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Case Report

Perioperative management of a patient with Rett syndrome

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Abstract: Rett syndrome is a neurodevelopmental disorder that results from mutations in the genes encoding methyl-cytosine-guanosine binding protein 2 located on the X chromosome. Clinical features of central nervous system involvement include regression of developmental milestones in the late infant and early toddler stages, mental retardation, seizures and other electroencephalographic abnormalities. Given the invariable association of this degenerative disorder with orthopedic deformities including scoliosis, patients with Rett syndrome may present for anesthetic care during various surgical procedures. The complexity of the end-organ involvement, specifically the progressive nature of respiratory and cardiac involvement, makes the anesthetic care of such patients challenging. Specific perioperative concerns include potential difficulties with airway management, an underlying seizure disorder, an increased sensitivity to anesthetic agents, prolonged QT syndrome, and diabetes mellitus. We present an 11-year-old girl with Rett syndrome who required anesthetic care for posterior spinal fusion. Previous reports of anesthetic care for these patients are reviewed, the end-organ involvement discussed, and options for anesthetic care presented.

Keywords: Rett syndrome, long QT syndrome, diabetes mellitus

Introduction

Rett syndrome is a neurodevelopmental disorder of the grey matter of the brain. Genetically, Rett syndrome results from mutations in the genes encoding methyl-cytosine-guanosine (CpG) binding protein 2 (MECP2) located on the X chromosome. Given its location on the X chromosome and the necessity of MECP2 for survival, the disease is generally lethal *in utero* to males. The loss of MECP2 alters the function of cells in the locus ceruleus thereby affecting the noradrenergic innervation to the cerebral cortex and hippocampus [1]. The diagnosis of Rett syndrome is made through observation of the classical signs and symptoms that manifest during early development [2]. Clinical features of central nervous system (CNS) involvement include loss or regression of developmental milestones, mental retardation, seizures and other electroencephalogram (EEG) abnormalities. Genetic testing of the MECP2 mutation is available to confirm the clinical diagnosis of the disorder [3]. There is a high incidence of sudden death with some series reporting 22-25% of all recorded deaths from Rett syndrome were characterized as sudden [4, 5]. Electrocardiogram (ECG) abnormalities and respiratory disorders including alternating tachypnea and apnea may be associated with sudden death. Cardiac arrhythmias may result from an associated prolonged QT syndrome or poor autonomic integration with altered central control of ventilation [4, 6].

Given the invariable association of this degenerative disorder of the CNS and orthopedic deformities with scoliosis affecting up to 50% of patients, patients with Rett syndrome may require anesthetic care for various surgical procedures. In addition to orthopedic issues, perioperative care may be necessary during tonsillectomy for the treatment of obstructive sleep apnea (OSA) or placement of a gastrostomy for feeding difficulties. The complexity of the end-organ involvement, specifically the progressive

nature of the respiratory and cardiac disease, makes the anesthetic care of such patients challenging. To date, there are a limited number of publications reporting the anesthetic management of patients with Rett syndrome. We present an 11-year-old female with Rett syndrome who required anesthetic care for posterior spinal fusion. Previous reports of anesthetic care for these patients are reviewed, the end-organ involvement discussed, and options for anesthetic care presented.

Case report

Institutional Review Board approval is not required at Nationwide Children's Hospital (Columbus, Ohio) for the presentation of single case reports. The patient was an 11-year-old, 22.1 kilogram female who presented for posterior spinal fusion for the treatment of progressive scoliosis. Her past history was significant for Rett syndrome with a seizure disorder and mental retardation; bronchomalacia and severe obstructive sleep apnea that required home bilevel positive airway pressure (BiPAP) at night for the past 2 years; insulin-dependent diabetes mellitus; and a prolonged QT interval. The patient had been delivered at 35 weeks via normal spontaneous vaginal delivery with a birth weight of 1843 grams. Initial respiratory difficulties required the administration of oxygen. Pregnancy was complicated by twin gestation and maternal tobacco use. The patient initially did well, but began to show signs of mental retardation and delayed motor developmental at approximately 6 months of age. The progression of these concerns and further investigation led to the diagnosis of Rett syndrome at 5 years of age. Her past surgical history included gastrostomy tube (G-tube) placement as well as adenotonsillectomy for the treatment of OSA. Current home medications included insulin (twice daily injections of a long-acting subcutaneous insulin with intermittent dosing of regular insulin based on blood glucose checks), ranitidine (37.5 mg per G-tube twice daily), and inhaled therapy with fluticasone, dornase alfa, ipratropium, and albuterol. Home BiPAP settings while sleeping were 18/10 cm H_2O. Preoperative physical examination revealed a cachectic girl with multiple joint contractures. Airway examination revealed a Mallampati III view with limited mouth opening (1.5 centimeters) and moderate micrognathia (thyromental distance of 2 centimeters). There was limited range of motion (flexion and extension) of the neck. Preoperative laboratory evaluation including electrolytes, renal function, coagulation function, and liver function were normal except for serum sodium of 157 mEq/L. A recent ECG revealed a corrected QT interval (QTc) of 480 msec which had progressed from 440 msec on a previous examination. The patient was admitted the day before surgery to manage her preoperative condition including blood glucose and electrolytes. A glucose infusion (5% glucose in 0.45% saline) was started at a maintenance infusion rate and half of her usual morning dose of insulin was administered. She was held *nil per os* for 6 hours. Her preoperative blood glucose was 141 mg/ml with a room air oxygen saturation of 96-98%. She was transported to the operating room and routine American Society of Anesthesiologists' monitors were applied. Anesthesia was induced with propofol (60 mg or 2.7 mg/kg) and fentanyl 50 μg (2.2 μg/kg) which were administered intravenously through a pre-existing peripheral intravenous line. Bag-valve-mask ventilation was provided without difficulty. Neuromuscular blockade was provided with rocuronium 10 mg (0.4 mg/kg) and direct laryngoscopy was performed with a Miller 2 blade. Laryngoscopy revealed a Cormack and Lehane grade II-III view and a 6.0 mm cuffed endotracheal tube (ETT) was placed on the first attempt using a stylet to direct the ETT under the epiglottis. Anesthesia was maintained with a propofol infusion (60-150 μg/kg/hr) which was titrated to maintain the bispectral index at 50-60 and a remifentanil infusion (0.1-0.3 μg/kg/min) to maintain the mean arterial pressure (MAP) at 55-65 mmHg. After the induction of anesthesia, arterial and central venous accesses were obtained. Additionally, using ultrasound guidance a 14 gauge intravenous cannula was placed in a right forearm vein and a 5 French catheter (Cook Micropuncture introducer, Cook Medical, Bloomington, Indiana) was placed in the upper aspect of the left arm. A 5% dextrose solution in lactated ringer's was provided at a maintenance rate. An insulin infusion was administered ranging from 0.02 to 0.04 units/kg/hour to maintain the blood glucose at 80-160 mg/dL throughout the case. Tranexamic acid was administered for prevention of fibrinolysis (50 mg/kg followed by an infusion at 5 mg/kg/hr). The patient was turned and posi-

tioned prone. Baseline neurophysiological monitoring including motor evoked potentials (MEP) and somatosensory evoked potentials (SSEP's) were obtained. Magnesium sulfate (25 mg/kg) was administered intraoperatively for the prevention of arrhythmias. Clevidipine was added for controlled hypotension once the remifentanil infusion had been increased to 0.3 μg/kg/min. The MAP was maintained at range of 55 to 65 mmHg for controlled hypotension to minimize intraoperative blood loss. Heart rates varied from 80 to 100 beats per minute with a normal sinus rhythm. No bradycardia or arrhythmias were noted. During the procedure, the amplitude of the MEP was noted to be decreased. At that time, the clevidipine infusion was discontinued and phenylephrine administered as needed to maintain the MAP ≥70 mmHg, which resulted in the return of the MEP to baseline. Intraoperative fluids included 268 mL of packed red blood cells, 95 mL of cell saver (autologous blood), 500 mL of 5% albumin and 2180 mL of isotonic crystalloid solution. The estimated blood loss was 300 mL. Following completion of the surgical procedure, the patient was transferred to the pediatric intensive care unit (PICU). Mechanical ventilation was provided overnight. On postoperative day 3, her trachea was extubated to BiPAP at her usual settings of 18/10 cm H_2O. For the initial 48 hours, the BiPAP was provided continuously and then transitioned to her usual home regimen of night-time use only. Postoperative pain control was provided with hydromorphone delivered via nurse-controlled analgesia. The remainder of postoperative course was uncomplicated and she was discharged home on postoperative day 14. Discharge was delayed due to feeding issues related to a postoperative ileus and constipation.

Discussion

Given the significant co-morbidities associated with Rett syndrome, there are several specific perioperative implications which may significantly impact the risk for perioperative morbidity and mortality. As with the anesthetic care of all patients, the focus of effective perioperative care begins with the preoperative examination and the identification of end-organ involvement by the primary disease process. Previous reports regarding the perioperative care of patients with Rett syndrome are summarized in **Table 1** [7-15].

Of primary concern to anesthesia providers is the potential for difficult endotracheal intubation related to limited mouth opening, micrognathia, and limited neck movement as were noted in our patient. Although we were able to successfully accomplish endotracheal intubation using direct laryngoscopy, the glottis view was less than optimal given the above-mentioned problems. Other authors have noted similar problems with direct laryngoscopy and endotracheal intubation [10, 11]. As such the ability to accomplish adequate bag-valve mask ventilation should be demonstrated prior to the use of neuromuscular blocking agents. Additionally, the appropriate equipment for dealing with the difficult airway should be readily available including indirect laryngoscopy tools [16].

Issues related to airway management may be further complicated by gastroesophageal reflux resulting in an increased risk for aspiration. In patients with a true aspiration risk, rapid sequence intubation (RSI) with cricoid pressure may be considered. In this setting, a rapidly acting neuromuscular blocking agent may be required. Although a higher dose of rocuronium (1 mg/kg) would be one option; however, an exaggerated and prolonged response may be seen in patients with CNS disorders with hypotonia. Given the associated involvement of the CNS, the use of succinylcholine is controversial because of possible hyperkalemia [8]. In addition, succinylcholine has been reported to increase the QTc interval, which may predispose the patient to fatal arrhythmias [17, 18]. If available, rocuronium in combination with sugammadex would provide not only rapid neuromuscular blockade during RSI, but also rapid return of neuromuscular function following the surgical procedure or in the setting of a cannot intubate-cannot ventilate scenario [10]. Alternatively, RSI can be accomplished using a combination of propofol and remifentanil to avoid the need for neuromuscular blockade [19-22].

In addition to the perioperative aspiration risk, as is noted in our patient, poor airway tone including bronchomalacia and obstructive sleep apnea may predispose these patients to developing respiratory failure in postoperative period. These issues may be compounded by pre-existing respiratory dysfunction from hypotonia, poor cough effort, chronic aspiration or

recurrent pneumonia. Previous anecdotal reports of anesthesia in children with Rett syndrome have noted postoperative respiratory problems including atelectasis and respiratory infections which have required postoperative mechanical ventilation or reintubation of the trachea. Non-invasive techniques of respiratory support such as BiPAP would facilitate postoperative tracheal extubation in these patients [23, 24]. Preoperative assessment with identification of patients with an abnormal respiratory pattern, hypercarbia on preoperative arterial blood gas analysis, a history of recurrent pneumonia, the presence of gastroesophageal reflux, or swallowing problems may identify patients with increased risk for perioperative respiratory complications. Preoperative preparation should include aggressive treatment of respiratory infections and as cognitive function permits, instruction regarding the use of techniques such as incentive spirometry with the consideration of extubation to non-invasive ventilation techniques.

Various anecdotal reports and one case-controlled trial have demonstrated that patients with Rett syndrome may be excessively sensitive to sedative agents, opioids, and volatile anesthetics thereby resulting in a greater risk of perioperative respiratory complications including apnea as well as delayed awakening [11-13, 15, 25]. Tofil et al. conducted a retrospective case-controlled study, consisting of 21 patients with Rett syndrome and 21 control patients undergoing lumbar puncture under deep sedation with propofol. The dose requirements for patients with Rett syndrome were significantly less than the control group was (310 ± 160 versus 520 ± 270 μg/kg/min, p=0.004). Additionally, 7 of 21 patients with Rett syndrome compared with none of the control patients experienced a serious adverse event, most of which were prolonged apnea. As the residual effects of anesthetic agents may impact both upper airway control and postoperative respiratory function, whenever feasible, short acting agents whose effects dissipate rapidly such as remifentanil should be considered. Khalil et al. recommended using an insoluble inhalational anesthetic agent (desflurane or sevoflurane) with bispectral index (BIS) monitoring [13].

As appropriate based on the surgical procedure, regional anesthesia may also be used as an adjunct to providing adequate postoperative analgesia. This will decrease intraoperative anesthetic requirements, including opioids, which may reduce the likelihood of postoperative respiratory depression. Anecdotal, the use of an epidural infusion of a local anesthetic agent and opioid has been suggested as a means of providing postoperative analgesia while limiting systemic opioid needs in these patients [26, 27]. It has also been postulated that patients with Rett syndrome have a high pain threshold from abnormal pain processing and increased endogenous β-endorphin concentrations in cerebrospinal fluid [28]. Regardless of the agents used, given the airway and respiratory co-morbid conditions seen in Rett syndrome, postoperative monitoring of respiratory function is recommended.

Given the progressive deterioration of CNS function, seizures are a frequent co-morbid condition in patients with Rett syndrome. Preoperative management to limit the potential for perioperative seizures includes optimizing and confirming therapeutic anticonvulsant levels prior to the surgical procedure. Routine anticonvulsant medications should be administered the morning of the procedure despite concerns of the patient's *nil per os* status. The ongoing administration of maintenance doses is suggested intraoperatively. When enteral administration is not feasible, alternative routes of delivery including either intravenous or transrectal administration should be considered. Consultation with the neurology or pharmacology service is suggested when questions arise concerning dosing conversion from enteral to intravenous administration or intraoperative redosing.

The choice of anesthetic agents in patients with seizure disorders remains controversial. Although it has been assumed that specific agents may activate the EEG resulting in stimulation of seizure activity, the inhalational and intravenous anesthetic agents are generally considered to have potent anticonvulsant properties. Many of these agents including the barbiturates, propofol, and the volatile agents have been used successfully to treat status epilepticus that is refractory to conventional therapy [29]. Although seizure-like activity and even occasional spike and wave activity on the EEG has been reported with the use of sevoflurane, these effects generally occur only when the

Table 1. Previous reports of anesthesia for patients with Rett syndrome

Authors and reference	Patient demographics	Intraoperative management	Postoperative problems and management
Dearlove OR et al [7].	15-year-old, 21 kilogram girl undergoing Luque spinal stabilization for scoliosis.	No intraoperative events. Blood loss was 1500 mL (90% circulating volume).	The patient was transferred to ICU for ongoing mechanical ventilation which was weaned after 48 hours. Postoperative complications included a chest infection requiring antibiotics and an episode of bacteremia secondary to a urinary tract infection. Both were successfully treated and she was discharged on the 11th postoperative day.
	11-year-old, 30 kg girl presented for two stage spinal surgery. Preoperative arterial blood gas analysis revealed carbon dioxide retention.	The first stage consisted of bilateral thoracotomies and removal of the intervertebral discs. Access was extremely difficult for both venous and arterial cannulae. Posterior spinal stabilization with Luque/Galveston instrumentation was performed as a second stage eight days later.	Although the patient's trachea was extubated three days after the first surgery, reintubation was required. She remained ventilated until the second surgery. Tracheal extubation was accomplished 24 days later after the second surgery. Unexpected death occurred one month after discharge.
	14-year-old, 45 kg girl presented for two stage scoliosis surgery. She had a history of hyperventilation followed by apnea and tonic clonic seizures. The ECG was unremarkable.	The first stage of surgery consisted of a left thoracoabdominal anterior spinal release. There were no intraoperative problems and the patient's trachea was extubated at 48 hours. Posterior spinal stabilization with Luque/Galveston instrumentation was performed one week later. Mechanical ventilation for 48 hours after second surgery.	After the first surgery, the frequency of seizures increased and additional anticonvulsant medications were required. After transfer to the inpatient ward following the second surgery, the patient developed left lung atelectasis. This slowly resolved with conservative therapy, physiotherapy, oxygen and antibiotics.
Kimura F et al [8].	8-year-old, 21.4 kg girl presented for bilateral tonsillectomy and adenoidectomy.	Monitored with BIS and neuromuscular monitoring during total intravenous anesthesia with propofol, remifentanil, ketamine, and rocuronium.	No perioperative issues were noted.
Pierson J et al [9].	7-year-old, 15.2 kg girl presented for an open feeding gastrostomy because of progressive feeding difficulties.	Premedication with oral midazolam was followed by inhalation induction with nitrous oxide and sevoflurane. Anesthesia was maintained nitrous oxide and sevoflurane. Rocuronium was used for neuromuscular blockade.	No perioperative issues were noted.
Kawasaki E et al [10].	18-year-old, 29 kg female undergoing laparoscopic fundoplication and gastrostomy.	Fiberoptic intubation was performed because of expected difficult airway due to trismus and micrognathia. Anesthesia was induced with thiopental and neuromuscular blockade achieved with rocuronium. Maintenance anesthesia included 1-1.5% sevoflurane and remifentanil infusion (0.1-0.2 μg/kg/min) with the BIS value ranging from 30 to 50.	The patient recovered smoothly from anesthesia using sugammadex (50 mg). The patient immediately demonstrated trismus and attack of apnea with shivering, which were successfully resolved by warming the body and intravenous fentanyl (50 μg bolus and subsequent infusion at a rate of 10 μg/hr). The postoperative course was uneventful.

Nho JS et al [11].	19-year-old, 23 kg female for ophthalmologic surgery for immature cataracts.	Anesthesia was induced with propofol (40 mg) and neuromuscular blockade achieved with rocuronium (15 mg). Anesthesia was maintained with 50% nitrous oxide and 1.0-2.0% sevoflurane.	The patient's recovery was slow and complicated by episodes of shaking. After 20 minutes, the patient began breathing spontaneously. Return to her baseline state required 24 hours.
Kim JT et al [12].	12-year-old, 43 kg girl scheduled for a T3-L4 posterior spinal fusion	No premedication was administered. Anesthesia was induced via the inhalational route with sevoflurane. Anesthesia was maintained with propofol (100-125 μg/kg/min) and remifentanil (0.1-0.15 μg/kg/min) titrating to keep the BIS at 30-50.	There was prolonged recovery following the anesthetic requiring postoperative mechanical ventilation. The patient's trachea was successfully extubated 4 hours after arrival in the ICU.
Khalil SN et al [13].	7-year-old, 14 kg girl for dental restoration	No premedication was administered. Anesthesia was induced via mask using 65% nitrous oxide and halothane. Neuromuscular blockade was achieved with rocuronium. Anesthesia was maintained with 0.3-0.6% halothane.	No perioperative complications were noted.
Maguire D et al [14].	14-year-old, 24 kg girl for posterior spinal fusion.	Anesthesia was induced by mask with halothane and nitrous oxide without premedication. Pancuronium was used for neuromuscular blockade. Anesthesia was maintained with 55% nitrous oxide, 0.5-1.0% isoflurane, and morphine.	Postoperative mechanical ventilation was provided for 24 hours postoperatively.
Tofil NM et al [15].	Cohort of 21 patients with Rett syndrome requiring propofol sedation for lumbar puncture. Age-matched control group.	Patients with Rett syndrome required significantly less propofol than case and age-matched controls (310 ± 160 versus 520 ± 270 μg/kg/min, P=0.004)	Seven of the 21 patients with Rett syndrome experienced apnea with propofol versus 0 of 21 control patients.

ICU: intensive care unit, BIS: bispectral index.

inspired concentration is rapidly increased during anesthetic induction when there is accompanying hypocarbia [30, 31]. However, Gibert and colleagues recently reported that the median concentration of sevoflurane causing major epileptiform activity on EEG recordings was 4.3%, or 1.75 minimum alveolar concentration (MAC), which the authors suggest represents an "epileptic threshold" [32]. Therefore, the use of sevoflurane in this population deserves further investigation.

Most patients with Rett syndrome have multiple joint contractures. Limited range of motion (flexion and extension) of the limbs can make insertion of invasive arterial cannulae and intravenous access difficult. Additionally, anatomical malposition of the vessels may occur in these patients. As was noted with our patient and other reports, the use of ultrasound guidance may be invaluable to aid in gaining adequate vascular access for major surgical procedures [33, 34]. The muscle wasting and joint contractures also mandates close attention to surgical positioning [14].

End-organ involvement may also include the cardiovascular system with a propensity of these patients to develop a prolonged QT interval, which has been suggested as a potential etiologic factor in the sudden death in these patients. Sekul et al. evaluated 61 standard 12-lead ECG's obtained in 34 patients with Rett syndrome and 41 ECG's obtained in 41 normal female subjects [4]. The patients with Rett syndrome had a significantly longer QTc interval ($p<0.001$) and more T-wave abnormalities than were found in age-matched, healthy girls. The proportion of corrected QT interval prolongations and T-wave changes increased with advancing stages of the syndrome. These ECG abnormalities are considered as one of the causes of sudden death in patients with Rett syndrome. However, abnormalities of the QTc interval have not been uniformly noted in patients with sudden death [7]. Others have demonstrated abnormalities in the central control of ventilation [5, 6].

Given these concerns, the routine preoperative assessment should include a 12-lead ECG, calculation of the baseline QTc as well as questioning regarding previous episodes of syncope. Ready access for the treatment of arrhythmias, including a defibrillator, should be available intraoperatively. Anesthetic considerations for patients with prolonged QTc interval include avoidance of potential factors that may further prolong the QT interval including an increase in sympathetic tone; hypothermia; electrolyte abnormalities including hypokalemia, hypomagnesemia, and hypocalcemia; as well as various medications which may be administered during the perioperative period [35, 36]. A usual reference for the anesthesia provider regarding the effects of medications on the QT interval can be found at WWW.QTDRUGS.ORG. Aside from medications, other intraoperative events may lead to a further prolongation of the QT interval including increased sympathetic tone, which has been demonstrated to occur during endotracheal intubation [37, 38]. To minimize this response, an adequate depth of anesthesia should be ensured during such procedures. As the synthetic opioids are free of effects on the QT interval, their use should be considered during noxious stimuli [39]. The volatile agents including sevoflurane, desflurane and isoflurane have been reported to prolong the QTc interval [40-43]. However, recent evidence has suggested that the QTc interval is a poor predictor of torsadogenicity, while the peak to end of the T wave interval (Tp-e) reflects the risk of myocardial repolarization dispersion, which most closely correlates with the risk of arrhythmias. Sevoflurane does not affect the Tp-e interval in children [43-45]. Given the concerns regarding QT prolongation and the need for neurophysiologic monitoring of spinal cord function in our patient, we chose to use a total intravenous anesthetic technique with a combination of remifentanil and propofol. Previous studies have demonstrated the negligible effects of propofol on the QTc interval and Tp-e in the pediatric population [41, 43]. The QTc interval and QT dispersion are also unaffected by remifentanil infusion [46]. In addition to these precautions, we chose to use intermittent bolus doses of magnesium because of its effects on the QTc interval, its anti-arrhythmic properties, and studies demonstrating its mitigation of postoperative pain following spinal surgery [47, 48]. Although postoperative mechanical ventilation was anticipated in this patient, consideration must be given to the antagonism of neuromuscular blockade and the emergence from anesthesia when circumstances dictate. Saarnivarra and Simola studied the effects of four anticholinesterase-anti-

cholinergic combinations on the QTc interval. There was a significant increase in the QTc interval approximately one minute after administration of any drug combination and, again, immediately after extubation [49]. In his retrospective cohort study of children with long QT syndrome, Nathan reported that all adverse events occurred during emergence from anesthesia and were confined solely to patients who received a combination of ondansetron and neuromuscular blocking reversal agents [50]. This indicates an important role for suggamadex, as suggested earlier. In addition, the sympathetic discharge accompanying extubation and emergence must be managed appropriately.

Our patient also had type 1 diabetes mellitus as has been described in association with Rett syndrome [51]. In the diabetic patient with absolute or relative insulin deficiency, surgical procedures and the associated stress response can lead to marked hyperglycemia and even diabetic ketoacidosis [52]. Hyperglycemia also can impair wound healing and increase the risk of surgical site infections [53-55].

Although clinical studies have not consistently demonstrated a significant relationship between perioperative glycemic control and short-term risk of infection or morbidity, tight glucose control has been recommended by others with a demonstration of decreased perioperative morbidity [56-58]. Additionally, hyperglycemia may result in glucosuria, polyuria, and electrolyte disturbances. Given these concerns, appropriate control of intraoperative glucose homeostasis may be beneficial. For major surgical procedures, a continuous intravenous infusion of insulin has been shown to be superior to subcutaneous injections in achieving perioperative optimal glycemic control [59, 60]. When feasible, surgery for patients with diabetes should be scheduled as the first case in the morning to avoid prolonged and potential mistakes involving the administration of insulin without glucose. Preoperative assessment should include investigation for the presence of ketonuria, an evaluation of serum electrolytes, and a hemoglobin A1c value. The goal of perioperative glycemic management should include maintenance of blood glucose in the target range of 100–200 mg/dL with hourly measurement of blood glucose concentration (bedside point-of-care testing) and adjustment of either insulin or dextrose infusions based on the results. In our patient, we chose to administer a 5% dextrose solution at maintenance with the use of isotonic, non-glucose containing fluids to replace 3rd space losses. An insulin infusion (0.02 to 0.04 units/kg/hour) maintained the plasma glucose in the desired range. Given the complexity and variability of current diabetes treatment options, consultation with the pediatric endocrinology service should be considered [61].

In summary, Rett syndrome is a neurodevelopmental disorder that results from mutations in the genes encoding MECP2 located on the X chromosome. Given the progressive nature of the disorder and its end-organ manifestations, various surgical procedures may be required in these patients. Specific perioperative concerns include potential difficulties with airway management, underlying seizure disorder, an increased sensitivity to anesthetic agents, associated respiratory compromise which may result in perioperative respiratory failure, prolonged QT syndrome, and diabetes mellitus. Preoperative examination, the assessment of end-organ impairment by the primary disease process, and close postoperative monitoring are mandatory for the effective perioperative care of patients with Rett syndrome.

Conflict of interest statement

All authors have no commercial associations that might pose as a conflict of interest in connection with the manuscript.

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