CASE REPORT

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General Anaesthesia Management in a Patient Diagnosed with Kabuki Syndrome and Review of the Literature

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ABSTRACT Kabuki syndrome is a rare genetic syndrome characterized by specific facial features, as well as neurological, cardiac, respiratory, and musculoskeletal system abnormalities. The craniofacial and multisystem abnormalities, latex allergy and suspicion of malignant hyperthermia may complicate anaesthesia management. In this case report, we present perioperative anaesthesia management of a 6-year-old patient diagnosed with Kabuki syndrome who underwent general anaesthesia for strabismus surgery. We preferred to use a laryngeal mask instead of an endotracheal tube for ventilation due to the tendency to hypotonia, malignant hyperthermia and avoiding the use of muscle relaxants. However, after the placement of the laryngeal mask, the peak inspiratory pressure increased and a significant amount of oral secretions were observed. A muscle relaxant was administered and the patient was intubated without difficulty. Anaesthesiologists should be careful about possible difficult airways, cardiac issues, and neurological problems during the perioperative period of patients diagnosed with Kabuki syndrome.

Keywords: Anaesthesia; general; genetic diseases; inborn; pediatrics

Kabuki syndrome (KS) is a rare genetic disorder characterized by specific facial appearance and multiple congenital anomalies. It was first described in Japan in 1981, with an estimated incidence of 1/32,000 in this population. The syndrome is named after the resemblance of the affected individuals' facial features to the makeup face of traditional Japanese theatre artists. Various chromosomal abnormalities have been described in the pathology of KS.[1]

The phenotypic features and organ involvements frequently encountered in KS are presented in Table 1.[1-5] The significant craniofacial abnormalities and multisystem involvements may complicate anaesthesia administration. Additionally, the literature highlights the need for caution regarding the risk of malignant hyperthermia (MH) and the association with latex allergy (LA) during the perioperative period in patients diagnosed with KS.[5,6] we aimed to present our anaesthesia management in a patient diagnosed with KS who underwent general anaesthesia for strabismus surgery. Written informed consent was obtained from the family for this case report. The article also adheres to the EQUATOR guidelines for case reports (CARE guidelines).

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TABLE 1: Specific craniofacial features and multisystemic abnormalities in Kabuki syndrome.

	Abnormalities
Nose	Flattened nose tip
Ear	Prominent auricle, preauricular pit, hearing problems
Mouth	High-arched palate, cleft palate, cleft lip, tonsillar hypertrophy, malformations of teeth, microdontia, micrognathia
Eye	Eversion of the inferior and lateral portion of the lower eyelids, long palpebral fissures, arched eyebrows structure, reduction in hair on the lateral part of the eyebrows, epicanthal folds, epiblapharon, amblyopia, exotropia, esotropia, ptosis, myopia, hyperopia, astigmatism, strabismus, nystagmus, blue sclera, coloboma, cataract, disc anomalies
Neurologic	Seizures, electroencephalogram abnormalities, microcephaly, coronal synostosis, mental retardation, developmental delay, speech delay
Cardiac	Atrial septal defect, ventricular septal defect, aortic coarctation, bicuspid aortic valve, mitral valve prolapse, hypertrophic cardiomyopathy
Respiratory	Bronchomalacia, bronchial stenosis, recurrent pneumonia attacks, obstructive sleep apnea
Musculoskeletal	Clubbing of the fingers, dislocation, short fingers and metacarpals, hypothenar region abnormalities, fingertip pad, vertebral abnormalities (butterfly vertebra, intervertebral space narrowing, scoliosis, sagittal aperture), short stature, hypotonia
Endocrine	Congenital hypothyroidism, growth hormone deficiency, thelargia, ovarian dysfunction
Genitourinary	Renal cryptoorchidism, renal malposition, hydronephrosis, renal dysplasia/hypoplasia, horseshoe kidney, megaureter, ureteropelvic junction abnormalities, hydroureter
Gastrointestinal	Anal atresia, diaphragmatic hernia, biliary atresia, sclerosing cholangitis, malnutrition
Immun system	Recurrent infections, autoimmune hemolytic anaemia, idiopathic thrombocytopenic purpura
Others	Latex allergy, resistance to non-depolarizing muscle relaxants

CASE REPORT

A 6-year-old male patient, 22 kg and 110 cm, diagnosed with KS, was scheduled for strabismus surgery. The ophthalmologic examination revealed that the patient has bilateral epicanthal fold and bilateral primary inferior oblique overaction (Figure 1). In the preoperative evaluation, several physical examination findings such as a high-arched palate, long palpebral opening, arched brow structure, flattened nose, mild mental and developmental delay, and mild hearing loss were noted. In the preoperative musculoskeletal examination of our patient, the muscle strength in all extremities was 4/5 and there was no significant hypotonia. During the airway assessment, the Mallampati score was 2. No abnormalities were detected during cardiac and respiratory system auscultation. It was learned that the patient is taking levothyroxine due to congenital hypothyroidism. The patient had a history of allergies to several medications such as paracetamol, pseudoephedrine, ibuprofen, chlorpheniramine, metoclopramide, and trimethobenzamide. It was also learned that the patient had a history of cesarean delivery as preterm (32nd week). The patient also had a history of an uncomplicated inguinal hernia operation. Electrocardiography (ECG) was in sinus rhythm and there were no abnormalities in

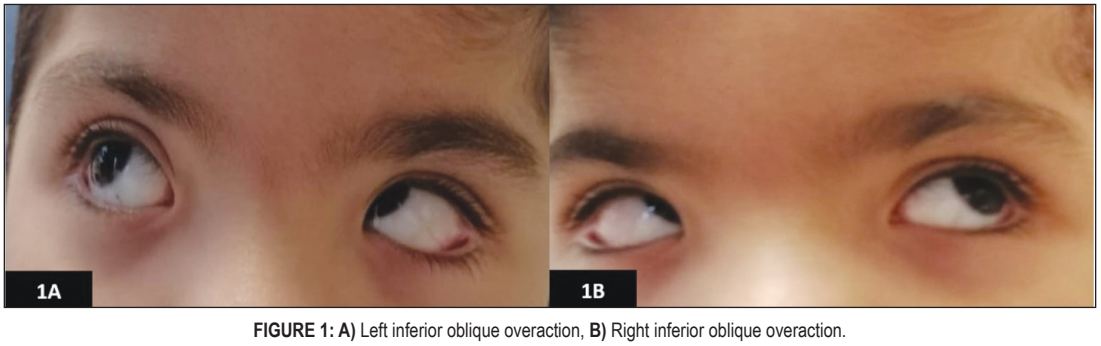

FIGURE 1: A) Left inferior oblique overaction, **B)** Right inferior oblique overaction.

chest X-ray, echocardiography and laboratory results.

The patient, whose an intravenous line was accessed in the ward, was administered 1 mg intravenous midazolam and taken to the operation room (OR). ECG, pulse oximetry (SpO_2) and noninvasive blood pressure monitoring (NIBP) were performed. The patient's basal vital signs were as follows: ECG: 83 beats/minute, NIBP: 89/69 (69) mmHg, SpO_2: 97%. Difficult ventilation and intubation devices were kept ready in the OR. Due to the probability of LA, which was previously reported in the literature, the OR was prepared as a latex-free environment. For induction, propofol 2 mg/kg, lidocaine 1 mg/kg, and fentanyl 1 mcg/kg were administered. During mask ventilation, there were no problems encountered.

After discussing with the surgeon, a size 2 laryngeal mask airway (LMA) was placed successfully without any issues. Since no muscle biopsy was performed in the patient, an infusion of 0.05 mcg/kg/min remifentanil and 6 mg/kg/hour propofol was started to reduce the risk of MD. The mechanical ventilator was adjusted to deliver 2 L of O2 and 2 L of air, with a tidal volume of 160 mL, a frequency of 20 breaths per minute, and an end-tidal carbon dioxide pressure of 30-40 mmHg. However, 5 minutes after the placement of LMA, the peak inspiratory pressure was increased before the surgical procedure started. Upon opening the patient's face, it was observed that there was a significant amount of oral secretions. After suctioning the oral cavity, 10 mg of rocuronium was administered. The patient was intubated with a 4.5 size cuffed endotracheal tube (ETT) in the neutral position due to the risk of joint lability in the cervical. There were no difficulties during laryngoscopy and intubation (Cormack-Lehane Score 1). To reduce the risk of airway oedema, 20 mg methylprednisolone was administered. For postoperative analgesia, 20 mg tramadol was given intravenously. Bilateral inferior oblique recession surgery lasted for 70 minutes. The patient was extubated when sufficient muscle strength was observed after 80 mg sugammadex was administered. No respiratory or cardiac instability was observed during the extubation and all perioperative period. The patient was transferred to the postoperative anaesthesia care unit and subsequently sent to the ward. On the first postoperative day, the patient was discharged without any complications during the perioperative period.

DISCUSSION

Patients with a rare genetic syndrome may require surgery in emergency or elective conditions. The anaesthesia management may be complicated due to possible difficult airways, cardiac anomalies, musculoskeletal issues, and neurological dysfunction in patients diagnosed with KS. High-arched palate, cleft palate or lip, and micrognathia can make mask ventilation and intubation challenging.[1,7,8] Intubation could not be performed and initially, LMA was applied due to reasons such as patients' tendency to hypotonia, obstructive sleep apnea syndrome, MH, and avoiding the use of muscle relaxants. In our case, there was LMA incompatibility and increased secretions. However, we did not consider trying another LMA number due to the risk of aspiration of increased secretions.

Hypotonia is a common finding in patients diagnosed with KS.[1,2] Therefore, caution should be exercised for the risk of MH during the perioperative process.[6] For this reason, we applied TIVA instead of inhalation agent in the maintenance of anaesthesia. However, there are case reports in the literature suggesting the safe use of inhalation agents in patients diagnosed with KS.[7,8]

Although pulmonary function is often normal in patients diagnosed with KS, obstructive sleep apnea has been reported in many cases.[1] The presence of obstructive sleep apnea and hypotonia may complicate the extubation process. Therefore, extubation should be performed in this patient population once muscle strength has fully recovered. And if a muscle relaxant agent has been used, it should be appropriately antagonized. We thought that it would be more appropriate to reverse the effect of the rocuronium with sugammadex. This specific and hypotonic patient group requires close neuromonitoring. In our case, the patient had to use muscle relaxants. TOF monitoring could have been performed and control

could have been achieved after extubation. However, we couldn't use it due to there are no routine neuromonitorization techniques in our clinic.

Various congenital cardiac defects may be encountered in up to 50% of patients diagnosed with KS.[1,2] It is important to carefully evaluate cardiac function in patients diagnosed with KS during the preoperative period and choose an anaesthesia technique that minimally affects hemodynamics during the perioperative period. Therefore, we used LMA instead of ETT to cause fewer hemodynamic changes during intubation.

The association between KS and LA has been reported in the literature.[5] In the previous anaesthesia administration of the patient, no information regarding LA was available. Therefore, we did not encounter any complications by providing a latex-free surgical and ward environment.

In conclusion, a detailed evaluation of airway, cardiac, neurological and musculoskeletal systems should be performed during the preoperative period in patients diagnosed with KS. Although a definitive association between KS, LA and MH has not been clearly demonstrated, anesthesiologists should take necessary precautions to reduce the risks in the perioperative period. Furthermore, sugammadex can be administered as a safe and effective muscle relaxant antagonist in patients diagnosed with KS.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Sibel Çatalca;* ***Design:*** *Sibel Çatalca;* ***Control/Supervision:*** *Nesrin Bozdoğan Özyılkan, Aysel Pelit;* ***Data Collection and/or Processing:*** *Ceren Kahraman;* ***Analysis and/or Interpretation:*** *Sibel Çatalca;* ***Literature Review:*** *Sibel Çatalca;* ***Writing the Article:*** *Sibel Çatalca;* ***Critical Review:*** *Nesrin Bozdoğan Özyılkan, Aysel Pelit;* ***References and Fundings:*** *Sibel Çatalca;* ***Materials:*** *Sibel Çatalca.*

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