PERIOPERATIVE CARE OF A CHILD WITH ULLRICH CONGENITAL MUSCULAR DYSTROPHY

- Case Report -

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Abstract

Ullrich congenital muscular dystrophy (UCMD) is a severe form of congenital muscular dystrophy manifesting axial muscle contractures and distal joint hyperlaxity. Severe hypotonia and associated respiratory failure may occur early in the disease process. Given the various associated orthopedic conditions, anesthetic management may be required during surgical interventions to correct skeletal deformities or these patients may present with surgical conditions unrelated to their primary illness. We present a 4-year-old with UCMD who required operative intervention for a ruptured appendix. Anesthetic care implications included the need for a rapid airway control to limit the risks of aspiration due to the intra-abdominal process, choice of neuromuscular blocking agent for rapid sequence intubation, associated airway issues related to micrognathia and limited mouth opening, and the potential for involvement of the cardiovascular and respiratory systems. The perioperative management of patients with UCMD is discussed including the use of propofol and remifentanil for rapid sequence intubation to avoid the need for neuromuscular blocking agents.

Introduction

Ullrich’s congenital muscular dystrophy (UCMD) is a severe form of congenital muscular dystrophy manifesting axial muscle contractures and distal joint hyperlaxity. It generally presents as hypotonia at birth. The disorder was first described in 1930 by Otto Ullrich, who encountered two children with proximal joint contractures and severe distal joint hyper-extensibility. He subsequently named the disorder congenital atonic-sclerotic muscular dystrophy, but over the years, it has become known as Ullrich’s congenital muscular dystrophy. UCMD is inherited as an autosomal recessive trait although cases of spontaneous mutation have been described.

Other distinctive clinical features include a high-arched palate, protuberant calcanei, and rigid spine syndrome. Despite the extensive muscular involvement, intelligence and development are generally normal. Early involvement of the diaphragm leads to early respiratory failure in many patients as well as resulting in the predisposition to recurrent chest infections.
Given the various associated orthopedic conditions, anesthetic management may be required during surgical interventions to correct skeletal deformities. Additionally, these patients may present with surgical conditions unrelated to their primary illness. We present a 4-year-old with UCMD who required operative intervention for a ruptured appendix. The perioperative management of such patients is discussed.

Case Report

Review of this patient’s medical records and presentation of this case report were approved by the Institutional Review Board of the University of Missouri. A 4-year-old, 14 kg girl presented with a 48 hour history of nausea, vomiting, and abdominal pain. Computed tomography scan was suggestive of appendicitis with rupture and she was scheduled for an emergency laparoscopic appendectomy. The patient’s past medical history was positive for UCMD diagnosed by muscle biopsy at 19 months of age when she presented with hypotonia and failure to achieve developmental milestones. During her hospitalization, the patient had been receiving morphine and ketorolac for pain and antibiotic coverage with cefoxitin.

Physical examination revealed a well developed child in moderate distress with complaints of abdominal pain. Her vital signs were stable with no evidence of respiratory distress. Airway examination revealed micrognathia with a thyromental distance of less than 2 centimeters and microstomia with a mouth opening of 1.5 centimeters between the upper and lower central incisors. The lungs were clear and cardiac auscultation was unremarkable. Neurological examination revealed mild hypotonia with strength of 4/5 in all 4 extremities. An intravenous cannula was present in the right antecubital space and flowed easily by gravity. Ranitidine (0.5 mg/kg) and metoclopramide (0.1 mg/kg) were administered intravenously.

Premedication included midazolam (0.07 mg/kg) and glycopyrrolate (5 µg/kg) intravenously and the patient was transported to the operating room where routine monitors were placed. The patient was preoxygenated for 3 minutes with 100% oxygen and this was followed by the administration of propofol (3 mg/kg) and remifentanil (3 µg/kg) for rapid sequence intubation with cricoid pressure. The first attempt at laryngoscopy with a MacIntosh 2 blade was difficult due to the microstomia and limited mouth opening. This attempt at laryngoscopy was aborted and while cricoid pressure was maintained, a second attempt at laryngoscopy with a Wis-Hipple 1.5 laryngoscope revealed a short epiglottis with a grade II view of the airway. The patient’s trachea was intubated with a 5.0 mm uncuffed ETT. Maintenance of anesthesia consisted of desflurane (expired concentration 4-8%) in 50% air/oxygen supplemented with fentanyl (total of 3 µg/kg). No neuromuscular blocking agents were administered. The laparoscopic procedure was completed without difficulty in approximately 75 minutes.

After completion of the procedure, a caudal epidural block was performed with 1.2 mL/kg of 0.25% bupivacaine with 1 µg/kg of clonidine. She was transported to the post-anesthesia care unit. No supplemental pain medication was required for the initial 10 postoperative hours. Subsequently, pain was easily controlled with ketorolac (0.5 mg/kg) administered every 6 hours around the clock, supplemented with as needed doses of nalbuphine (0.05 mg/kg). The remainder of her postoperative course was uneventful.

Discussion

The congenital muscular dystrophies are comprised of a heterogeneous group of diseases affecting muscular architecture including Ullrich congenital muscular dystrophy (UCMD), merosin-deficient congenital muscular dystrophy, and rigid spine syndrome. The congenital muscular dystrophies present similarly during infancy and the neonatal period with decreased intrauterine movement, hypotonia, and delays in the achievement of motor milestones. However, there are specific signs and symptoms which may suggest the diagnosis of UCMD including spinal rigidity, hyperlaxity of the joints of the hands and feet, and early diaphragmatic involvement with chronic respiratory infections or respiratory failure.

Biochemically, collagen type VI is a large, ubiquitous, extracellular matrix protein which forms a highly branched, microfilbrillar network of the skeletal muscle providing structural support including cell-to-cell adhesions and stability. Interactions have
been described between collagen type VI and the major constituent of the muscle basement membrane, collagen type IV indicating that it functions as an anchor for the basement membrane to underlying connective tissue\textsuperscript{2,3}. Likewise, a variety of other matrix components have been shown to interact with collagen type VI particularly proteoglycans and other types of collagen to form structurally critical cellular networks for skeletal muscle\textsuperscript{4,6}. The interactions between proteoglycans such as chondroitin sulfate, biglycan, and decorin and collagen VI provides important mechanisms for transmembrane signaling in a variety of tissues including: skeletal muscle, blood vessels, and cartilagenous tissues throughout the body\textsuperscript{4,6}. These molecular interactions aid in cellular maintenance of homeostasis as well as processes of wound healing through interactions with fibronectin microfibrillar networks\textsuperscript{4,6}.

Structurally, collagen type VI is composed of 3 separate α-chains which are encoded by 3 separate genes located on chromosomes 2 and 21. Mutations in these genes result in 2 specific types of muscular dystrophies including Bethlem myopathy and UCMD\textsuperscript{2}. Although Bethlem myopathy is generally a more benign disease with a more variable onset and a slower progression, UCMD presents in the neonatal period with severe wasting of the axial musculature and distal joint hyperlaxity. Of significant importance to the perioperative care of these patients is the frequent early involvement of the diaphragmatic musculature which may progress to early and severe respiratory failure. However, there remains significant interpatient variability depending on the severity of the mutations in the collagen VI gene resulting in a wide range of clinical presentations and manifestations. These can range from as mild as scoliosis or abnormal scar formation and wound healing to neonatal hypotonia with failure to achieve independent ambulation and an early requirement for ventilatory support.

In our patient, anesthetic considerations included not only her primary disease process, but also the need to secure the airway using rapid sequence intubation due to the presence of an intra-abdominal process with delayed gastric emptying and the associated risk for aspiration. In an effort to avoid the potential for aspiration during anesthetic induction, we pretreated our patient with an H\textsubscript{2}-antagonist and the motility agent metoclopramide, followed by rapid sequence intubation with cricoid pressure. Of primary concern in such patients is the choice of medications to allow for the rapid accomplishment of endotracheal intubation. Given the risks of rhabdomyolysis, hyperkalemia and cardiac arrest with succinylcholine, this agent is absolutely contraindicated in patients with muscular dystrophies\textsuperscript{7,8}. Conversely, non-depolarizing neuromuscular blocking agents (NMBA's) are considered safe in patients with various muscular dystrophies. However, even with intermediate-acting agents such as atracurium or vecuronium, doses which are normally used for endotracheal intubation can result in a prolonged duration of action as increased sensitivity to these agents has been established in patients with muscular dystrophies\textsuperscript{9,10}.

Prior to their withdrawal, rapacuronium and mivacurium, two short-acting NMBA's, could have been considered in this scenario although rapacuronium may have been preferred given its rapid onset. Frankowski et al. reported their experience with the use of rapacuronium in 2 patients (9-years of age and 10-years of age) with Duchenne muscular dystrophy\textsuperscript{11}. There was a prolonged clinical duration (return of T\textsubscript{1} to 25% of its baseline, (16.4 and 18.4 minutes vs. 13.8 ± 7.2 minutes in the general population), a doubling of the recovery index, and doubling of the spontaneous recovery time (return of T4/T1 to ≥ 70%). Mivacurium has also been suggested as a possible agent in patients with muscular dystrophy\textsuperscript{12}. In a cohort of 7 patients with Duchenne muscular dystrophy, a dose of 0.2 mg/kg resulted in complete suppression of all four twitches of the train-of-four in 1.5 to 2.6 minutes. Time to recovery of the first twitch varied from 12 to 18 minutes.

Given that these short-acting neuromuscular blocking agents are no longer available, we chose to use an alternative technique of rapid sequence intubation without a neuromuscular blocking agent. Several investigators have reported the successful use of a combination of remifentanil and propofol to allow for endotracheal intubation without the need for neuromuscular blocking agents\textsuperscript{13-16}. Batra et al. reported that propofol (3 mg/kg) and remifentanil (3 µ/ kg) could be used to allow for endotracheal intubation.
within 90 seconds without the use of a NMBA in children ranging in age from 5 to 10 years\textsuperscript{13}. Similar efficacy has been reported in a cohort of adult patients when using propofol (2 mg/kg) and remifentanil (3 µg/kg)\textsuperscript{14}. In adult patients, Alexander et al. evaluated the suitability of tracheal intubation 60 seconds following the administration of propofol (2 mg/kg) and remifentanil in doses ranging from 2 to 5 µg/kg. Good or excellent conditions were present in 95% of patients who received 4 µg/kg of remifentanil versus only 60% of those who received 3 µg/kg.

In our patient, the combination of propofol (3 mg/kg) and remifentanil (3 µg/kg) produced excellent conditions within 60-90 seconds although a second attempt at laryngoscopy was necessary due to our patient’s airway abnormality and the need to use a direct laryngoscope blade.

Although anecdotal, previous reports exist regarding the potential for difficulties with airway management in patients with various muscular dystrophies including both Duchenne and Emery-Dreifuss variants\textsuperscript{17,18}. As with our case, these difficulties resulted from the combination of limited mouth opening and restricted flexion/extension of the neck. These issues are likely related to fibrotic changes in the associated muscle groups including the masseter muscles which may limit mouth opening. Furthermore, in these cases reports and our patient, associated micrognathia and a short thyromental distance further complicated airway management. It remains unknown whether these issues are sporadic occurrences or somehow related to the muscle dystrophy.

In addition to the concerns outlined above regarding rapid sequence intubation and airway management, the underlying muscular dystrophy may also predispose these patients to both respiratory and cardiac problems. Of particular importance would be the risk of postoperative respiratory failure. The effects of residual anesthetic agents combined with poor muscular function may predispose these patients to upper airway obstruction. Poor cough reflex, pre-existing muscle weakness, and diaphragm impairment may further increase the risk for postoperative atelectasis and respiratory failure. Although our patient underwent a laparoscopic block at the completion of the procedure to ensure adequate postoperative analgesia\textsuperscript{19}. Supplemental postoperative analgesia was then easily achieved with a combination of ketorolac and nalbuphine thereby avoiding the need for strong opioids and their potential for associated adverse effects. We would suggest that use of a regional anesthetic technique with a combination of local anesthetic and clonidine may be beneficial in patients with UCMD by eliminating the deleterious physiologic effects of pain as well as avoiding the need for agents which may potentially impair respiratory function.

Possible cardiac involvement posed an additional anesthetic concern in our patient. Although commonly associated with Duchenne and Becker muscular dystrophy, there does not seem to be a strong association between cardiac involvement and UCMD. Brockington et al. reviewed a case series of fifteen patients with UCMD patients. Both cardiac functional and electrical conduction were examined with echocardiogram and serial electrocardiograms. The entire study group had an unremarkable echocardiogram and all but one patient had normal electrocardiograms. Despite these findings, the possibility of cardiac involvement is raised by one child of the cohort who died suddenly from an arrhythmia\textsuperscript{1}.

In conclusion, we present a 4-year-old with UCMD who required operative intervention for a ruptured appendix. Anesthetic care implications included the need for a rapid airway control to limit the risks of aspiration due to the intra-abdominal process, choice of neuromuscular blocking agent for rapid sequence intubation, associated airway issues related to micrognathia and limited mouth opening, and the potential for involvement of the cardiovascular and respiratory systems. The use of propofol and remifentanil for rapid sequence intubation eliminated the need for neuromuscular blocking agents. However, some potential issues with airway management were noted including micrognathia and limited mouth opening. Additional involvement of respiratory or cardiovascular performance may impact the perioperative care of these patients.
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References


