Brief Communication

Crouzon Syndrome: a fibroblast growth factor receptor 2 gene mutation

Farhad Safari[1], Kamran Mottaghi[1], Rofeideh Fallahinejadghajari[1], Masoud Nashibi[1*]

Abstract

Crouzon syndrome is a rare autosomal dominant premature cranyosynostosis, caused by fibroblast growth factor receptor 2 gene mutation on chromosome 10. The predominant skull and facial malformations with potential compromised airway make the crouzon syndrome a demanding issue for anesthesiologists and surgeons, required dynamic team work. In this report we describe a child, a known case of Crouzon syndrome who was a candidate for optic nerve decompression through endoscopic surgery. The anesthetic considerations and management are presented.

Keywords: Crouzon Syndrome, FGFR2 gene, Difficult Intubation, Anesthesia

Please cite this article as: Safari F, Mottaghi K, Fallahinejadghajari R, Nashibi M. Crouzon Syndrome: a fibroblast growth factor receptor 2 gene mutation. J Cell Mol Anesth. 2017;2(1):15-8.

1. Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Corresponding Author: Masoud Nashibi, MD, Assistant Professor, Anesthesiology Research Center, Anesthesiology Department, Loghman Hospital, Kargar Ave, Shahid Beheshti University of Medical Sciences, Tehran, Iran; e mail: masoudnashibi@sbmu.ac.ir

Introduction

Rare genetic disorders are great challenges for anesthesiologists (1, 2). Crouzon syndrome is a rare, complex craniosynostosis of autosomal dominant transfer, with a highly variable phenotypic appearance and mutations in the fibroblast growth factor receptor 2 (FGFR2) gene on chromosome 10 are known to cause it (3, 4). Due to a FGFR2 gene mutation, the disease is characterized by premature craniosynostosis, hypertelorism, orbital proptosis, psittichorhina (beaklike nose), hypoplastic maxilla and mandibular prognatism (5).

Numerous findings from animal studies imply a critical role for FGFRs in the regulation of skeletal development (6). The majority of mutations in FGFR2 are missense substitutions clustered around the third extracellular immunoglobulin-like domain, encoded by exons IIIa and IIIca (7). Most FGFR2 mutations affect the structure of the extracellular domain of the FGFR2 protein, are de novo when found in sporadic cases, segregate with the syndrome in familial cases, and are not found in the normal population (8). There are various kinds of mutations which have been studied with different phenotypes. A C342R mutation in FGFR2 with elbow deformity in Chinese patients (6), a firstly identified mutation s267p in FGFR2 (8), a novel sFGFR2-L617F mutation in tyrosine kinase domain related to premature suture closure (9) and mutations in the interleukin receptor IL-11RA cause of autosomal recessive Crouzon-like cranyosynostosis (10) are few examples of ongoing progression in figuring out this mysterious puzzle.

Although there are different kinds of mutation with various expressivity, the same affected area in all types, the skull, is the major part that may need to undergo lots of therapeutic, corrective and cosmetic surgery thorough a patient's life. Since these surgeries require multidisciplinary management, the anesthesiologist and the surgeons should be aware of and prepared for all difficulties may occur in perioperative period.

Brief Report

A 6 years old boy, known case of crouzon syndrome was admitted to our hospital due to acute deteriorating visual acuity, hydrocephaly and orbital mass. The nasal endoscopic surgery was scheduled for decompressing the optic nerve bilaterally.

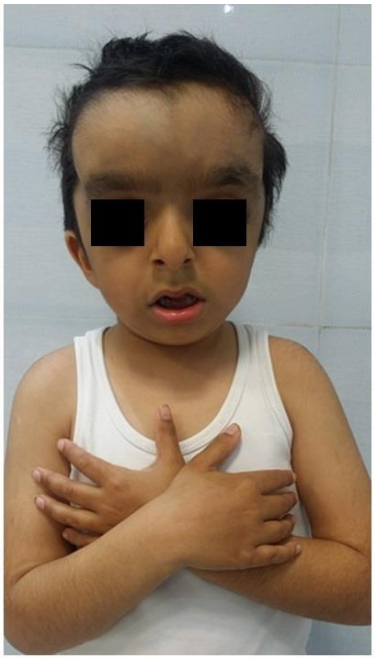

Figure 1. Anterior view

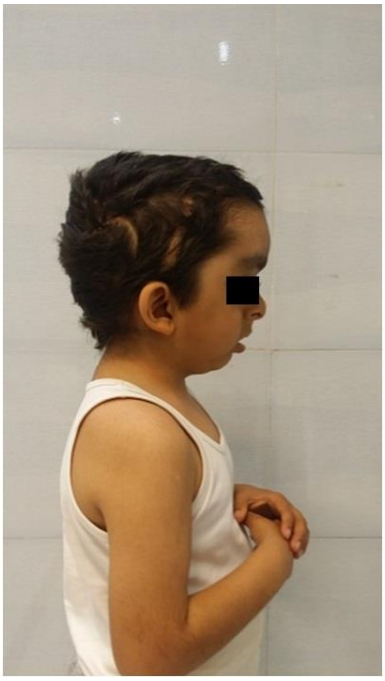

Figure 2. Lateral view

He was an adopted child without any birth documents and family history. The caregivers did not have data about his milestones and the syndrome was diagnosed in pediatric ward based on clinical features of the disease.

He had undergone three surgeries during his infancy and toddler years. The former was a shunt placement and the latter was medial and lateral tarsorrhaphy. The second surgery was a brain surgery without any documents.

In preoperative assessment he was an alert child with stable vital signs and 21 kg weight. He had no limitation in physical activity and the mental development was acceptable for his age.

In head and neck, the prominent forehead, hypertelorism, orbital proptosis, strabismus, low lying ears and micrognatia were conspicuous. There was no limitation in mouth opening and the mallampati score was II. In oral cavity inspection, there was an arched palate and some lost primary teeth. There was some limitation for neck extension.

His visual exam demonstrated visual loss limited to perception of hand motion. The physical exam revealed no remarkable sign in cardiovascular and respiratory systems. The consultant neurosurgeon did not mention any problem like rising Intracranial pressure (ICP).

In operation theatre the whole arsenal was prepared for compromised airway management, including different sizes of endotracheal tubes and laryngeal masks, stylete, bougie and quick track. The surgeon has been there already and prepared, in case of probable need for tracheotomy.

Due to the certain concern about difficult intubation, the inhalation induction with sevoflurane with gradual rising percentage was chosen for the patient to maintain the spontaneous breathing. The depth of anesthesia has been assessed with Cerebral State Monitoring (CSM). The laryngoscopy was performed after the provider was assured about the enough depth of anesthesia through monitoring data. The Cormack score was 1 and the intubation with number 4 cuffed tube was done uneventfully. Fentanyl 50 µg and atracurium 10 mg were given after securing the airway. While the bilateral sphenoidectomy, posterior and anterior etmoidectomy and bilateral optic nerve decompression was being performed, the child was on maintenance of 1.5 % Sevoflurane, 50% O2, 50% N2O. Repeated doses of 5mg Atracurium and 25 µg fentanyl were given during 255 minutes procedure. The hemodynamic indices, oxygen saturation and end tidal CO2 were in acceptable range. At the end the muscle relaxant was reversed with 1.5 mg Neostigmine and 0.5 mg Atropine. The child was extubated and

transferred to the recovery unit. After reaching full awake state and met the discharge criteria, he was transferred to a ward.

Discussion

Crouzon syndrome is a complex craniosynostosis of autosomal dominant transfer, with a highly variable phenotypic appearance. Although of variable penetrance, is thought to be caused in part by a mutation in the fibroblast growth factor receptor-2 (FGFR2) on chromosome 10q 25.3-q26 (4, 11) and more than 30 different mutations within the gene have been documented in separate families (11). Aside from craniofacial malformations, the disease can also cause hearing loss and airway challenges due to malformations in the nasal cavity and nasopharyngeal airway (4).

Differential diagnosis of Crouzon's syndrome are Apert syndrome and other problems including Carpenter syndrome, Pfeiffer syndrome, Seatre-Chotzen syndrome, and Jackson Weiss syndrome (11). Before the novel achievements in mutation detection in genes, the diagnosis of Crouzon syndrome was made according to the clinical signs of the patients, including acrocephaly, exophthalmos and maxillary hypoplasia with ''parrotbeak'' nose, short upper lip, high narrow palate, narrowly spaced teeth and prognathism (7). Although the severity of these signs and symptoms varies among affected children (3), most of them need therapeutic, corrective and cosmetic surgeries from their infancy to older ages even adulthood including pregnancy (12). Craniofacial abnormalities are common at birth and may progress with time (3), thus anesthesiologists and surgeons are involved in challenging even life threatening situations.

From the perspective of an anesthesiologist, difficult intubation is the most important consideration in perioperative management in patients with abnormalities in head and neck and providing a secure airway in the same common surgical field is a demanding issue, required dynamic teamwork in the perioperative period. Even though the elective fiberoptic intubation is recommended in various literatures (12, 13) the device may not be available in the operating room, or the patient is uncooperative for the procedure. According to these issues, the anesthesiologists should be prepared and skilled enough in providing a secure airway with other alternative approaches.

Our patient was uncooperative for awake elective fiberoptic intubation and he had a history of undergoing general anesthesia three times in the past without any documentation of the techniques and methods. We decided to provide general anesthesia with inhalation induction and maintain the spontaneous breathing. The surgery team was available in the operating room with all equipments in case of need to secure the airway through establishing emergency tracheostomy. Despite the fact that the operation lasted more than 4 hours, we did not face any untoward conditions in terms of bleeding, malposition, thermal and ventilation problems.

Conclusion

As a result of novel achievements in genetic and cellular studies and uprising hope to treat the patients with rare genetic disorders like Crouzon syndrome, anesthesiologists find themselves in new era required skillful adaptable individuals who can work in dynamic situations. The airway management, the most important breath taking issue in the perioperative period, requires full knowledge about the underlying disease, the perioperative probable events, the available equipment and making the best decision to use the least harmful technique

Acknowledgment

The authors would like to thank the kind help of physicians and nurses, operating room and anesthesiology ward staffs, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran for their kind help and support.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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