Shimane J. Med. Sci., Vol.37 pp.61-65, 2020

# Anesthetic Management in an Infant Patient With Carnitine Palmitoyltransferase II Deficiency: A Case Report

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（Received March 30, 2020; Accepted June 8, 2020）

Carnitine palmitoyltransferase（CPT）II deficiency, a very rare inherited disorder of mitochondrial fatty acid oxidation, is characterized by myalgia attacks leading to rhabdomyolysis, hyperkalemia, and acute renal failure. Here, we report an anesthetic management in an infant patient with CPT II deficiency. A 16-month-old child underwent implantation of a totally implantable central venous access device. General anesthesia was performed with sevoflurane, fentanyl, and rocuronium. No complications occurred during the perioperative period. In patients with mitochondrial fatty acid oxidation disorders such as CPT II deficiency, it is important to ensure continuous glucose infusion with blood sugar monitoring. Avoiding drugs associated with rhabdomyolysis and maintaining normothermia are keys for safe anesthetic management.

Key words: carnitine palmitoyltransferase（CPT）II deficiency, anesthetic management, pediatric anesthesia

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## INTRODUCTION

Carnitine and long-chain fatty acids are transported into the mitochondria for beta-oxidation. Carnitine palmitoyltransferase（CPT）II, an enzyme located on the inner mitochondrial membrane, transforms an acylcarnitine into long-chain acyl coenzyme A（CoA）and carnitine. Long-chain acyl-CoA is used for energy production in mitochondrial beta-oxidation. In healthy individuals, energy is produced primarily from glucose produced by gluconeogenesis, secondarily by the β-oxidation of fatty acids, and finally from the decomposition of muscle tissue when there is a decrease in consumption under conditions of stress, such as infections, starvation, excessive exercise, or strong emotion.

CPT II deficiency is classified into three different forms, a lethal neonatal form, a severe infantile hepatocardiomuscular form, and a myopathic form. The lethal neonatal form becomes apparent soon after birth with disorder develop respiratory failure, seizures, liver failure, cardiomyopathy, and arrhythmia. The severe infantile hepatocardiomuscular form produces symptoms hypoketotic hypoglycemia, seizures, hepatomegaly, cardiomyopathy, and arrhythmia. The symptoms usually appear within the first year of life. The myopathic form is mild form, characterized by myalgia attacks, rhabdomyolysis and myoglobinuria［1］. The symptoms set up during childhood or adolescence.

In patients with CPT II deficiency, energy production from fatty acids is impaired; thus, catabolism tends to be accelerated, leading to rhabdomyolysis and hypoglycemia. During the perioperative period, CPT II can be triggered by fasting, infection, cold, emotional stress, and drugs. There have been several case reports describing general anesthesia in adults

with CPT II deficiency [2-4], but only few reports have reported CPT II deficiency in pediatric patients.

Here, we report an anesthetic management in an infant with CPT II deficiency. This study was approved by Shimane University Institutional Committee (3841), and written informed consent was obtained from the child's family.

## CASE DESCRIPTION

The patient was a 16-month-old infant (height: 77 cm and weight: 8.7 kg). When several weeks old, he was diagnosed with CPT II deficiency (a myopathic form) by acylcarnitine analysis and genetic testing, which was conducted because he had a family history of CPT II deficiency. He grew up and developed without any complications caused by taking levocarnitine 90 mg/day by mouth. However, he sometimes exhibited elevated creatine kinase (CK) levels due to fever, hypoglycemia and rhabdomyolysis following upper respiratory infections or acute tonsillitis. Each time any of the infections, the patient was admitted to hospital where he underwent symptomatic therapy, such as rehydration, continuous glucose infusion, and antipyretic drug administration. Consequently, he was hospitalized 17 times by the time he was 16 months old. Because of the difficulty of venous catheter insertion and blood drawing, the implantation of a totally implantable central venous access device was scheduled.

Table 1. Time course of blood test results during perioperative duration

| Characteristics | X-10days | X-4days | X-1day | operation day(X) | X+1day |
|---|---|---|---|---|---|
| WBC (/μL) | 7930 | 5610 | 8560 | | 6290 |
| AST (U/L) | **302** | **77** | | | 29 |
| ALT (U/L) | **59** | **56** | | | 13 |
| BUN (mg/dL) | | 10 | | | 3.8 |
| Cr (mg/dL) | | 0.24 | | | 0.24 |
| CK (U/L) | **13020** | **979** | 88 | | 92 |
| LDH (U/L) | **597** | **526** | | | 319 |
| CRP (mg/dL) | **1.56** | 0.12 | 0.05 | | 0.44 |
| Glucose (mg/dL) | | | | 106 | |

ALT: alanine aminotransferase, AST: aspartate aminotransferase, BUN: blood urea nitrogen, CK: creatine kinase, Cr: creatinine, CRP: C reactive protein, LDH: lactate dehydrogenase, WBC: white blood cell.
Boldface means higher than maximum of normal range.

Eleven days before the surgery, the patient had acute gastroenteritis with fever and vomiting. The following day, he was hospitalized and underwent treatment for rhabdomyolysis caused by hypercatabolism because a blood test showed elevated CK levels with AST and LDH (Table 1). We thought CK was increased also by fever, mild inadequate oral intake. His general condition recovered, and the blood findings showed improvement. Therefore, he was discharged 4 days before the surgery. The day before surgery, he was hospitalized as scheduled without exacerbation, and there were no findings of any other infections or of hypercatabolism. The surgery was therefore performed as scheduled.

Before fasting, we commenced administration rehydration with 10% glucose for the maintenance infusion to prevent hypoglycemia and catabolism caused by carbohydrate shortage. We did not administer any premedication before anesthesia. General anesthesia was induced with thiopental 5 mg/kg, and tracheal intubation was facilitated with fentanyl 3 μg/kg and rocuronium 1 mg/kg. We measured the patient's blood glucose after the intubation with a rapid test kit, which confirmed no hypoglycemia (108 mg/dL).

Anesthesia was maintained with sevoflurane 2.0%–2.5%, and fentanyl was added as necessary (the total amount used was 60 μg). During the anesthesia, the maintenance infusion adjusted to 10% glucose was administered at 40 mL/h (glucose infusion rate, GIR about 0.46 g/kg/hr). The patient's blood pressure and heart rate remained stable. His body temperature was monitored with a rectal thermometer and controlled by a circulation water system; this resulted in good control, without hypo- or hyperthermia, with his temperature maintained at 36.6–37.5°C. There were no circulation, respiratory, or consciousness problems, and no indications of hypoglycemia after extubation, such as tachycardia, sweating, tremor, or a bad mood. Therefore, we did not measure the blood sugar level again and allowed the patient to leave the operating room. The operative time was 78 min and the total anesthesia time was 139 min.

The operation was successful. Throughout the rest of the day, the patient experienced no obvious

Table 2. Selection of anesthetic drugs in patients with Carnitine Palmitoyltransferase II deficiency

| | |
|---|---|
| To be avoided | Propofol, Depolarizing Muscle relaxant, Ibuprofen |
| Careful | **Inhalation anesthetic, Non-depolarizing Muscle relaxant**, Benzodiazepine |
| Safe | **Barbiturate**, **Opioid**, Local anesthetics |

Boldface means drugs used in this case.

pain, postoperative nausea, or vomiting. There were no abnormal blood test findings such as catabolism, so the patient was discharged the day after surgery (Table 1).

## DISCUSSION

In total, there have been more than 350 published case reports of CPT II deficiency worldwide. However, it has an estimated incidence of 1 in 260,000 newborns in Japan. There have been reports of perioperative complications, including an adult who experienced acute renal failure, pregnant women with rhabdomyolysis, and a child who exhibited symptoms suggesting malignant hyperthermia [2-5]. There has been no previous pediatric anesthetic report that focused on blood glucose management.

There are four key factors to take into account during the preoperative and anesthetic management of patients with CPT II deficiency:

First, glycemic control is important for preventing hypoglycemia and catabolism. When patients with CPT II deficiency fast, they are more likely than healthy people to develop hypoglycemia and catabolism. It is therefore essential to minimize the time spent without eating and drinking, and to commence continuous glucose infusion at time of the fasting [6]. During the anesthesia, it is important to monitor blood glucose. If hypoglycemia is observed, 20% glucose infusion 1 mg/kg should be administered and the analgesia, sedation, moisture, and body temperature management should be reviewed to relieve stress. In the present case, management by blood glucose monitoring and an appropriate infusion containing glucose ensured that hypoglycemia was avoided. We did not measure the blood sugar level again after extubation, but we should pay attention about hypoglycemia. Since the symptoms of hypoglycemia do not appear as long as the glucose is supplied to muscles sufficiently even if patient have hypoglycemia [4].

Second, drugs with suspected associations with rhabdomyolysis should be avoided when selecting the anesthetic for patients with CPT II deficiency (Table 2) [2,4]. There are some reports of CPT deficiency patients had adverse events associated with anesthetic agents in perioperative period (Table 3). In the present case, we used barbiturate, opioid, sevoflurane, and rocuronium; these drugs caused no complications. We selected inhalation anesthetic rather than propofol, because propofol may cause rhabdomyolysis [2].

However, Hogan et al. reported a pediatric case in which the patient developed malignant hyperthermia-like symptoms after exposure to succinylcholine and halothane [5]. Inhalation anesthetics and depolarizing muscle relaxants are associated with malignant hyperthermia [7]. On the other hand, Litman et al. showed that CPT II deficiency had little relation to malignant hyperthermia [8]. It is important to pay attention to any symptoms of malignant hyperthermia regardless of whether or not the patient has CPT II deficiency. We also regarded that clear airway and immobilization were necessary for a safe operation. Hence, we chose barbiturate, opioid, sevoflurane, and rocuronium.

Third, temperature management is also important. Hypothermia should be avoided because it triggers shivering [9]. During this short surgical procedure, we maintained normothermia by using a circulation water system.

Fourth, selection of an appropriate day for the surgery is crucial. If the patient has symptoms of upper respiratory infection, it is better to postpone the surgery if possible because this can lead to respiratory complications [10], and the extra stress of complications may accelerate catabolism. In the present case, the patient had a frequent history of

Table 3. Anesthetic drug and adverse event in perioperative period

| author | Age/Sex | diagnosis of CPT II deficiency | disease/operation | anesthetic drugs | adverse events |
|---|---|---|---|---|---|
| Hogan (5) | 4y/F | no | recurrent cerebellar astrocytoma / resection | atropine meperidine thiopental succinylcholine pancuronium halothane nitrous oxide | malignant hyperthermia-like symptoms (tachydysrhythmia, tachypnea, fever, metabolic acidosis, hyperCKemia, myglobinemia) |
| Liker (4) | 30y/F | done | delivery | (epidural anesthesia) lidocaine bupivacaine fentanyl | elevation of CK asymptomatic hypoglycemia |
| Katsuya (3) | 42y/M | no | gastric cancer / gastric resection | thiamylal halothane nitrous oxide succinylcholine | postoperative acute renal failure |
| Nakamura (2) | 42y/M | no | gastric cancer / gastric resection | thiamylal halothane nitrous oxide succinylcholine | postoperative acute renal failure |
| Nakamura (2) | 67y/M (same person above) | done | cancer of residual stomach / resection of the gastric remnant | thiamylal rocuronium remifentanil sevoflurane ropivacaine | none |

CPT: carnitine palmitoyltransferase, CK: creatine kinase, y: year, M: male, F: female

upper respiratory inflammation; however, the surgery was performed on an appropriate day without inflammation. Evaluation of the patient's symptoms, physical findings, and blood test results was helpful for this.

## CONCLUSION

We described here the general anesthesia management for an infant case of CPT II deficiency. The key points for performing safe anesthetic management were a continuous infusion of glucose, not administering any drugs that may cause rhabdomyolysis, the avoidance of hypothermia and hypoglycemia, and the selection of an appropriate day for the anesthesia.

ACKNOWLEDGEMENTS: None.

## CONFLICTS OF INTEREST

We checked ICMJE Form and declare that there is no conflict of interest.

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