabolic state is precipitated. OTCD can present as a severe neonatal-onset disease affecting mostly males or as a late-onset partial disease in males or heterozygous females [1]. Even in asymptomatic patients or in those with mild disease, a hyperammonemic crisis can be precipitated by stress and become a life-threatening event. The perioperative period inherently predisposes the body to a catabolic state due to NPO status in addition to the psychological and physical stress of surgery. This emphasizes the importance of an anesthetic plan maintaining the body within an anabolic state throughout the perioperative period.

We present an adult female patient with OTCD who underwent L5-S1 transforaminal lumbar interbody fusion. The anesthetic management of this patient

aimed at avoiding conditions that could stimulate protein catabolism.

CASE REPORT

A 41 year old female with heterozygous OTCD presented for L5-S1 transforaminal lumbar interbody fusion for the treatment of symptomatic lumbar stenosis. Her OTCD was diagnosed via blood and urine testing after her first born son died shortly after birth. Manifestations of OTCD were absent and her pre-operative blood urea nitrogen level was normal at 8 mcg/dl. She weighed 55 kg, was 163 cm high, and had a Mallampati class 2 airway with limited neck range of motion secondary to two previous uncomplicated C-spine fusions. The anesthetic plan was general anesthesia with endotracheal intubation. Standard American Society of Anesthesiologists' recommended monitors were used (pulse oximetry, electrocardiography, non-invasive blood pressure measurement, temperature measurement, and capnography). Prior to transferring the patient to the operating room hydration was started with intravenous 5% dextrose/lactated ringer's solution, and midazolam 2 mg was given intravenously for sedation. Upon arrival to the operating room cefazolin 1gm was given intravenously and denitrogenation with 100% oxygen

via face mask was completed. Anesthesia induction was accomplished with lidocaine 40mg and propofol 150mg. The patient was easy to ventilate by face mask. Rocuronium 30mg was given for muscle relaxation and the patient was intubated atraumatically with a size 7.5 endotracheal tube. Anesthesia was maintained with desflurane and ventilation was controlled throughout the 3-hour procedure which was performed in the prone position. The patient's temperature was maintained above 36°C with the help of an air-heated blanket (Bair Hugger^R, Augustine, MN, USA). Dexamethasone 10mg was given immediately after induction for anti-nausea prophylaxis, ephedrine (a total of 50mg) was titrated as needed to support the blood pressure, and ondansetron 4mg was given IV shortly before emergence from anesthesia. Fentanyl 450mcg was titrated IV during the case to supplement the desflurane anesthesia. The estimated blood loss was 200 ml and a total of 1500 ml 5% dextrose/lactated ringer's solution was given during the case. At the end of the procedure neuromuscular blockade was successfully reversed and the endotracheal tube was removed once extubation criteria were met. In the post anesthesia care unit (PACU) the patient was kept warm and well hydrated. Her neurologic status was closely monitored and remained stable.

DISCUSSION

Ornithine transcarbamylase deficiency, an X-linked, inherited condition, is the most common urea cycle disorder with an incidence of 1:14,000 live births. It is characterized by failure of citrulline formation [2, 3]. Normally, ornithine transcarbamylase facilitates the synthesis of citrulline from carbamoyl phosphate and ornithine. Citrulline ultimately facilitates ammonia detoxification and urea formation. Consistent elimination of ammonia is important due to the constant ammonia production from cell turnover and the breakdown of protein obtained from diet. Impairment of this enzyme and this reaction leads to hyperammonemia associated with the accumulation of glutamine and carbamoyl phosphate, and to decreased synthesis of citrulline, arginine and urea. This may result in episodes of encephalopathy that can progress to brain injury and death [2, 3]. The most dramatic form of the disease occurs in newborn boys and presents as catastrophic hyperammonemic encephalopathy. Those who survive the neonatal period have poor neurologic outcome with a high incidence of mental retardation, cerebral palsy, and seizures. The late-onset (partial) form of OTCD can present from infancy to later childhood, adolescence, or

adulthood. It can affect males or heterozygous females. Only females may be heterozygous patients and thus carriers. The extent of their symptoms is variable due to the random inactivation of X chromosomes. For all individuals with OTCD, typical neuropsychological complications include developmental delay, learning or intellectual disability, and attention deficit hyperactivity disorder. Even asymptomatic patients are at risk of developing a hyperammonemic crisis in response to stress.

The female patient described is heterozygous for the ornithine transcarbamylase gene deficiency. She never experienced a prior episode of hyperammonemia. Despite being asymptomatic she was still at risk of developing a hyperammonemic crisis during surgery and general anesthesia. Symptoms in such patient may be triggered by infections, physical or psychological stress, and drugs; provoked by trauma, pain and fear, or by episodes of protein catabolism such as during gastrointestinal bleeding, during cancer therapy, in the postpartum period, or as a result of fasting [4]. Drugs to be avoided in these patients are high-dose steroids, valproate and haloperidol [1].

The patient's care was coordinated by a clinical geneticist experienced in the treatment of metabolic diseases whose recommendations were that every effort was made to minimize the risk of catabolism. To achieve that goal adequate sedation was established in the preoperative area, glucose was administered before the start and during the case to prevent protein catabolism, and she was kept warm and well hydrated throughout the case. In view of her normal preoperative ammonia blood level no more interventions were felt to be necessary. Nonetheless, her neurological status was closely monitored in the PACU. In patients with high blood ammonia levels perioperative administration of drugs that increase waste-nitrogen excretion and close monitoring of blood ammonia levels are important.

Our rationale for administering dexamethasone to this patient was that it would be beneficial to minimize the potential stress associate with vomiting. However, this can be criticized in view of the catabolic effect of steroids.

CONCLUSION

Patients with asymptomatic OTCD are at risk of developing hyperammonemic crisis as a result of the

stress of surgery and anesthesia. This complication can be avoided by paying close attention to minimizing perioperative factors that increase the risk of protein catabolism.

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