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CLINICAL REPORT

Anesthetic case in a child with congenital neuromuscular disease with uniform type 1 fibers (CNMDU1)

Ryu Okutani · Daisuke Arashi · Kenji Tsujii

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Abstract Congenital neuromuscular disease with uniform type 1 fibers (CNMDU1) is an extremely rare, non-progressive, congenital neuromuscular disorder. Although the etiology is unknown, ryanodine receptor gene mutation is reportedly involved. No descriptions of anesthetic practice in patients with this disease have been reported around the world. We report a case of safe perioperative management with general anesthesia, using total intravenous anesthesia, propofol, fentanyl and a non-depolarizing muscle relaxant but avoiding the use of any inhaled anesthetics or depolarizing muscle relaxants to prevent malignant hyperthermia and postoperative respiratory failure, during anesthetic management for cranioplasty for premature synostosis of the cranial sutures in a pediatric patient of CNMDU1.

Keywords Congenital neuromuscular disease with uniform type 1 fibers (CNMDU1) · General anesthesia · Malignant hyperthermia

Introduction

Since the first report of congenital neuromuscular disease with uniform type 1 fibers (CNMDU1), by Oh and Danon [1], fewer than 20 cases have been reported worldwide [1–14], and no reports have described anesthetic practice for this extremely rare congenital neuromuscular disorder. The muscle fibers that form skeletal muscle can be classified into two types based on characteristics. Type 1 fibers are referred to as slow-twitch or red muscle fibers; these have a slower rate of contraction but the ability to contract for longer periods of time. They are activated during continuous motion. Type 2 fibers are referred to as fast-twitch or white muscle fibers, and display a faster rate of contraction along with the ability to instantly produce substantial force.

In normal individuals, type 1 fibers account for $\leq$55% of muscle fibers [13], whereas in CNMDU1, at least 99% are type 1 fibers, resulting in respiratory failure immediately after birth due to respiratory muscle weakness. Symptoms present from infancy, as feeding disorders or delayed growth, but the prognosis is not poor considering the non-progressive nature of the symptoms and mild proximal weakness. This disease is also characterized by normal levels of muscle enzymes, and a definitive diagnosis may be reached on the basis of muscle biopsies [15]. Mutation of the ryanodine receptor gene, a sarcoplasmic reticulum calcium release channel, is reportedly found in about 40% of pediatric patients with CNMDU1 [15]. Given the speculation that ryanodine receptor gene mutation may also be involved in the onset of malignant hyperthermia (MH) [16, 17], sufficient precautions concerning the risk of MH must also be taken during anesthesia in patients with this disease.

We report our experience of anesthetic management during expansion cranioplasty for premature synostosis of the cranial sutures in a pediatric patient diagnosed with CNMDU1.

Case presentation

This 19-month-old boy was 75 cm tall and weighed 7.8 kg. His family history was unremarkable. In terms of current

R. Okutani (✉) · D. Arashi · K. Tsujii
Department of Anesthesiology, Osaka City General Hospital and Children's Hospital, 2-13-22 Miyakojima-hondori, Miyakojima-ku, Osaka, Osaka 534-0021, Japan
e-mail: ryu0909@kcat.zaq.ne.jp

history, the patient was born by vaginal delivery, with unstable respiratory status and floppy infant syndrome since birth, necessitating immediate tracheal intubation followed by mechanical ventilation for about 1 month postnatally. Despite repeated subsequent compromised sputum excretion and aspiration, the patient was able to live while breathing spontaneously. At 1 year old (0 months), at another hospital, the patient underwent orchiopexy under general anesthesia for cryptorchidism, and a muscle biopsy was performed for diagnostic purposes, resulting in a definitive diagnosis of CNMDU1. Surgery was completed rapidly, with no apparent complications from the anesthesia during or after the operation, but the specific details are not known. CNMDU1 continued to be observed, but as premature closure of the anterior fontanelle resulted in pronounced cranial expansion, the patient was referred to our hospital, and cranioplasty was scheduled.

When the patient was admitted, growth and developmental disorders were evident, but no respiratory disorders were present. He was able to eat on his own and pull himself up, and he was capable of meaningful utterances.

Electrocardiography (ECG), chest radiography, hematology, blood biochemistry, and electrolyte tests all yielded normal results. Serum CK levels of 72 IU/L were within the normal range, and all other muscle enzymes (ALT, LDH) were normal.

Anesthesia course

A drip infusion route was prepared preoperatively on the left hand, and fluid therapy was performed. No premedication was used. After the patient had been brought into the operating room, ECG and percutaneous oxygen saturation were monitored. Anesthesia was then induced with propofol 30 mg and fentanyl 10 μg, vecuronium 1 mg was used for muscle relaxation, and the patient was easily intubated (tracheal tube with inner diameter of 3.5 mm). Anesthesia was maintained with oxygen, air, propofol at 5–10 mg/kg/h, continuous intravenous administration of vecuronium at 0.8 mg/kg/h, and intravenous administration of fentanyl as needed. After the induction of anesthesia, an arterial line was established for the direct measurement of invasive blood pressure, and a central venous catheter was placed using a 4-Fr catheter through the right femoral vein.

During the operation, arterial blood pressure and percutaneous oxygen saturation were stable. Body temperature was between 36 and 37°C, heart rate was 80–120 beats/min, and end tidal CO_2 was 32–40 mmHg. Muscles were relaxed, with no findings suggestive of MH, and surgery was concluded uneventfully. As both respiratory status and hemodynamics were stable, muscle relaxation was reversed with atropine sulfate 0.15 mg and neostigmine 0.4 mg, and the patient's trachea was extubated. Surgery lasted 8 h 42 min, and anesthesia lasted 11 h 32 min. Estimated blood loss during surgery was 200 mL, but crystalloid fluid (1000 mL), red cell concentrates (RCC; 4 units), and fresh frozen plasma (FFP; 4 units) were administered based on changes in hemodynamics and blood loss volume results. The results of blood analysis at the conclusion of the surgery revealed: hemoglobin, 10.1 g/dL; hematocrit, 29.9%.

Postoperative body temperature, respiratory condition, and vital signs were all stable, serum creatine kinase (CK) was 91 IU/L, other muscle enzymes were within their normal ranges, and the patient was discharged in good condition on postoperative day 52.

Discussion

A review of the 14 cases (17 patients) of this disease reported previously [1–14] revealed delayed motor development and muscle weakness in all cases, but serum CK levels were within normal ranges in most of the cases (Table 1). Mental retardation was noted in 3 cases (cases 7–9). Acute respiratory disorders since birth were found in 6 cases (cases 6, 10, 14–16, 18), including the case presented here, necessitating mechanical ventilation. In severe cases with respiratory disorders, patients had suffered from feeding disorders since birth, but only 1 death was described, and symptoms improved and stabilized as the patients grew older in the other cases. In addition, 13 of the 18 reported cases were from East Asia (including 10 from Japan), suggesting possible regional involvement.

Our case was also considered severe, as the patient experienced neonatal respiratory failure necessitating mechanical ventilation, albeit briefly. However, no dysphagia or respiratory disorders were apparent at the time of surgery, only muscle weakness, and symptoms improved and stabilized.

Our review of the literature revealed not a single article on anesthesia for CNMDU1. Although the cause of this serious disease is unknown, involvement of ryanodine receptor gene mutation has been reported [16, 17], and in light of reports on anesthesia in central core disease, which is a similar nonprogressive congenital muscular disease that is often complicated by ryanodine receptor gene mutation [18, 19], we focused on preventing MH during anesthetic management.

Volatile inhalation anesthetics and depolarizing muscle relaxants are anesthesia-related drugs with the potential to induce MH. MH is essentially abnormal hypermetabolism of skeletal muscle, but it can be caused by volatile

Table 1 Summary of cases with congenital neuromuscular disease with uniform type 1 fibers (CNMDU1)

Case	Reference	Gender	Age (year)	Symptom	Respiratory failure	Mental retardation	Serum CK (IU/L)	Family history	Mortality	Nationality
1	[1]	F	2	Difficulty in walking	−	−	Normal	−	Alive	USA
2	[1]	M	1	Delay in motor milestones	−	−	Normal	−	Alive	USA
3	[1]	M	1	Delay in motor milestones	−	−	Normal	−	Alive	USA
4	[2]	M	1	Muscle weakness	−	−	Normal	−	Alive	Italy
5	[3]	F	Neonate	Difficulty in sucking	−	−	Normal	−	Alive	Italy
6	[4]	M	Neonate	Difficulty in sucking	+	−	Normal (33)	−	Alive	Japan
7	[5]	M	Neonate	Difficulty in sucking	−	+	Normal	−	Alive	Japan
8	[6]	F	Neonate	Difficulty in sucking	−	+	Normal	−	Alive	Taiwan
9	[7]	F	2	Difficulty in walking	−	+	Normal	−	Alive	Japan
10	[8]	F	Neonate	Poor sucking	+	−	Normal	+	Alive	Taiwan
11	[9]	M	1	Unstable gait	−	−	Normal (73)	+	Alive	Japan
12	[10]	F	12	Swelling of the mandible	−	−	Normal (102)	−	Alive	Japan
13	[11]	F	8/12	Bilateral ptosis	−	−	Normal	−	Alive	Korea
14	[12]	M	Neonate	Severely hypotone	+	−	Normal (75)	+	Alive	Japan
15	[12]	M	Neonate	Severely hypotone	+	−	Normal (123)	+	Dead	Japan
16	[13]	M	Neonate	Weak muscle tonus	+	−	Normal	−	Alive	Japan
17	[14]	F	60	Muscle weakness	−	−	Mild elevation	−	Alive	Japan
18		M	Neonate	Severely hypotone	+	−	Normal (72)	−	Alive	Japan

Case 17 is our reported patient

F, female; *M*, male

inhalation anesthetics stimulating the mechanism involved in the release of calcium ion from the endoplasmic reticulum of skeletal muscle, and by depolarizing muscle relaxants stimulating muscle contractions and increasing cellular membrane permeability. Nitrous oxide, nondepolarizing muscle relaxants, and narcotic analgesics (fentanyl) do not trigger MH. Propofol, as used in this case, has often been reported to have been used safely, even in patients susceptible to MH, and the results of animal experiments have also shown that this agent exhibits no action in inducing MH [20]. Although use of a muscle relaxant was not particularly needed during this operation, we did use a muscle relaxant during surgery in this case because intraoperative immobility was an important consideration, and a nondepolarizing muscle relaxant could be safely used. About the same dose as is used for the same operation on patients of the same age was used, but prolonged muscle relaxation was not observed.

Safe perioperative management was achieved, without any intra- or postoperative MH or respiratory failure, by means of total intravenous anesthesia using propofol, fentanyl, and vecuronium, while avoiding the use of any inhalation anesthetics or depolarizing muscle relaxants, during anesthesia for expansion cranioplasty in a child with CNMDU1.

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