CASE REPORT

Anesthesia in a child with Maroteaux-Lamy syndrome undergoing mitral valve replacement

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INTRODUCTION

Mucopolysaccharidoses (MPSs) are a group of metabolic diseases transmitted in an autosomal recessive fashion. MPSs are due to deficiencies of the specific enzymes responsible for the catabolism of dermatan sulfate, heparin sulfate, and keratan sulfate, resulting in the accumulation of glycosaminoglycans (GAGs). MPSs have a chronic, progressive course with multisystemic involvement. The incidence of MPSs is approximately 1/50,000 (1). As GAGs begin to accumulate in lysosomes, functional disturbances occur in cells, tissues, and organs. Diagnosis is based on elevated mucopolysaccharide levels in the urine and enzyme deficiencies in the serum or in fibroblast cultures (2).

MPS type VI (Maroteaux-Lamy syndrome) is characterized by a deficiency of N-acetylgalactosamine-4-sulfatase, which is responsible for the catabolism of dermatan sulfatase. The clinical features of MPSs include coarse face, short stature, kyphoscoliosis, upper airway thickening, hearing loss, corneal opacity, hepatosplenomegaly (3), and symptoms that vary according to the GAG accumulation sites (1). Sinus tachycardia, atrial dilatation, valve involvement, endocarditis, myocarditis, and ventricular aneurysms might be observed due to cardiovascular system involvement (4,5). In contrast to the other types of MPSs, there is no mental retardation in patients with MPS type VI.

There are only a limited number of reports of heart surgery in patients with MPSs (6,7). To the best of our knowledge, the literature is devoid of any reports of pediatric patients with Maroteaux-Lamy syndrome undergoing valve replacement surgery. Herein, we present the anesthetic management of a pediatric patient with Maroteaux-Lamy syndrome during mitral valve replacement surgery and a discussion based on the literature.

CASE DESCRIPTION

A 9-year-old, 96-cm-tall, and 18-kg female patient whose sister died at the age of 14 years due to MPS type VI was also diagnosed as having Maroteaux-Lamy syndrome at the age of 2.5 years. She had undergone an inguinal hernia operation in the same year that she was diagnosed, and there were no complications in airway control or the anesthetic course. Follow-up echocardiography when she was three years old revealed mitral valve prolapse, moderate mitral valve insufficiency, and a bicuspid aorta. Although she had no limitation in exercise capacity at earlier ages, she developed exercise dyspnea at age 7. The patient had been treated with recombinant N-acetylgalactosamine-4-sulfatase enzyme (Naglazyme®, Biomarin, USA) 15 $mg/kg^{-1}/week^{-1}$ and digoxin drops 2.5 mg/d^{-1} for the last three years. Her preoperative echocardiography showed an ejection fraction of 83%, along with mitral valve prolapse, severe mitral insufficiency, mild aortic valve stenosis, and mild aortic incompetence. Based on these findings, mitral valve replacement surgery was scheduled.

The pre-anesthetic examination showed failure to thrive, microcephaly, macroglossia, coarse face, corneal opacity, gum hypertrophy, short neck, and kyphoscoliosis (Figures 1 and 2). The patient's ASA score was class III, and her Mallampati score was class II. The physical examination revealed no hepatosplenomegaly. Findings in other systems and biochemical analyses were within the normal limits, except for exercise dyspnea. The platelet count and coagulation tests were also in the normal ranges (platelets: 312×10^9/L; prothrombin time: 12.4 seconds; international normalized ratio: 1.06; activated partial thromboplastin time: 39.7 seconds).

The patient was premedicated with midazolam 1 mg i.v. in the operating room, and five-derivation ECG, SpO_2, non-invasive arterial pressure and invasive arterial pressure were monitored. Her heart rate was 112 bpm, her arterial blood pressure (ABP) was 105/66 mm Hg, her SpO_2 was 95%, and her ECG showed a sinus rhythm. During the induction of anesthesia, the necessary devices and materials for adequate airway control were available, and the surgical team was prepared to perform a tracheostomy.

Following pre-oxygenation, induction of anesthesia was achieved with sevoflurane and midazolam 3 mg i.v. Once ventilation was determined to be non-problematic, the patient received propofol 50 mg i.v., fentanyl 25 μg, and vecuronium 2 mg i.v. During direct laryngoscopy, the Cormack-Lehane classification was determined to be class IV. Intubation via direct laryngoscopy was unsuccessfully attempted four times. Patient ventilation using a mask was satisfactory between intubation attempts. The patient was successfully intubated with a TrueView laryngoscope (Truphatek, USA) and a No. 5 tube on the fifth attempt.

A 5-F internal jugular vein catheter with three lumens was inserted. Following intubation, the patient's heart rate was 140 bpm, her ABP was 92/40 mm Hg, her central venous pressure (CVP) was 26 mm Hg, and her SpO_2 was 99%. The

No potential conflict of interest was reported.

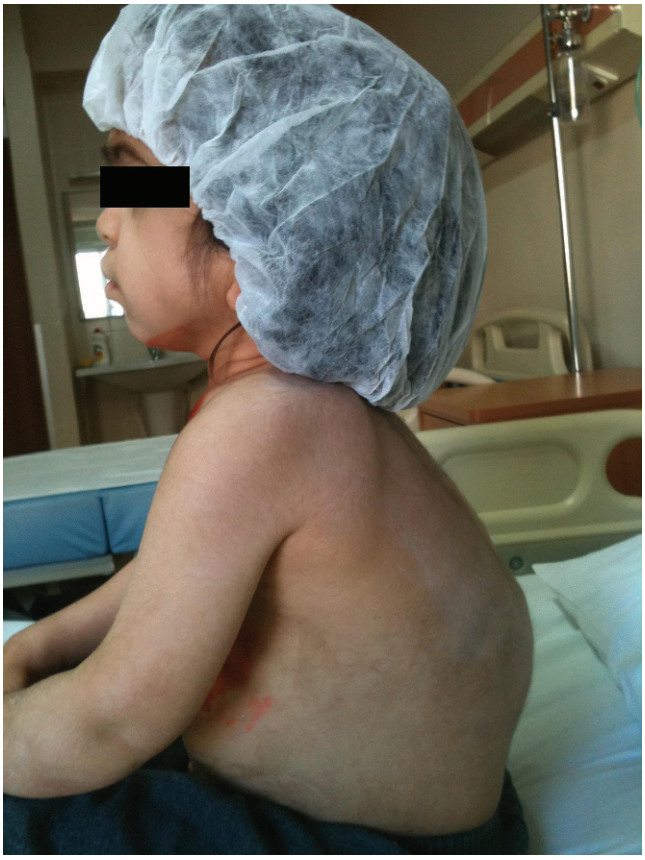

Figure 1 - Lateral position showing kyphoscoliosis and short stature.

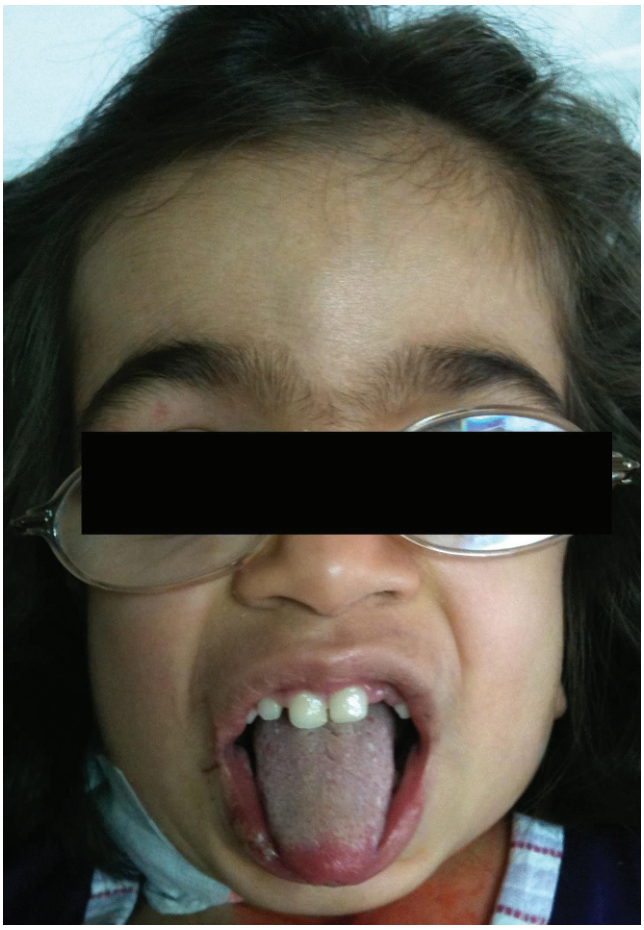

Figure 2 - Coarse face - one of the confirmatory feature of Maroteaux-Lamy syndrome.

arterial blood gas parameters were as follows: pH: 7.39, $PaCO_2$: 41.1 mm Hg, PaO_2: 200 mm Hg, SpO_2: 99.1%, Hb: 12 g/dL^{-1}, Hct: 36.8%, glucose: 164 mg/dL^{-1}, lactate: 0.6 $mmol/L^{-1}$, Na: 139 $mmol/L^{-1}$, K: 3.5 $mmol/L^{-1}$, Cl: 106 $mmol/L^{-1}$, Ca: 0.92 $mmol/L^{-1}$, BE: 0.1 $mmol/L^{-1}$, and HCO_3: 24.4 mmol L^{-1}. Volume-controlled mechanical ventilation was maintained as follows: V_T: 180 mL, frequency: 20 min^{-1}, I/E: ½, FiO_2: 0.5, and PEEP: 4 cmH_2O. The peak airway pressure was 22 cm H_2O, and $EtCO_2$ was 31 mm Hg.

The cardiopulmonary bypass circuit (Dideco EOS Pediatric Oxygenator, Biodevices Inc., Italy) was primed with 650 mL of crystalloid and mannitol solution. After a median sternotomy, anticoagulation was provided with a single dose of 6,000 U heparin. The activated clotting time was measured at 525 seconds. Cardiopulmonary bypass (CPB) was conducted under moderate hypothermia. Myocardial protection during aortic cross-clamping was achieved with cold crystalloid cardioplegia (Plegisol, Hospira Inc., USA). Following standard mitral valve implantation (St. Jude Medical No. 25 mechanical valve, St. Jude Medical, USA), the patient was weaned off CPB with 10 μg/kg/min of dobutamine. Conventional ultrafiltration was also used, and a volume of 600 mL was removed.

The duration of anesthesia was 245 min, including 165 min for surgery, 50 min for cross-clamping, and 78 min for CPB. In total, 400 mL of isotonic NaCl and 340 mL of erythrocyte suspension were administered intraoperatively. The urine output was 300 mL, and the bleeding volume was 150 mL. The patient was taken to the intensive care unit under dobutamine support with a normal sinus rhythm and the following parameters: heart rate: 123 bpm; SpO_2: 100%, ABP: 90/48 mm Hg, and CVP: +28 mm Hg. Dobutamine infusion was administered for 3 h postoperatively. After considering and preparing for re-intubation, the patient was intubated when she was fully awake and met the standard extubation criteria at the 18^{th} hour. She was transferred to the general patient ward at the postoperative 48^{th} hour. The patient was discharged from hospital on the 5^{th} postoperative day under Coumadin treatment.

Histopathological examination of the resected mitral valve revealed a macroscopic nodular appearance, microscopic hyalinization, fibrotic thickening, and single or clustered histiocytes with large, granular cytoplasms.

DISCUSSION

Based on the deficient lysosomal enzyme, there are six types of MPSs. The incidences of MPSs have been reported at between 1/25000 and 1/500000, depending on the type (1,6). Maroteaux-Lamy syndrome accounts for 1% of all MPSs. Treatment of MPS type VI involves recombinant N-acetylgalactoseamine-4-sulfatase administered p.o. Additionally, one patient was reported who experienced a definite cure with bone marrow transplantation (6,8). The family histories of MPS patients are important during pre-anesthesia examinations (7). In MPS patients, the most critical problems related to

anesthesia are difficult intubation and airway control. It has been reported that 25%-50% of MPS patients have problematic airways (1,5,9,10). In total, 82% of MPS patients receiving anesthesia require urgent airway interventions (11). A rapid tracheostomy in such cases can be difficult due to the short neck and kyphoscoliosis. Additionally, the presence of GAG accumulation within the entire tracheobronchial tree must always be a consideration.

Macroglossia, deformation of the skull and facial bones, short neck, gum disorders, limited mouth opening, the anterior position of the larynx, and thoracic malformations all contribute to airway control difficulty. Limited head and neck movements and instability of the atlanto-axial joint also require special attention during intubation (1,12,13). Previous surgeries, especially in pediatric patients with MPS at an early age, might not be associated with airway problems; however, with increasing age, morphological and anatomical changes that occur due to mucopolysaccharide accumulation result in airway control difficulties (1,6,14). The patient presented here underwent complication-free inguinal hernia repair at the age of 2.5 years under general anesthesia.

Preoperative evaluation is important, especially when dealing with a difficult airway; in such cases, radiological imaging might be necessary (1). In the presented case, we did not obtain radiological imaging because we foresaw the possibility of a difficult airway and made the necessary preparations prior to intubation.

It was reported that loss of tonicity in the supraglottic region due to neuromuscular blockade might cause airway obstruction during manual ventilation. As such, it is recommended that neuromuscular blocking agents not be used until the airway is secure (15).

Awake intubation via fiberoptic bronchoscopy has been suggested by some researchers (5,9,16,17). Laryngeal mask use has also been reported (11). As we used sevoflurane for the induction of anesthesia in this case, we were able to preserve the patient's spontaneous respiration. Following the induction of anesthesia, it was observed that ventilation with a mask was preserved before and after neuromuscular blockade. We were also prepared for fiberoptic bronchoscopy. Intubation was successfully accomplished on the 5^{th} attempt using a TrueView laryngoscope in the neutral position.

Intravenous or general anesthesia can be used during the surgery (1,11). When selecting the type of anesthesia, disease stage, systemic involvement and its severity, and airway difficulties must be considered. Although the difficult airway issues in MPS patients undergoing non-cardiac surgery have been resolved, the common involvement of the cardiovascular system makes it more difficult to manage anesthesia and increases the complications. It is well known that patients with Maroteaux-Lamy syndrome have stenoses and mitral and tricuspid valve insufficiencies (2,6). The severity of cardiac involvement might not always be correctly predicted clinically because of limited activity due to limited joint movement (6).

In most individuals with MPS VI, both the liver and spleen become enlarged due to storage of mucopolysaccharides (hepatosplenomegaly). However, the enlarged liver does not usually cause liver problems or lead to liver failure. Furthermore, a significant reduction in the liver volume is observed with enzyme replacement therapy (18). In the patient presented here, preoperative tests revealed normal liver function and coagulation status that might have affected coagulation management and the choice of anesthetic drugs during the CPB. Contrary to expectations, no intraoperative adverse events have been reported related to cardiac anesthesia (6).

Although this patient had serious heart valve problems, there were no significant hemodynamic alterations following the induction of anesthesia, either before or after CPB, and the patient was transferred to the intensive care unit with stable hemodynamics under dobutamine support.

Enlargement of the tongue, tonsils, and adenoids, thickening of mucus membranes, and stenoses very deep in the lower airway can lead to respiratory complications, especially during the post-extubation period. Additionally, obstructive sleep apnea can occur in such patients (19,20). This patient was extubated 18 h after surgery and did not experience any respiratory problems following extubation.

In conclusion, currently used anesthetic methods and drugs can be safely used in patients with Maroteaux-Lamy, but anesthesia protocols must be mindful that MPSs are a group of progressive diseases, and in such patients, histories of non-problematic airways and anesthesia management should not mislead anesthesiologists, who should always prepare vigilantly for difficult airways and systemic complications.

AUTHOR CONTRIBUTIONS

Sayilgan C wrote the manuscript and was one of the responsible anesthesiologists. Yuceyar L collected the data and was one of the responsible anesthesiologists. Akbas S was the resident anesthesiologist responsible for collecting the data. Erolcay H was the supervising anesthesiologist responsible for the patient consultation. All the authors declare that they participated sufficiently in the work to take public responsibility for the appropriate portions of the content.

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