Journal of Spine and Neurobiology
Volume 1 | Issue 1

Case Report Open Access

Perioperative Management of a Pediatric Patient with Zhu-Tokita-Takenouchi-Kim Syndrome Undergoing Urologic Surgery: A Case Report

Adina Weiss MD[1*], Yaniv Hen MD[1], Mohammad Jaber MD[1], Ilan Z, Kafka MD[2], Yaacov Gozal MD, Ph.D[1]

[1]Department of Anesthesiology, Perioperative Medicine and Pain Treatment, Shaare Zedek Medical Center, affiliated with the Hebrew University Hadassah Medical School, Jerusalem, Israel

[2]Departments of Urology, Faculty of Medicine, Shaare Zedek Medical Center, Hebrew University, P.O.B 3235, 91031, Jerusalem, Israel

[*]**Corresponding author:** Adina Weiss MD Department of Anesthesiology, Perioperative Medicine and Pain Treatment, Shaare Zedek Medical Center, affiliated with the Hebrew University Hadassah Medical School, Jerusalem, Israel Tel: 972-532771770 E-mail: adina505@gmail.com

Citation: Adina Weiss MD[1*], Yaniv Hen MD[1], Mohammad Jaber MD[1], Ilan Z, Kafka MD[2]. et al (2022) Perioperative Management of a Pediatric Patient with Zhu-Tokita-Takenouchi-Kim Syndrome Undergoing Urologic Surgery: A Case Report. J Spine Neurobiol 1(1): 103

Abstract

Zhu-Tokita-Takenouchi-Kim syndrome (ZTTK) is a rare autosomal dominant genetic disorder that affects many organ systems, the more cardinal ones being developmental delay and intellectual disability[1],[2]. The potential hazard in anesthetizing children with musculoskeletal abnormalities, heart defects, and neurologic deficiencies amongst other things that may be found in ZTTK syndrome, is high. In this report, we present our experience in the management of anesthesia during urologic surgery that was performed on a 10-year-old pediatric patient diagnosed with ZTTK syndrome.

Glossary of Terms ZTTK: Zhu-Tokita-Takenouchi-Kim, EQUATOR: Enhancing the Quality and Transparency of Health Research Network, MRI: magnetic resonance imaging, ASA: American Society of Anesthesiologists Classification, PACU: post anesthesia care unit, PICU: pediatric intensive care unit, TIVA: total intravenous anesthesia.

Keywords: ZTTIK; EQUATOR; MRI; ASA; PACU; PICU; TIVA

Introduction

Zhu-Tokita-Takenouchi-Kim syndrome (ZTTK) belongs to the group of developmental disorders. It has an autosomal dominant inheritance pattern, and a heterogeneous clinical presentation that affects multiple organ systems. Patients with ZTTK suffer from intellectual disability, abnormal facial features, hypotonia, malnutrition, and visual abnormalities. In addition, most patients have musculoskeletal abnormalities, and some may have congenital heart and/or genitourinary system defects[1]. Brain imaging usually reveals cerebral abnormalities (e.g., cerebral cortical gyration changes, cortical and/or cerebellar atrophy, and thin corpus callosum)[2],[3]. In this report, we present the anesthetic challenge we experienced in the management of a child with ZTTK syndrome who underwent urologic surgery in our institution. To our knowledge, there are no reports of anesthesia for children with ZTTK syndrome. We hope to provide here a single point of reference for successful anesthesia management in a child with ZTTK. This report follows the appropriate EQUATOR guidelines.

Written informed consent for publication of this case was obtained from the parents.

Case Presentation

Chief Complaint A 10-year-old boy, weighing 23kg and 122cm in height, was scheduled for a ureteroscopy and endoscopic extraction of nephrolithiasis. The patient presented with pain upon urination for the past year. Abdominal computed tomography and ultrasound revealed renal calculi, 7mm and 4mm in size in the right kidney, with mild hydronephrosis. The patient underwent evaluation for failure to thrive and developmental delay at the age of 8, and was diagnosed with ZTTK syndrome. Genetic testing showed a de novo heterozygous mutation of the SON gene at 21:34821927, c.393_396del, p. Arg131SerfstER17. System review included:

• Neurology: the patient suffers from developmental delay, mental retardation, failure to thrive, and has a history of seizures treated with levetiracitam. At the age of 2 he underwent magnetic resonance imaging (MRI), that revealed mild ventriculomegaly. Computed tomography scans performed following trauma at the age of 6 and 8 were normal, as well as MRI performed 7 months prior to the present surgery.

• Cardiovascular: Normal echocardiography, no atrial or ventricular septal defect, no pulmonary hypertension.

• Ophthalmology: exotropia, surgically corrected in October 2020.

• Endocrinology: subclinical hypothyroidism. Growth retardation expressed as short stature. The child is due to start growth hormone therapy.

• Musculoskeletal: hypotonia, hyper flexibility.

• Urogenital: hypospadias and unilateral inguinal hernia repaired in infancy, no records of the operative and anesthetic course available.

Physical Examination Physical examination revealed a child in good general condition, with moderate facial dysmorphism. The child made little eye contact and lacked verbal communication. His chest appeared barrel shaped. No abnormal findings were noted when auscultating his heart and lungs, nor when checking his abdomen. Airway assessment included neck exam, he had full range of motion. Hyoid-mental distance was estimated as 4cm. The child was given an American Society of Anesthesiologists Classification (ASA) of 2. Intubation was expected to be difficult due to the patient's abnormal appearance. Vital signs: Blood pressure 114/76mmHg, Heart rate 87bpm, Temperature 36.4°C, Oxygen saturation 98% on room air. Laboratory tests were in normal range. Electrocardiogram showed normal sinus rhythm.

The patient was scheduled for ureteroscopy and endoscopic removal of renal calculi. He was the first on the schedule the day of the surgery, and the surgery was booked to be performed in a main operating room and not in the urology institute. All our operating rooms are latex free as standard of care. Although most cases of older children with hypotonia are not associated with malignant hyperthermia, the lack of literature regarding perioperative management of patients with ZTTK caused us to approach this case with extra precaution, namely ensuring non-triggering agents for malignant hyperthermia or hyperkalemia. We washed the anesthetic machine for 20 minutes and replaced all tubing. Dantrolene was prepared for emergency administration. The child was placed on a food and fluid fast for 6 hours prior to surgery. The child was accompanied by his mother into the operating room, the mother left only after the child was deeply sedated. The room was pre-warmed, a hotline was connected for warming of fluids. The patient was monitored for non-invasive blood pressure, electrocardiogram, and pulse oximeter. Pre-oxygenation was given via face mask. General anesthesia was induced with 30mcg fentanyl, three consecutive doses of propofol: 50mg, 20mg, and 40mg. Mask ventilation was easy and did not necessitate the use of an oral airway. Due to an expected difficult intubation, a video laryngoscope with a Macintosh blade size 2 was used for intubation from the initial attempt. A cuffed endotracheal tube 5.0mm in size with a guide placed inside it was used. External manipulation was needed to improve the view of the larynx from grade 3 to grade 1 on the Cormack-Lehman scale. Once the tube was secured in the trachea normal and equal breath sounds were auscultated bilaterally. Satisfactory ventilation values were achieved with pressure control ventilation: tidal volume of 180ml, peak inspiratory pressure of 20cmH2O.

Following the induction, the patient's position was adjusted, silicon pads were used to avoid any pressure points. Next a nasopharyngeal thermometer was inserted to the patient's mouth, an orogastric tube was placed, an entropy monitor was attached, and an active warming device (bair hugger) was connected. Maintenance of anesthesia was provided via continuous propofol infusion at 0.2mg/kg/min, and inhaled 45% nitrous oxide. Multimodal analgesia included 1.5mg morphine, 360mg paracetamol, and a continuous remifentanil drip at 0.27mcg/kg/min. For postoperative nausea and vomiting prevention, the patient was given 2 mg dexamethasone, 3mg ondansetron, and an infusion of 300mL Hartmann's solution. During the operation, the patient's heart rate was stable around 100bpm, while the mean blood pressure was 80mmHg. The end tidal CO2 fluctuated between 36 and 48 mmHg, and the nasopharyngeal temperature was 36°C. The operation lasted approximately 20 minutes. An oxygen mask with a reservoir was attached. Extensive suction was performed secondary to hypersalivation.

The patient recovered from anesthesia, was awake, and cough and swallowing reflexes were witnessed. He was transferred to the post anesthesia care unit (PACU), and after two hours was transferred to the general hospitalization ward. Upon discharge from PACU vital signs were: Blood pressure: 125/78mmHg, Heart rate: 80bpm, Oxygen saturation: 98% on room air.

The following morning, he was discharged home.

Discussion

ZTTK syndrome is a severe multisystem developmental disorder characterized by delayed psychomotor development and intellectual disability. It is very rare with a prevalence of <1/1000000. Affected individuals have characteristic dysmorphic facial features, hypotonia, poor feeding, poor overall growth, and eye or visual abnormalities. Most patients also have musculoskeletal abnormalities, and some have congenital defects of the heart and urogenital system. Brain imaging usually shows developmental abnormalities such as gyral changes, cortical and/or cerebellar atrophy, and thin corpus callosum. ZTTK is caused by a heterozygous mutation with a 4-bp deletion in *SON* gene (OMIM accession number: 182465). It has an autosomal dominant inheritance pattern.

The child we presented had previous surgeries. They were performed before the diagnosis of ZTTK syndrome was made. We decided to approach the anesthetic plan for this patient with extra care. The lack of literature regarding ZTTK and anesthesia management led us to approach this case with the goal of avoiding any unknown potential risks. These included difficult intubation and ventilation, and difficult positioning due to musculoskeletal deformities. Even though no association has been reported between

ZTTK and malignant hyperthermia, upon searching the literature the issue of malignant hyperthermia arose in conjunction with other pediatric syndromes that have shared features with ZTTK[1,2]. For that we took precautions to avoid the potential albeit unreported risk of malignant hyperthermia.

To start, we ensured a safe setting for surgery by booking a centrally located operating suite rather than a satellite location that is sparse in extra staff and equipment. We ensured the presence of difficult intubation equipment, we notified our ear nose and throat team, and ensured an available bed in the pediatric intensive care unit (PICU).

No information is known concerning the safety of anesthetic drugs in patients with ZTTK syndrome. In our case, total intravenous anesthesia (TIVA) proved to be a safe and effective approach. The use of small incremental propofol, remifentanil, and morphine did not lead to respiratory depression in our patient. We excluded the use of volatile anesthetics because of their ability to cause malignant hyperthermia. Muscle relaxants were not necessary in this surgery, but we would have avoided the use of succinylcholine as well if muscle relaxation was indicated.

Since ZTTK syndrome is associated with dysmorphic facial features resulting in a difficult airway, we recommend using video assisted laryngoscopy to reduce risks associated with this physical appearance. In our patient, we needed manual manipulation to improve laryngeal view.

After surgery, there was careful monitoring of ventilation and oxygenation. Based on our experience we recommend performing deep suction for prevention of salivary secretions.

In conclusion, general anesthesia was safely performed in this child with ZTTK syndrome. Although our case did not show any complications, this syndrome has the potential for difficult intubation, hemodynamic instability due to cardiac anomalies, positioning problems, and malignant hyperthermia. More cases should be presented in the literature to determine the best anesthesia management in these patients.

References

1. Yang Y, Xu L, Yu Z, Huang H, Yang L (2019) Clinical and genetic analysis of ZTTK syndrome caused by SON heterozygous mutation c.394C>T. Mol Genet Genomic Med. 7(11): e953. doi:10.1002/mgg3.953

2. Ueda M, Matsuki T, Fukada M, Eda S, Toya A, Iio A, et al. (2020). Knockdown of Son, a mouse homologue of the ZTTK syndrome gene, causes neuronal migration defects and dendritic spine abnormalities. Molecular Brain, 13(1) 80 10.1186/s13041-020-00622-4

3. Online Mendelian Inheritance in Man, OMIM®. Johns Hopkins University, Baltimore, MD. MIM Number: {617140}: {12/01/2016}: World Wide Web URL https://omim.org/entry/617140#description

4. Yang L, Yang F (2020) A de novo heterozygous variant in the SON gene is associated with Zhu-Tokita-Takenouchi-Kim syndrome. Mol Genet Genomic Med 8(11): e1496. doi:10.1002/mgg3.1496

5. Kushary ST, Revah-Politi A, Barua S, et al (2021) ZTTK syndrome: Clinical and molecular findings of 15 cases and a review of the literature. Am J Med Genet A 3740-53. doi:10.1002/ajmg.a.62445

6. Miller CR, Lee K, Pfau RB, Reshmi SC, Corsmeier DJ, Hashimoto S, et al (2020) Disease-associated mosaic variation in clinical exome sequencing: a two-year pediatric tertiary care experience. Cold Spring Harb Mol Case Stud. a005231. Published 2020 Jun 12. doi:10.1101/mcs.a005231

7. Bamaga AK, Riazi S, Amburgey K, et al (2016) Neuromuscular conditions associated with malignant hyperthermia in paediatric patients: A 25-year retrospective study. Neuromuscul Disord. 201-6