

Anaesthesia in a child with Rubenstein-Taybi syndrome

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Introduction

We report on the anaesthetic management of a child with Rubenstein-Taybi syndrome who required eye surgery. This is a rare congenital syndrome characterised by severe learning difficulties, cardiac abnormalities, gastro-oesophageal reflux and craniofacial abnormalities, e.g. micrognathia and a small mouth. There is the possibility of a difficult intubation.

Case report

An 18-month-old male child with Rubenstein-Taybi syndrome with congenital glaucoma and poor vision was booked for viscocanuloscopia and viscocanuloplasty. Despite there being nothing remarkable in the perinatal and family history, the child had delayed milestones and a diagnosis of gastro-oesophageal reflux. The family history was incompatible with recurrent chest infections or obstructive sleep apnoea and the child had not been prescribed any regular medication. At 16 months of age, he had an uneventful anaesthetic for examination under anaesthesia. He was administered an inhalational gas induction, followed by the insertion of a laryngeal mask airway and maintenance of anaesthesia with sevoflurane. The examination revealed an underweight child (10 kg), placing him on the 10th centile,¹ with dysmorphic facial features (a prominent forehead, slanting eyes, hypertelorism and low-positioned ears) (Figure 1 and 2). The patient also had a high-arched palate. It was also noted that the child had broad hands and broad laterally deviated thumbs (Figure 3). A clinical evaluation revealed no cardiac or respiratory abnormalities.

The patient was starved from 02h00 on the morning of surgery. Clear glucose-containing fluids were offered to the child at 05h00. Premedication with benzodiazepines and antihistamines was avoided because they depress the respiratory centre, and are not suitable as these patients may have obstructive sleep apnoea.^{2,3} Metoclopramide

0.1 mg/kg (2 mg) was administered orally at 07h00. It was decided to omit any sedative medication preoperatively.

In the theatre, the patient was made comfortable and covered to keep him warm. Monitoring comprised electrocardiography, noninvasive blood pressure, pulse oximetry, capnography, rectal temperature and a peripheral nerve stimulator. The capnograph and the temperature probe were used to monitor end-tidal carbon dioxide and temperature because patients with congenital abnormalities are prone to malignant hyperthermia. A non-triggering method, total intravenous anaesthesia, would have been ideal, but this did not apply to this patient because we did not have a paedfusor.⁴

General anaesthesia was induced at 09h00. The patient was preoxygenated via a face mask with 100% oxygen, followed by gas induction with sevoflurane at 8% in 100% oxygen. After induction, a peripheral intravenous 24 G cannula was placed at the cubital fossa and an infusion of Ringer's lactate solution was commenced at a rate of 4 ml/kg/hour. The trachea was intubated with a 4-mm internal diameter cuffed endotracheal tube. The cuff was inflated to a pressure below 20 cmH₂O.⁵ After confirming correct placement of the endotracheal tube clinically, and using capnography, atracurium 5 mg (0.25 mg/kg) was administered because microsurgery requires a totally motionless patient. The patient was ventilated with a ventilator at a tidal volume of 6-8 ml/kg using a Humphrey ADE[®] closed circuit. The respiratory rate settings ranged from 20-25, depending on the end-tidal carbon dioxide concentration. Six litres of fresh gas flow was administered. Fentanyl 2 µg/kg (20 µg) was given intravenously for analgesia. General anaesthesia was maintained with a 1.5% setting on the vaporiser in 50% oxygen and 50% medical air. The end-tidal isoflurane was maintained between 1.2% and 1.3%.

Both surgery and anaesthesia were uneventful. The patient's vital signs were stable throughout the procedure. These



Figure 1: Slanting eyes and hypertelorism



Figure 2: Prominent forehead and low-positioned ears



Figure 3: Broad hand and a broad laterally deviated thumb

were a heart rate of 130 beats/minute, blood pressure of 90/65 mmHG, oxygen saturation of 100%, end-tidal carbon dioxide of 37 mmHg and a temperature approximating 36.9°C. On completion of surgery, the isoflurane was turned off and the patient was left to breathe 100% oxygen. Neuromuscular blockade was antagonised with 0.4 mg (0.04 mg/kg) neostigmine and 0.2 mg (0.02 mg/kg) atropine. The nerve stimulator was used to confirm adequate reversal of the neuromuscular blockade.

Mechanical ventilation was stopped when the patient could breathe spontaneously with adequate breaths sufficient to blow end-tidal carbon dioxide to a reading that ranged between 35-45 mmHg and to maintain normal oxygen saturation with a range of 96-100%. The patient's oropharyngeal secretions were suctioned under vision using a laryngoscope. The cuff of the endotracheal tube

was deflated. The patient was extubated when he was fully awake and could cough up secretions. To minimise the risk of postoperative hypoxia, oxygen therapy via face mask was continued. After extubation, the patient's heart rate was 134 beats/minute, blood pressure, 98/45 mmHg, oxygen saturation 100% and temperature 36.7°C. The patient was transferred to the recovery room.

Discussion

Rubenstein-Taybi syndrome, was initially reported by Michail et al in 1957 as the broad thumb-hallux syndrome. Dr Jack Herbert Rubenstein and Dr Hooshang Taybi did not know each other while independently preparing to publish a report of this syndrome. A third physician, known to both of them, realised that the descriptive features in their case reports were the same. Rubenstein and Taybi then jointly published the first paper in 1963 on children with broad thumbs and big toes.³

Rubenstein-Taybi syndrome is a sporadic autosomal dominant disorder which occurs in nature and which has been linked to microdeletion at 16p13.3-encoding cyclic adenosine monophosphate-responsive, element-binding protein (CREB)-binding protein (CREBBP) genes. CREBBP is a transcriptional co-activator that is involved in the cyclic adenosine monophosphate mediated induction of intracellular protein synthesis. Production of this coactivator is stimulated by protein kinase A. There is a genetic heterogeneity. However, the disease can also be caused by a mutation in the gene EP300. The incidence ratio is 1:100 000- 125 000 at birth.^{3,6,7}

The cause of this syndrome remains widely unknown, but has been linked to microdeletion and/or the absence of chromosome 16p13.3.

Typical abnormalities associated with Rubenstein-Taybi syndrome include, but are not limited to:

- *Periocular and intraocular features:* Of the periocular and intraocular features, patients with strabismus have an increased possibility of developing malignant hyperthermia. However, when managing patients for open-eye surgery, for example glaucoma, iris coloboma and cataracts, certain drugs should be avoided, such as suxamethonium and ketamine, as these increase intraocular pressure which may be exacerbated in patients with glaucoma. Other abnormalities, e.g. palpebral fissures (slanting downwards toward the ears), hypertelorism, high-arched eyebrows, ptosis and refractive errors, have no direct impact on anaesthesia.^{8,9}
- *Perinasal and intranasal features:* Choanal atresia makes nasal intubation impossible, while a deviated nasal septum will make nasal intubation difficult. Other abnormalities, such as nasolacrimal duct stenosis and a prominent or beaked nose, do not have any direct impact on anaesthesia.^{3,8,9}
- *Perioral and intraoral:* Microstomia and micrognathia make oral intubation difficult. Other abnormalities, like a short upper lip and pouting lower lip, high-arched palate and dental crowding and malocclusion, do not impact on anaesthesia.^{2,3}

- **Ears:** The patient may present with malpositioned ears with dysplastic helices, as well as abnormalities of the Eustachian tubes. However, enlarged adenoids may predispose the patient to obstructive sleep apnoea of which certain pre-, intra- and postoperative pharmacological interventions, like the use of benzodiazepines, opioids, and other drugs that will sedate the patient, must be used with caution.^{2,3}
- **Airway:** The patient may present with a collapsible larynx. A case of congenital tracheal stenosis has been reported. These conditions may make endotracheal intubation difficult or impossible.³
- **Chest:** Aspiration, caused by gastro-oesophageal reflux and hypotonia, may lead to the inability to cough up secretions. These factors predispose these patients to recurrent respiratory infections, which may lead to pneumonia and chronic lung disease. The patients may have sternal anomalies, such as pectus excavatum.^{3,9}
- **Cardiovascular:** Acynotic cardiac defects (atrial septal defect, ventricular septal defect, patent ductus arteriosus, coarctation of the aorta and pulmonic stenosis) have been reported to occur in 24-38% of patients who are affected with Rubenstein-Taybi syndrome.⁹⁻¹¹
- **Neuromuscular:** Neuromuscular abnormalities that are associated with Rubenstein-Taybi syndrome include, but are not limited to, mental retardation (with an intelligence quotient typically between 35 and 50), speech delays and a stiff and unsteady gait. These patients may present with seizures, a large foramen magnum and agenesis of the corpus callosum. However, hyperreflexia may make patient positioning difficult if regional anaesthesia is contemplated. Anaesthetic management of patients with hypotonia is complicated by both cardiac and pulmonary manifestations. The use of suxamethonium is best avoided because of the unpredictable response and the risk of inducing malignant hyperthermia.^{11,12}
- **Orthopaedic:** Scoliosis and cervical kyphosis may lead to difficulties in patient positioning during anaesthesia. Other orthopaedic abnormalities (a short stature, broad thumbs and first toes, clinodactyly of the finger, flaring of the ilia, slipped capital femoral epiphyses and flat feet, a stiff gait, spina bifida occulta, retarded osseous maturation and patellar dislocation and joint laxity) are presenting features of Rubenstein-Taybi syndrome, but have no direct impact on anaesthesia.^{3,6}
- **Genitourinary tract:** Genitourinary tract abnormalities [cryptorchidism, overgrowth of the scrotal sac surrounding the penis (i.e. shawl scrotum), hypospadias and occasional renal agenesis anomaly (e.g. congenital absence of a kidney) are associated with Rubenstein-Taybi syndrome, but do not impact on anaesthesia directly.^{3,6}
- **Other abnormalities:** Gastro-oesophageal reflux may pose feeding difficulties that may lead to postnatal growth and nutritional deficiencies. There is an increased incidence of benign tumours and malignancies, e.g. leukaemia and lymphoma. Some dermatological manifestations that are common in patients with Rubenstein-Taybi syndrome include hirsutism, capillary malformations, keloid formation and pilomatricomas. Premature thelarche is

also a common feature in such patients. These features have no direct impact on anaesthesia.^{6,8}

By comparison with all of the above-mentioned features that are common in Rubenstein-Taybi syndrome, the only anaesthesia-related factor with which this particular patient presented was gastro-oesophageal reflux which puts the patient at risk of aspiration. To minimise this, the patient was starved and a premedication of metoclopramide administered. The patient was then intubated using a cuffed endotracheal tube to further eliminate any possibility of aspiration.

This patient had glaucoma as one of the presenting symptoms. The use of suxamethonium and ketamine was avoided because both increase intraocular and intra-abdominal pressure, and suxamethonium further increases the risk of malignant hyperthermia and cardiac arrhythmias.

Conclusion

Patients with Rubenstein-Taybi syndrome may present to hospital when they require surgery for the correction of varying conditions. Clearly, an assessment must be made on an individual basis because management strategies are symptomatic. Major anaesthetic considerations are a difficult intubation, patient positioning and gastro-oesophageal reflux with a risk of aspiration. Mental retardation with or without hypotonia may place these patients at risk of malignant hyperthermia.

Declaration

Informed consent to take photographs of the patient was obtained from the mother.

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