



General anesthesia application with the patient who has kabuki make-up syndrome

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Abstract

Kabuki Syndrome is disease derived from a rare genetic mutation that is particularly characterized by distinctive facial features, musculoskeletal malformations, mental retardation and cardiopulmonary anomalies and several pathologies. From anesthetic aspect, this syndrome may cause both cardiovascular and inspiratory problems, defects in palate and collum and also a number of difficulties in selecting medications and invasive procedures. Difficult intubation, prolonged neuromuscular blockage and malignant hyperthermia are frequently encountered problems in the patients with Kabuki Syndrome. An attentive examination of the patient in preoperative stage and appropriate medication preference is essential in order to prevent complications.

Keywords: Kabuki make-up, congenital anomaly, malignant hyperthermia, difficult intubation

1. Introduction

Kabuki Syndrome is a rare genetic syndrome which has distinct dysmorphic facial findings, postpartum growth restriction, mental retardation, skeletal and organ anomalies and anomalous dermatoglyphic patterns (1). For the first time in 1969, as a consequence of having reservations about an underlying undiscovered genetic disorder in a patient who has a different facial feature and mental retardation, it was studied by a Japanese genetic specialist Norio Niikawa (2). In the years that followed, as a result of the consideration of similar cases by being identified with two different groups from Japan in 1981, it took its place in literature (3). Due to the resemblance of characteristic facial features to Kabuki dance drama which belongs to the traditional Japanese theater, it is named after that.

First cases are reported in Japan and although the prevalence of Kabuki Syndrome according to Japanese data is estimated 1/32000, after that in New Zealand it is calculated as 1/86000 (4, 5). It is typically sporadic and has no family history (2). Despite the fact that many cytogenetic anomalies related to the syndrome are indicated, the most common mutation is seen in X chromosome (1). The genes whose pathogenic variants are determined as the cause of Kabuki Syndrome are KMT2D (MLL2) ve KDM6A (1, 6). The characteristics of facial features in patients are may be sorted as; long palpebral fissures, ectropion, thinness in the 1/3 lateral of eyebrows, short nasal septum, large and forward angled ears and preauricular sinus.

Moreover, these patients have additional pathologies as

microcephalia, cleft palate and lips, tooth abnormalities, hypotony, joint laxity, cardiac anomalies (typically VSD, bicuspid aorta, coarctation of aorta), skeletal anomalies (scoliosis, shortness in the 4th and 5th metacarpals, costa anomalies, hip dislocation et cetera) and urinary system malformations (7, 8).

2. Case Report

2.1. Medical history and physical examination

A 19 years old female patient who is diagnosed with Kabuki Make-up Syndrome consulted to our clinic for consideration whose operation is planned by orthopedy and traumatology clinic due to ulna distal fracture. According to the medical history received from the patient's relatives, being born weighing 2700 gr at the end of a eight month of pregnancy, the patient is diagnosed with Kabuki Make-up Syndrome when she was 23 months old as a result of the examinations made due to neuromotor growth deficiency and dysmorphism. In the 31st axis of the MLL-2 gene, heterozygous C6794delG mutation was detected in the gene analysis. As a result of the static kidney scintigraphy (DMSA), taken due to frequent urinary tract infection, stage 2 vesicourethral reflux was monitored and left kidney's functional capacity recorded as 20%. Despite the fact that premature thelarche was observed, based upon the normal hormone levels, the patient was followed up and patient's condition improved by itself at the age of 3. At the age of 2 years, the patient had bacterial pneumonia resulted in hospitalization with a frequent upper respiratory tract infection history. The patient was diagnosed with epilepsy

by an electroencephalogram when she had seizures two times in one month apart with tremors in the body and fixation in the eyes. In the cranial computed tomography (CT) a mass was monitored in the left ear and as a result of the biopsy performed on suspicion of glomus tumor. At the age of 7, the patient started primary school and learn to read and write in the first year. The patient was good at memorizing and she could keep the close relative's phone numbers in her mind. The patient's early IQ test score was stated as 62.

The patient has no cardiac and gastrointestinal system anomalies recorded. The patient had no operation, but before CT was taken at the age of 6, she was sedated and recovered in approximately 6 hours.

In the physical examination, significantly long palpebral fissures and thinness in the 1/3 lateral of the highly curved eyebrows was observed. She had eversion in her lower eyelids and ptosis in her left eye (Fig. 1).



Fig. 1. Lower eye lids, ptosis in her left eye, obese appearance

Her tooth gaps were wide, her nasal septum was low and her ears were low-set (Fig. 2).



Fig. 2. High palate

The patient's appearance was obese and her weight recorded as 90 kilograms. She had no scoliosis. The patient's hemithorax both took part in breathing and lung sounds were bilaterally normal on auscultation. In the cardiac examination, no additional sound or murmur was recorded. Neck movements were natural, mallampati score were 2 and mouth opening were normal. The patient had joint laxity and it was confirmed that her fingers were shorter than normal (Fig. 3).



Fig. 3. Short fingers, joint laxity

In the anterior posterior chest X-Ray, no pathological image was detected. The patient's electrocardiography was in normal sinus rhythm. In the hemogram and routine biochemical blood tests no pathological results were taken.

2.2 Anesthesia application

On the operation day, despite the fact that the patient's mallampati score was 2, essential precautions were taken against the potentiality of difficult intubation and because of the risk of malignant hyperthermia, dantrolene sodium vials were kept ready. The patient was monitored, blood pressure was 112/76 mmHg, heart rate was 92 beats/min, heart rhythm was regular and oxygen saturation was 98% in the room air. Opening the patient's vascular access, 0,5 mg/kg lidocaine, 1 mg/kg propofol and 1mcg/kg fentanyl were administered and induction was ensured. The patient was intubated with size 7.0 intubation tube without curarization due to the fact that the patient had no muscle biopsy history. Vital signs observed stable. After anesthesia, 4-6mg/kg/hour propofol and 0,05-0,2mcg/kg/min remifentanyl infusion was administered. There was not any complications observed. In the last half an hour of the operation, 1mg/hour paracetamol and 20 mg tenoxicam were administered to the patient to achieve analgesia. At the end of the operation, medication infusions were turned off and the patient was awakened due to the fact that there were no need for decurarization.

3. Discussion

Applying anesthesia to the patients with Kabuki Syndrome can actually be difficult in consequence of many

pathologies that may involve with this syndrome. Accompanied by micrognathia, cleft and high palate can cause difficult intubation. Despite the fact that pulmonary functions are generally normal, in hypotonic child obstructive apnea syndrome may go along with this syndrome. In the meantime scoliosis may also accompany with this syndrome and may cause respiratory restrictiveness. In addition immunodeficiency and associated recurrent pneumonias should not be overlooked. Many cardiac pathologies as coarctation of aorta, bicuspid aorta, mitral valve prolapse, ventricular septal defect, valvular stenosis, tetralogy of Fallot, transposition of great arteries may pose a risk in terms of anesthesia.[10] In this regard, it is highly essential to consider these patients about cardiac and pulmonary issues in detail before anesthesia. Another significant point on selecting anesthesia agent is the risk of deepening of neuromuscular blockage and the possibility of malignant hyperthermia in hypotonic patients. In this respect, remifentanyl is considered as a low risk alternative from the point of complications.[9] Additionally, there are also examples in the literature that neuromuscular blocking agents must be administered at higher doses in the patients with Kabuki Syndrome, due to their regular anticonvulsant treatment.[9,10] In this case, in the pre-anesthetical examination, despite the fact that cardiac and pulmonary complication risks were lower than the cases with severe Kabuki Syndrome, precautions were taken particularly in terms of malignant hyperthermia. As recommended in the literature, remifentanyl infusion was preferred and the patient was awakened without any complication.

Although Kabuki Syndrome is rarely seen, patients with Kabuki Syndrome has significant pathognomonic phenotype features and therefore they should be carefully evaluated in preoperative evaluation in terms of possible

anesthesia risks. Necessary precautions should be taken in these patients, particularly in terms of cardiac and pulmonary complications, difficult intubation possibility and malignant hyperthermia.

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