Perioperative total intravenous anesthesia in a child with Walker-Warburg syndrome: A case report

ABSTRACT

Purpose: Walker-Warburg syndrome is a rare autosomal recessive congenital muscular dystrophy presenting with hydrocephalus, type II lissencephaly, cerebellar malformation, and ocular anomalies. Here, we describe the use of perioperative total intravenous anesthesia in a pediatric patient with Walker-Warburg syndrome.

Clinical Features: A 2-month-old girl with Walker-Warburg syndrome was admitted for urgent ventriculoperitoneal shunt insertion. Anesthesia was induced using intravenous atropine (100 µg), ketamine (10 mg), and fentanyl (15 µg). The patient was monitored for various clinical parameters based on American Society of Anesthesiologists standards. Anesthesia was maintained using intermittent doses of 0.5 mg intravenous midazolam and 5–10 µg fentanyl in incremental boluses. The postoperative course was uneventful.

Conclusions: To our knowledge, no published cases have reported the use of total intravenous anesthesia in patients with Walker-Warburg syndrome who have potential risks for anesthetic-induced malignant hyperthermia. This report described the key features, potential anesthetic management plan, and current literature review of Walker-Warburg syndrome.

Key words: Congenital muscular dystrophy; malignant hyperthermia; perioperative; ventriculoperitoneal shunt

Introduction

Walker-Warburg syndrome (WWS) is an autosomal recessive disorder characterized by congenital muscular dystrophy (CMD) associated with ocular and brain abnormalities. In 2016, a survey in northeastern Italy reported an incidence rate of 1.2 per 100,000 live births.[1] Dobyns et al.[2] established the diagnostic criteria for WWS, including type II lissencephaly, cerebellar malformation, retinal malformation, and CMD with or without ventricular enlargement and anterior chamber malformation. Nevertheless, WWS may also present with cleft lip and/or cleft palate developmental delay, mental retardation, and seizures.[3] It is considered the most severe form of CMD such that, most children with WWS die before the age of 3 years [Genetic and Rare Diseases (GARD)] usually due to respiratory failure, pneumonia, seizures, hyperthermia, or ventricular fibrillation.

The classical signs of WWS can be detected via routine maternal ultrasound and fetal magnetic resonance imaging
in the early weeks of gestation. However, molecular genetics, postabortion MRI, and/or histopathology may be needed to confirm the diagnosis during or shortly after birth.\textsuperscript{4,5}

**Case Description**

Informed and written consent was obtained from the parents of the child. A 2-month-old girl was admitted for urgent ventriculoperitoneal shunt insertion.

Birth and maternal history revealed that the patient was delivered at 37 weeks of gestation by elective cesarean section. Prenatal maternal ultrasound showed Chiari II malformation with cerebral atrophy. Genetic tests conducted during pregnancy were negative for trisomy 13, 18, and 21. Immediately after delivery, the patient was admitted to the neonatal intensive care unit (NICU) due to hydrocephalus and episodic apnea, which required gastric tube insertion for feeding.

Family history showed that the parents were relatives and consanguineous. Our patient had four siblings in total. The first sibling who died at the age of 14 months in Saudi Arabia had clinical features of WWS, which required ventriculoperitoneal shunt insertion at the age of 2 months. The second sibling who was immediately admitted to the NICU upon delivery died after 1 month. The third sibling also had clinical features of WWS, which required ventriculoperitoneal shunt insertion at the age of 2 months. However, during the induction of anesthesia, the patient died due to cardiac arrest. Her fourth sibling was a healthy 16-year-old boy. Other detailed records of these events were unavailable for further review.

Anthropometrics revealed that her weight was 3.6 kg, which was below the 5\textsuperscript{th} percentile, WHO Child Growth Standards.\textsuperscript{6} Physical examination revealed dysmorphic features including severe macrocephaly, low nasal bridge, frontal bulging, micrognathia, receding mandible, moderate hypotonia, exophthalmos with hazy cornea on the left eye, and sluggish pupillary reflexes to light. Preoperative vital signs were within normal ranges (heart rate: 137 bpm; blood pressure: 89/52 mm Hg; respiratory rate: 20 bpm; oxygen saturation at room air: 95%; temperature: 36.9°C). Cardiorespiratory examination revealed normal heart and lung sounds on auscultation. Laboratory investigations showed no abnormalities in hemoglobin, serum electrolytes, blood glucose, and creatinine kinase levels. The renal function tests were normal.

The whole paragraph is rephrased as follow: Postdelivery cranial MRI revealed (1) marked supratentorial hydrocephalus with a normal-sized fourth ventricle, (2) marked thinning of brain parenchyma with no evidence of acute infarction or intracranial hemorrhage, (3) severe thinning of the corpus callosum, (4) enlarged posterior fossa with hypoplasia of cerebellar vermis, and (5) brainstem kinked to Z shaped [Figure 1]. Cranial computed tomography (CT) performed 4 days before surgery showed worsening of the supratentorial hydrocephalus with posterior fossa cysts [Figure 2]. All of these findings are suggestive of WWS.

**Anesthetic Management**

After obtaining written informed parental consent, the patient underwent fasting for 4 hours. Difficult airway equipment was prepared in anticipation of difficult intubation. Precautions to prevent malignant hyperthermia (MH) were observed during preparation and surgery. Pulse oximetry, noninvasive oscillometry, electrocardiography, and rectal thermometer were used for monitoring based on the standards of the American Society of Anesthesiologists (ASA) standard.

Preoxygenation with 100\% O\textsubscript{2} for 2 min was performed, followed by induction of anesthesia with intravenous atropine (100 \(\mu\)g), ketamine (10 mg), and fentanyl (15 \(\mu\)g). Once apneic, the baby on the head extension was intubated using the midline approach with anterior cervical pressure. Direct laryngoscopy with a curved-size zero blade showed a grade IV laryngoscopic view. The view was further optimized using external laryngeal manipulation, which made the epiglottis visible (Grade III laryngoscopic view). A 3.5-mm cuffed endotracheal tube (ETT) over the stylet was successfully passed on the first attempt. Endotracheal intubation was confirmed by capnography and inspection of bilateral chest expansion. Auscultation was not performed due to restrictions related to the coronavirus disease 2019 (COVID-19) pandemic. Upon fixation of the ETT, the patient was positioned for surgery.

Anesthesia was maintained with intermittent doses of intravenous anesthetic agents according to the intraoperative monitoring results. This was achieved with 0.5 mg intravenous midazolam and 5–10 \(\mu\)g fentanyl in incremental boluses (Total fentanyl: 50 \(\mu\)g/over 90 min). Mechanical ventilation was achieved at a pressure of 20 cm H\textsubscript{2}O, positive end-expiratory pressure of 3 cm H\textsubscript{2}O, and respiratory rate of 30 bpm to target an end-tidal CO\textsubscript{2} in the range of 30–35 mm Hg. The gas consisted of 40\% O\textsubscript{2}. Intravenous fluid management was performed using 60 mL of 0.45\% saline with 5\% glucose. A forced-warm-air warming system (3M\textsuperscript{TM} Bair Hugger\textsuperscript{TM}) with a thermostat mattress was used to maintain the
The patient was placed in the supine position during surgery. The head was placed on a ring pad and rotated to the left side with the placement of a shoulder roll pad. Insertion of the ventriculoperitoneal shunt was performed by the neurosurgical team. The total operation time was 76 min. The postoperative course was uneventful. The patient was transferred to the NICU and was maintained with 0.5 mg/h midazolam for sedation. She was extubated 4 h after surgery. For the first 24 h, 60 mg intravenous paracetamol was administered every 6 h for pain management. On the second day, paracetamol was given on demand. The doses were subsequently given once daily and then as needed. The patient stayed in the NICU for monitoring and close observation for a week. On the 6th postoperative day, the patient was discharged with no surgical complications. During the latest followup, the patient was alive at 1 year of age.

Discussion

The perioperative anesthetics considerations for the management plans of WWS cases are challenging. The approach of anesthetic management may depend on the degree of organ dysfunction, type of surgery, and urgency. In our case, the patient presented with a difficult airway and a possible family history of anesthesia-related mortality, necessitating the need for special care and attention.

A potentially difficult airway should always be anticipated for timely management. The management of difficult airways requires competent human resources (e.g. anesthesiologist and head and neck surgeon), and functional equipment (i.e., pediatric difficult airway cart).[7,8] In our case, despite the poor visualization, intubation was successful in the first attempt. Nevertheless, we were prepared with the necessary resources for the management of potentially difficult airways, including the fiberoptic scope and video scope. Another common method for the management of the anticipated difficult airway in pediatric patients is inhalation induction with inhaled anesthetics while maintaining spontaneous ventilation. However, this alternative was not suitable for the patient due to concerns regarding malignant hyperthermia, as suggested by the family history of unexplained intraoperative arrest and postoperative death. The use of succinylcholine, muscle relaxants, and volatile anesthetics may trigger an exaggerated potassium release, causing fatal cardiac dysrhythmias and MH.

Choosing the type of anesthesia was challenging for our case as the risk for MH in the patient was unclear based on her family history alone. Fortunately, the patient’s perioperative and postoperative courses were uneventful.

WWS is considered the most severe type of CMD, with a potential association with MH. Rhabdomyolysis and unspecific hypermetabolic responses triggered by volatile anesthetics (e.g., sevoflurane) or succinylcholine have been described in CMD and various myopathies.[9,10] Because of the timing of the case (i.e., early COVID-19 period) and the surgical urgency, we decided to use total intravenous anesthesia, considering the possibility of drug-induced MH. Other important considerations include the presence of a dedicated anesthesia machine for MH, ease of access to dantrolene, and continued monitoring. Body temperature...
must be monitored during both the perioperative and postoperative periods to identify MH early.\[1\]

WWS may also present with cardiac and renal dysfunction. It is important to identify any systemic conditions, as these may increase the risk of perioperative cardiac arrest and renal failure. Fluid management should be maintained to avoid renal and cardiovascular complications. Furthermore, WWS may cause increased intracranial pressure in pediatric patients, necessitating the need for adequate cerebral circulation by maintaining mean arterial pressure within normal limits.\[2\]

The decision for an intensive care admission should be based on the clinical presentation. As mentioned previously, WWS is a severe form of CMD with multi-system involvement. In neonates, WWS may present with seizures, central apnea, cardiorespiratory failure, aspiration pneumonia, and dysphagia.\[2\]

**Conclusion**

Despite the limitations brought about by the COVID-19 pandemic, we have described the successful anesthetic management of an infant with WWS through total intravenous anesthesia. WWS may be associated with MH and rhabdomyolysis. Hence, it is important to avoid drugs that may trigger MH in patients who have potential risks for MH. Furthermore, the difficult airway should be anticipated and managed accordingly through the use of competent human resources and functional difficult airway equipment.

**Implication statement**

We describe the utility of perioperative total intravenous anesthesia during elective ventriculoperitoneal shunt insertion in a 2-month-old girl with Walker-Walburg syndrome. This study suggests a potential technique for the perioperative anesthetic management of patients with Walker-Walburg syndrome.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient’s consent forms. In the form, the patient’s parents have given their consent for the child images and other clinical information to be reported in the journal. The parents understand that their names (including child name) and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Vajsar J, Schachter H. Walker-Warburg syndrome. Orphanet J Rare Dis 2006;1:29.
2. Dobyns WB, Pagon RA, Armstrong D, Curry CJ, Greenberg F, Grix A, et al. Diagnostic criteria for Walker-Warburg syndrome. Am J Med Genet 1989;32:195-210.
3. Burton BK, Dillard RG, Weaver RG, Opitz JM, Reynolds JF. Walker-Warburg syndrome with cleft lip and cleft palate in two sibs. Am J Med Genet 1987;27:537-41.
4. Achiron R, Katorza E, Reznik-Wolf H, Pras E, Kidron D, Berkenstadt M. Very early in-utero diagnosis of Walker-Warburg phenotype: The cutting edge of technology. Ultrasound Int Open 2016;2:E54-7.
5. Lacalm A, Nadaud B, Massoud M, Putoux A, Gaucherand P, Guibaud L. Prenatal diagnosis of cobblestone lissencephaly associated with Walker–Warburg syndrome based on a specific sonographic pattern. Ultrasound Obstet Gynecol 2016;47:117-22.
6. WHO. Child growth standards. 2021.
7. Kose EA, Bakar B, Ates G, Aliefendioglu D, Apan A. Anesthesia for a child with Walker-Warburg syndrome. Braz J Anesthesiol 2014;64:128-30.
8. Yasar M, Huda AU. Anaesthesia management of a new-born baby with Walker-Warburg syndrome undergoing ventriculoperitoneal shunt insertion. J Coll Physicians Surg Pak 2020;30:1115-6.
9. Valk MJ, Loer SA, Schober P, Dettwiler S. Perioperative considerations in Walker-Warburg syndrome. Clin Case Rep 2015;3:744-8.
10. Veyckemans F. Can inhalation agents be used in the presence of a child with myopathy? Curr Opin Anesthesiol 2010;23:348-55.
11. Schneiderbanger D, Johannsen S, Roewer N, Schuster F. Management of malignant hyperthermia: Diagnosis and treatment. Ther Clin Risk Manag 2014;10:355-62.