

Anaesthesia for a child with α -dystroglycan-related congenital muscular dystrophy

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Abstract

α -Dystroglycanopathy is a newly emerging subcategory of autosomal recessive inherited muscular dystrophies which encompasses a wide spectrum of clinical severity. Mutation of at least 18 genes which are responsible for O-mannose glycosylation of α -dystroglycan has been linked to these congenital muscular dystrophy phenotypes. α -Dystroglycan-related congenital muscular dystrophy (α DG-CMD), which may be associated with multisystem involvement, poses a challenge in perioperative management. Yet, there is a dearth of resources available for reference. We report successful anaesthesia for a 6-year-old child with α DG-CMD who underwent bilateral hamstring lengthening, left Achilles tendon lengthening, and above-the-knee fibreglass for bilateral hamstring tightness. Anaesthesia was performed using total intravenous anaesthesia (TIVA) without muscle relaxant. Bilateral sciatic nerve blocks were performed for postoperative pain control, allowing opioid-free analgesia. The patient was extubated at the end of the surgery. Perioperative considerations in α DG-CMD include anticipation of difficult airway, maintenance of thermoregulation and precautions against malignant hyperthermia with the employment of TIVA, techniques that avoid opioids and neuromuscular blocking agents (particularly suxamethonium), as well as minimizing the risk of aspiration and of raised intracranial pressure.

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Introduction

α -Dystroglycanopathy is a newly emerging subcategory of muscular dystrophies which encompasses a wide spectrum of clinical severity: the most severe comprise congenital-onset phenotypes of Walker-Warburg syndrome (WWS), muscle-eye-brain (MEB) disease, and Fukuyama congenital muscular dystrophy (FCMD), while to the mildest end, adult-onset limb girdle muscular dystrophy (LGMD).¹ Mutations in at least 18 genes of autosomal recessive inheritance, commonly named *POMT1*, *POMT2*, *CRPPA*, *FKTN*, *FKRP*, and *LARGE1*, which are responsible for O-mannose glycosylation of α -dystroglycan (α DG), are linked to these congenital muscular dystrophy (CMD) phenotypes.^{2,3} Normally, α DG mediates cytoskeleton-extracellular matrix communication, thus stabilizing skeletal muscle fibres and facilitating the migration of neurons in early brain development as well as the formation of optic tissue.^{1,2} Malfunctioned α DG disrupts cell membrane integrity, leading to muscular dystrophy as well as brain and eye developmental aberrations.

α DG-related congenital muscular dystrophy (α DG-CMD) often presents at birth with varying degrees of brain and ocular anomalies on top of muscular dystrophy as well as reduced life expectancy, mainly due to systemic complications such as pneumonia, respiratory failure, and cardiac failure.³ WWS is the most severe

Table 1. Anomalies associated with α -dystroglycan-related congenital muscular dystrophy

Organ/system	Anomalies
Brain	Lissencephaly, hydrocephalus, encephalocele, cerebellar hypoplasia, cerebellar cyst, brainstem flattening
Eye	Retinal detachment, retinal atrophy, anterior chamber malformation, microphthalmia, buphtalmus, congenital cataract, myopia, nystagmus
Musculoskeletal	Hypotonia, motor developmental delay, contractures, bulbar weakness
Cognitive function	Mental retardation
Cranium/face	Macro- or microcephaly, micrognathia, cleft lip/palate, midface hypoplasia
Genitourinary	Hydronephrosis, cryptorchidism

form, with an estimated life expectancy of 3 years, followed by MEB/FCMD with an estimated life expectancy 10 to 30 years. Table 1 shows the associated anomalies reported in patients with α DG-CMD.

Children with α DG-CMD requiring surgery pose a challenge in anaesthetic management due to its multisystem involvement. Guidelines and literature on perioperative management for this condition, however, are limited. Hence, we present the anaesthetic management of a child with α DG-CMD as a reference.

Case presentation

A 6-year-old girl weighing 17 kg was scheduled for bilateral hamstring lengthening, left Achilles tendon lengthening, and above-the-knee fibreglass for bilateral hamstring tightness. She was born to a non-consanguineous couple via caesarean section for breech presentation at term. On day 11 of life, she was diagnosed with ventricular septal defect, which was then surgically repaired at 6 months of age. The surgery was uneventful, but no anaesthetic record was available. Her parents noted abnormal eye movement and failure to focus the eyes at 2 months of age. Ophthalmological consultation revealed high myopia with myopic degeneration, bilateral ametropic amblyopia, and nystagmus. As she grew, her parents started to express concern about her delayed developmental milestone and “floppiness”. Brain MRI at 6 months of age revealed dysplastic cerebellum with multiple cerebellar cysts in the subcortical region and vermis, small pons, and cerebral atrophy (Fig. 1). Genetic testing at 3 years of age confirmed *FKRP* mutation (c.891C>G and c.1309C>A) in this child with both parents being carriers, thus the diagnosis of α DG-CMD. However, the phenotype of α DG-CMD in this child was not established.

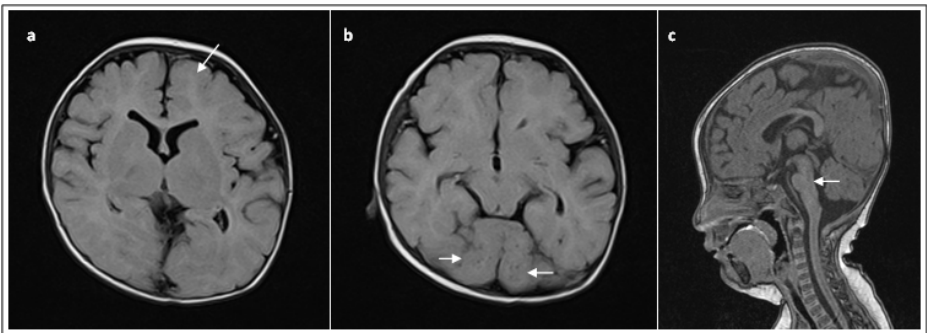


Fig. 1. Brain MRI for the patient taken at 6 months of age with anomalies associated with α -dystroglycan-related congenital muscular dystrophy. Shown by arrows: (a) pachygyria in the frontal region, (b) multiple cerebellar cysts, and (c) small pons.

Physical examination revealed soft dysmorphism (low set ears, depressed nasal bridge, and hypertelorism) and generalized hypotonia. The mouth opening was good and no physical features of difficult airway were noted. She was able to sit with support, feed by herself, and communicate in simple words. Vital signs were stable with blood pressure of 90/45 mmHg, heart rate of 101 beats per minute, and SpO₂ of 100% under room air. No murmur or cyanosis was detected. Laboratory investigations and echocardiography were normal.

Preoperatively, she was fasted for 6 hours with an allowance of clear fluid up to 2 hours before surgery. No sedative premedication was given. The general anaesthetic machine was flushed with 15 L/min oxygen for 15 minutes with the vaporizer removed and the CO₂ absorber changed. Paediatric difficult airway trolley and dantrolene were on standby in the operating room (OR). Standard monitoring was applied, and the patient was induced with target-controlled infusion (TCI) of propofol using the Paedfusor model (starting at a plasma target of 5 mcg/mL and titrated upwards until loss of consciousness) and mass rate infusion of intravenous remifentanil at 0.3 mcg/kg/min. No muscle relaxant was given. Her vocal cord was sprayed with lidocaine 2% using an atomizer and she was subsequently intubated via direct laryngoscopy using uncuffed endotracheal tube size 6, with no difficulty and haemodynamically stable. Additional monitoring for malignant hyperthermia – nasal temperature probe and capnography as well as bispectral index (BIS), were then attached. Anaesthesia was maintained with total intravenous anaesthesia (TIVA) (TCI propofol at 3–4 mcg/mL and intravenous infusion of remifentanil 0.2–0.3 mcg/kg/min) running through dedicated intravenous access, targeting BIS values of 40 to 60. She was ventilated using pressure-controlled ventilation mode to achieve a tidal volume of 6 to 8 mL/kg and respiratory rate titrated to achieve the desired end-tidal CO₂. Approximately 300 mL of Hartmann solution was used to correct preoperative fluid deficit as well as maintenance. Intravenous acetaminophen 250 mg was served as analgesia in addition to bilateral sciatic nerve block (popliteal approach), allowing avoidance of opioid use. Normothermia was maintained with an underbody Bair Hugger™ warming unit (Model 77500, 3M, Newark, DE, USA) and overhead radiant warmer. Tourniquet was applied intraoperatively to minimize bleeding. Intraoperative glucose level was 5.6 mmol/L.

The procedure was completed uneventfully within 2 hours with minimal blood loss. Intravenous propofol and remifentanil were stopped at the end of the surgery. The patient emerged fully from anaesthesia and regained good spontaneous breathing. Subsequently, she was extubated well and discharged to the paediatric high-dependency unit for close monitoring. Her postoperative stay in the hospital was uncomplicated with good pain control using syrup acetaminophen 250 mg QID and syrup ibuprofen 150 mg TDS. She was then discharged home 2 days later.

Discussion

α DG-CMD presents several perioperative considerations. One of the notable challenges is its relation to difficult airway, evidenced by case reports of difficult intubation in infants with WWS requiring paraglossal straight blade laryngoscopy approach.⁴ Macrocephaly, micrognathia, receding mandible, and presence of cleft lip/palate, which are commonly reported in children with α DG-CMD, make intubation challenging. Despite the absence of these features in this patient, a difficult airway trolley consisting of appropriate sizes of oral and nasopharyngeal airway, supraglottic airway device, and video laryngoscope was stationed in the operating room as a safety precaution. As the number of attempts at laryngoscopy is an independent predictor of severe complications, minimizing the number of direct laryngoscopy attempts and early transition to video laryngoscopy is highly recommended and hence necessitate immediate accessibility of video laryngoscope during a crisis.⁵

CMD was traditionally thought to be associated with malignant hyperthermia. However, the literature suggests that a significant association was found only in King-Denborough syndrome and central core myopathy.⁶ Despite the current opinion suggesting non-malignant hypothermia-triggering anaesthesia as the mode of choice, uncomplicated anaesthesia with inhalational agent in α DG-CMD has been reported in several articles.^{4,7} With TIVA gaining popularity among the paediatric age group, availability of TIVA facilities and endorsed guidelines in our centre drove us towards the decision of performing TIVA on this patient. Paedfusor model for TCI propofol and mass rate infusion for intravenous remifentanyl was chosen based on the patient's age as well as body weight as per guideline.⁸ BIS monitoring, although not compulsory, was applied to guide titration.

Another crucial anaesthetic concern for α DG-CMD is the use of neuromuscular blocking agents (NMBA). Firstly, avoidance of suxamethonium is mandatory, as it has catastrophic effects on patients with CMD. Administration of suxamethonium triggers massive potassium release from extrajunctional acetylcholine receptors, which are largely found in CMD, leading to fatal hyperkalaemia, rhabdomyolysis, and cardiac arrest.⁹ Secondly, judicious use of non-depolarizing NMBA has been suggested, as CMD shows augmented sensitivity to NMBA thus causing respiratory muscle weakness, sputum retention, and pneumonia. Neuromuscular monitoring is essential if NMBA use is necessary.⁹ In this case, we agreed on omitting NMBA with the aid of TIVA, aiming to reduce the risk of postoperative respiratory complications.

Bearing in mind that patients with α DG-CMD are predisposed to central and obstructive apnoea, which can be potentiated by anaesthetic medications and NMBA, cautious opioid use may alleviate the likelihood of postoperative respiratory compromise.¹⁰ A multimodal analgesia approach with the administration of regional

anaesthesia can reduce the requirement of opioids, as shown in this case where successful peripheral nerve block excluded the need for opioids. Other options for analgesia include caudal or epidural block. However, neuraxial block was not chosen for this case based on 2 considerations. Firstly, taking into account the presence of brain anomalies, although not a contraindication, we opted to avoid interference to the central nervous system. Secondly, sciatic nerve block (popliteal approach) provides reliable pain relief to a more targeted innervation for surgery below the knee and hence reduces the effect of motor and sensory block in non-related innervation of lower limbs in a patient with pre-existing neurological deficit.

Although raised intracranial pressure was not apparent in this case, caution should be taken to avoid a surge in intracranial pressure as α DG-CMD is often associated with brain anomalies such as hydrocephalus and encephalocele. Other considerations to take into account are the risk of pulmonary aspiration and thermoregulation. Gastrointestinal dysmotility and bulbar weakness increase the risk of pulmonary aspiration;¹⁰ therefore, fasting time should be tailored against the risk of hypoglycaemia and hypovolaemia. A standard fasting time was deemed adequate for this patient. However, if prolonged fasting time is required, glucose-containing intravenous fluid should be prescribed. Also, temperature control plays an essential role as hypothermia can delay recovery from NMBA and cause arrhythmias and coagulopathy, which may further complicate anaesthetic management.

The postoperative period is also crucial wherein organ failure, particularly respiratory compromise, may ensue. Ideally, the patient should be monitored closely in a specialized unit with trained personnel to observe for early signs of respiratory complications.

Conclusion

Despite being a complex multisystem disorder, safe anaesthesia for patients with α DG-CMD is possible with a detailed understanding of the disease, thorough planning of anaesthesia, and close monitoring for complications.

Declarations

Informed consent for publication

Written informed consent for the publication of the clinical data and images contained in this case report was obtained from the patient's mother.

Competing interests

None to disclose.

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