Clinical Case Reports

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CASE REPORT

Perioperative considerations in Walker–Warburg syndrome

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Funding Information
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Received: 22 January 2015; Revised: 25 May 2015; Accepted: 24 June 2015

Clinical Case Reports **2015; 3(9): 744–748**

doi: 10.1002/ccr3.334

Key Clinical Message

Walker–Warburg syndrome is a rare congenital disorder. Several features, including muscular dystrophy, hydrocephalus, and oropharyngeal abnormalities, have important implications in the perioperative setting. We present a case of general anesthesia in an infant and discuss perioperative considerations to guide clinicians faced with the management of patients with this syndrome.

Keywords

Anesthesia, hydrocephalus, muscular dystrophy, ventriculoperitoneal shunt, Walker–Warburg syndrome.

Introduction

Walker–Warburg syndrome (WWS) is a rare congenital disorder, characterized by muscular dystrophy combined with brain and eye abnormalities and other facultative malformations [1]. Perioperative management is challenging but has only scarcely been reported in the literature [2]. Muscular dystrophy might be associated with malignant hyperthermia (MH) or rhabdomyolysis and may cause postoperative respiratory complications. Patients may present with a difficult airway (i.e., difficulties to perform mask ventilation and tracheal intubation after induction of anesthesia) due to orofacial malformations. Other perioperative problems include increases in intracranial pressure in patients with hydrocephalus. Delayed gastric emptying as well as an increased risk for apnea and seizures have also been described in this patient category.

We present a case of general anesthesia in an infant with WWS. Best practice of perioperative management yet has to be established for such patients. Leading textbooks on general anesthesia, pediatric anesthesia, and perioperative medicine completely lack information on WWS [3–7]. We therefore discuss perioperative considerations to guide clinicians in the management of patients with this rare but challenging syndrome. Both parents of the patient gave written consent to publish the case and photographs.

Case History

A 29-days-old male infant of consanguineous parents weighing 2860 g was scheduled for placement of a ventriculoperitoneal drain due to increasing hydrocephalus. The child had been delivered by cesarean section due to fetal distress at a gestational age of 36 + 2 weeks. He was immediately admitted to the neonatal intensive care unit because of respiratory insufficiency, which was treated with continuous positive airway pressure and noninvasive positive pressure ventilation. Moreover, congenital hypothyroidism was noted and hormone replacement therapy was initiated.

Preoperative physical examination showed macrocephaly, microphthalmia, cataract of the left eye, and glaucoma of both eyes, a small mouth, retrognathia, low-set malformed ears, and a large anterior fontanel (Fig. 1A). The child had very little to no muscle tone, and the grasp reflex was absent. Blood pressure was

91/54 mmHg, pulse rate was 140 beats per minute and oxygen saturation was 100%. An electrocardiograph and chest X-ray were normal.

Laboratory investigation showed no abnormalities for parameters of renal function, hemoglobin, serum electrolyte levels, and blood glucose. Magnetic resonance imaging of the head (Fig. 1B/C) showed typical characteristics of WWS such as dilated ventricles, hydrocephalus, cerebellar hypoplasia, agenesis of the corpus callosum, cobblestone lissencephaly, a buphthalmos of the right eye and a persistent hyperplastic primary vitreous of the left eye. Electroencephalography showed moderate atypical cortical activity but no signs of convulsions.

Perioperative Treatment and Outcome

Preoperatively, the child was fasted for 4 h and received no sedative premedication. Pulse oximetry, ECG and noninvasive blood pressure monitoring were attached on arrival in the operating room. Difficult airway equipment was prepared, including an infant gum elastic bougie, Guedel oropharyngeal airway devices (size 00 and 0), a laryngeal mask airway device (size 1), as well as a video laryngoscope (Glidescope, Verathon Inc., Bothell, WA, USA). General anesthesia was induced with ~6% sevoflurane in oxygen using a facemask. After assuring that mask ventilation was possible, fentanyl (2 μg kg^{-1}), propofol (1 mg kg^{-1}), and atracurium (0.7 mg kg^{-1}) were administered intravenously. Laryngoscopy was performed using a straight Miller blade (size 1) with gentile backward pressure on the larynx, allowing direct visualization of the vocal cords. A cuffed tracheal tube (size 3) was passed through the nose and the trachea was intubated. Correct placement of the tracheal tube was confirmed by capnography and auscultation of both lungs.

After intubation, sevoflurane administration was discontinued and anesthesia was maintained intravenously with intermittent doses of fentanyl (3–5 μg kg^{-1}), midazolam 0.1 mg kg^{-1}) and s-ketamine (1 mg kg^{-1}). The patient was mechanically ventilated using volume-controlled ventilation mode with a tidal volume of 6–8 ml kg^{-1}, a respiratory rate adjusted to maintain normocapnia and a positive end-expiratory pressure of 5 mbar. A balanced electrolyte solution was used to correct preoperative fluid deficit and for maintenance. Body temperature was continuously monitored via a rectal temperature probe.

The surgical procedure was uneventfully completed after 42 min. At the end of surgery, the child was left sedated and transferred to the pediatric intensive care unit where he was extubated the same day a few hours later. Aside from occasional short episodes of hypopnea/apnea with decreases in oxygen saturation (to 80%), the postoperative course was uneventful. The patient was transferred to the general pediatric ward on the first postoperative day and was discharged home 5 days after the operation.

Discussion

Walker–Warburg syndrome is a genetically heterogeneous autosomal recessive disorder. The incidence is unknown but has been estimated to be 1.2/100,000 live births in Italy [8]. Its pathophysiology is not entirely understood, but involves defects in the dystrophin-glycoprotein complex [9]. Walker–Warburg syndrome is considered the most severe type of congenital muscular dystrophy (CMD) and most of the affected children die before the age of three years [9]. Common features include a cobblestone lissencephaly, cerebellar malformations, ventricular enlargement with hydrocephalus, as well as retinal and

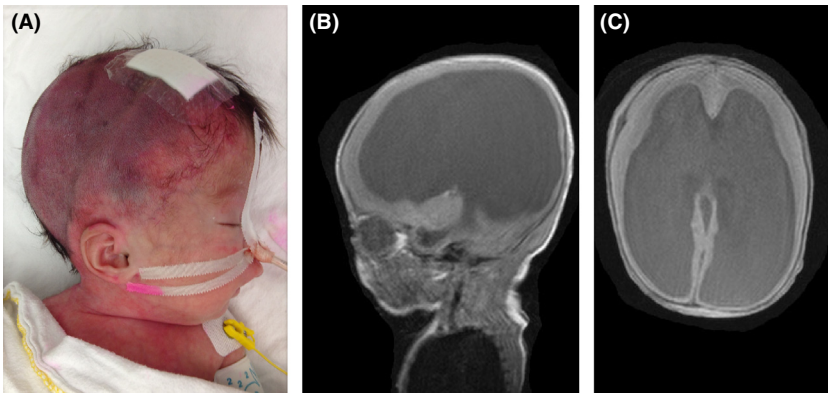

Figure 1. Postoperative photograph of the infant with retrognathia and low-set ears (panel A), as well as sagittal (panel B) and axial (panel C) magnetic resonance images showing massively dilated ventricles (preoperative situation).

anterior chamber malformations [1]. Facial and oropharyngeal abnormalities such as micrognathia, small mouth opening, cleft lip and cleft palate have also regularly been observed. Clinical features of WWS are summarized in Table 1.

Several of the features pose a unique challenge to anesthesiologists and increase the risk for complications in the perioperative period. A thorough knowledge of the patient's medical condition is crucial to allow adequate planning of any anesthesia procedure, and this is especially true in infants with complex syndromes like WWS. Planning should address preoperative requirements for sedative premedication and fasting, anticipation of problems during induction, maintenance and emergence of anesthesia, as well as precautions to avoid complications in the postoperative period.

Concerns about an increased risk for central and obstructive apnea prompted us to avoid preoperative sedation in this child with severe neurologic impairment and muscular hypotonia [2, 10]. Regarding preoperative fasting requirements, a previous publication suggested that WWS might be associated with reduced gastrointestinal motility and an increased risk for pulmonary aspiration of gastric contents [10]. We were unable to verify this information in the cited original literature [11, 12], but our patient indeed showed signs of gastric retention and gastroesophageal reflux shortly after birth. Since gastric retention had resolved by the time of the operation, and since prolonged fasting times in neonates are associated with hypoglycemia and hypovolemia, we determined that a standard fasting period was sufficient. However, clinicians should be aware of a possible association between WWS and delayed gastric emptying and should individually determine preoperative fasting requirements.

Table 1. Clinical features of Walker–Warburg syndrome (WWS).

Common features
Congenital muscular dystrophy
Cobblestone (or type II) lissencephaly
Cerebellar malformation
Ventricular enlargement
Hydrocephalus
Retinal malformation
Anterior chamber malformation
Facultative features
Micrognathia / retrognathia
Cleft lip and cleft palate
Glaucoma, cataract, microphthalmia, and colobomas
Encephalocele
Dandy–Walker malformation
Low-set malformed ears
Contractures
Cryptorchidism, small penis and testis
Hydronephrosis
Possible association with WWS
Central and obstructive apnea
Seizures
Delayed gastric emptying

During induction of anesthesia, we faced two problems: a potential association of CMD with MH and a potentially difficult airway. Associations of MH with CMD, or other myopathies have repeatedly been suggested but are only poorly established [13]. There have been no reports of MH in patients with WWS, but nonetheless such an association cannot be excluded. Moreover, rhabdomyolysis or unspecific hypermetabolic responses triggered by volatile anesthetics (such as sevoflurane) or succinylcholine have been described in a variety of myopathies [13]. Hence, it may be safest to avoid triggering substances. However, in our patient, a small mouth opening and retrognathia suggested that airway management might be difficult. We therefore determined that an inhalation induction with sevoflurane is the safest approach to maintain spontaneous ventilation until we could establish adequate mask ventilation. Sevoflurane is the only volatile anesthetic on the market that does neither have airway irritant effects nor a pungent odor, and is therefore currently the only available volatile anesthetic that is suitable for inhalation induction.

As soon as manual ventilation turned out to be appropriate, a muscle relaxant was administered to facilitate tracheal intubation. In this context, succinylcholine as a potential trigger of MH, rhabdomyolysis or massive potassium release in myopathic muscles was avoided. We used atracurium instead, and subsequent intubation was uneventful. After confirmation of tube positioning, sevoflurane was discontinued and anesthesia was maintained with total intravenous anesthesia.

During induction and maintenance of anesthesia, the patient was meticulously monitored for signs of MH or rhabdomyolysis, such as tachycardia, arrhythmias or muscle rigidity. Specifically, we monitored endtidal CO_2 partial pressure by continuous capnography, because excessive CO_2 production and marked hypercapnia is a sensitive early sign of MH [14]. After placement of the rectal temperature probe, we also monitored the patient for hyperthermia. The ECG was observed for signs of hyperkalemia, such as tall peaked T waves, widening of the QRS complex, or arrhythmias, which may occur as a result of MH or rhabdomyolysis. In the absence of any signs of MH or rhabdomyolysis, specific laboratory testing or arterial blood gas analyses were not performed.

Intraoperative management should also address other comorbidities. In particular, patients with WWS commonly present with hydrocephalus and are at risk of developing increased intracranial pressures (ICP). To

avoid any increases in ICP by coughing on the endotracheal tube, we paralyzed the patient. Subsequent ventilation targeted at normocapnia to avoid increases in ICP by hypercapnic cerebral vasodilation. Maintenance of anesthesia with fentanyl, midazolam, and s-ketamine resulted in stable hemodynamics, avoiding arterial hypotension and impairments in cerebral perfusion pressure.

Patients with WWS may develop postoperative respiratory complications due to muscular weakness and have an increased risk for seizures [9]. Patients should be transferred to a postoperative care unit capable of providing advanced pediatric life support. We transferred the intubated and sedated patient to the pediatric intensive care ward to allow gradual weaning from mechanical ventilation and to ensure that neuromuscular blocking effects of atracurium were completely abolished before extubation. After extubation, the patient received 30% oxygen through a nasal cannula. He showed several short incidents of hypopnea/apnea with drops in oxygen saturation to 80%, underlining that children with WWS need to be closely monitored in the postoperative period.

To our knowledge, only one previous report has described a case of general anesthesia in a patient with typical WWS [2]. The authors describe major difficulties in visualizing laryngeal structures during laryngoscopy using two different techniques, and eventually performed blind endotracheal intubation. This supports our approach of maintaining spontaneous breathing until adequate mask ventilation is established, and underlines the need to be well prepared for difficult airway management. A second report described a patient with possible WWS who also presented with a difficult airway [10]. However, this patient did not have CMD, which is considered a cornerstone in the diagnosis of WWS [1].

One case series[15] and one case report[16] describe general anesthesia in patients with muscle-eye-brain (MEB) disease. While this disease shares many characteristics with WWS, most authors consider WWS and MEB as two distinct entities [17–19]. Yet, due to its similarity, these reports may be of interest in the context of WWS. The case series describes a marked increase in creatine kinase activity after administration of succinylcholine and concludes that this drug should be avoided [15]. The case report describes anesthesia in a child with difficult airway in whom the authors completely avoided volatile anesthetics and secured the airway with fiberoptic intubation [16].

In summary, we describe successful perioperative management of an infant with typical WWS, which may help to guide other clinicians in similar circumstances. Preoperative fasting requirements and the need for sedating premedication should be determined individually in the context of potentially delayed gastric emptying and an increased risk of apnea. Patients should be evaluated for the presence of a difficult airway, and specialized equipment and expertise to handle difficulties should be readily available. A possible association of WWS with MH or rhabdomyolysis cannot be excluded, and caution is needed when triggering drugs are used. Increases in ICP as well as decreases in cerebral perfusion pressure should be avoided in patients with hydrocephalus. Patients are at increased risk for postoperative respiratory complications and seizures, and should be monitored accordingly.

Conflicts of Interest

None.

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