Anesthesiology considerations during maxillofacial surgery in a child with Noonan's syndrome: A Case Report

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ABSTRACT

Anesthesiology considerations during maxillofacial surgery in a child with Noonan's syndrome: A Case Report

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Noonan syndrome (NS) is an autosomal dominant disorder characterized by anatomic and patho-physiologic abnormalities.Anesthetic management in these cases has many challenges regarding airway management and cardiovascular stability.We present a case report of a 11-year-old male child who was scheduled for maxillofacial surgery under general anesthesia.

INTRODUCTION

Noonan syndrome (NS) is a common genetic disorder with multiple congenital abnormalities. The syndrome is transmitted as an autosomal dominant trait. It is characterized by congenital heart disease, short stature, a broad and webbed neck, sternal deformity, variable degree of developmental delay, cryptorchidism, increased bleeding tendency,lymphatic dysplasia's and characteristic facial features that evolve with age. The syndrome has a worldwide distribution and a reported incidence of 1 in 1000 to 1 in 2500 live births.NS is a clinical diagnosis. Establishing the diagnosis can be very difficult, especially in adulthood. There is a great variability in expression and the phenotype becomes less pronounced with increasing age. Several scoring systems have been devised to help the diagnostic process[1,2].

The problems regarding anesthesia of these patients are difficult airway/intubation because of high arched palate, micrognathia and short webbed neck,limited cardiovascular reserve which is associated with cardiovascular disease especially pulmonary stenosis/atrial septal defect (mostly right sided lesions), difficulties in

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performing awake procedures or obtaining consent because of mental retardation, difficulties with intravenous access because of lymphoedema/redundant skin, electrolyte disturbances because of congenital renal abnormalities, increased risk of spinal hematoma with regional procedures because of bleeding diathesis (decreased factor XI,XII, Von Willebrand's factor or platelet dysfunction) and technical difficulties with regional procedures because of kyphoscoliosis/short stature[3,4].

In this report, we describe the preoperative evaluation and anesthetic management of a child with Noonan's syndrome scheduled for a maxillofacial surgery (multiple teeth extraction) with general anesthesia.

CASE REPORT

An 11-year-old male (weight 22.5 kg, height 125 cm) with known Noonan syndrome, was referred for an anesthetic evaluation to be scheduled for a maxillofacial surgery with general anesthesia.

From his history, he was born at the end of the 35nd week after an abnormal pregnancy because it was complicated by preeclampsia. On the first year of his life a valvuloplasty of pulmonary valve and a surgical intervention to close the atrial septal defect was carried out, as he had an atrial and ventricular septal defect, pulmonary stenosis and regurgitation and aortic regurgitation. There were no postoperative complications and the baby was released without the need for further cardiac surgery. After that, he had been under annually cardiological evaluation throughout childhood and he didn't require any medications for his cardiac function.

The diagnosis of the Noonan Syndrome was probable from the 3rd year of his life from his clinical symptoms and the fact that there was a family member with characteristics of Noonan's syndrome (father), but molecular testing which offers the opportunity to confirm the diagnosis in many patients, hasn't been done yet due to economic insufficiency of the family. At the 7th year of his life he had another operation for undescended testicles.

Presently, the patient had no symptoms pointing toward any cardiac decompensation and according to his father his exercise tolerance was good.His last cardiac evaluation 10 months ago revealed mild remaining pulmonary stenosis and regurgitation and aortic regurgitation. There was no left ventricular outflow tract obstruction. The basal septum and left ventricular posterior wall motion appeared normal and there was no evidence of systolic anterior motion of the mitral valve.

Clinically, hehadcharacteristic features of Noonan syndrome including hypertelorism with down-slanting palpebral fissures, ptosis, low-set posteriorly rotated ears with a thickened helix, a webbed neck and short stat-

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ure.Furthermore, there was obvious mental retardation of the child. On pediatric examination pulse rate was 94bpm, blood pressure was recorded to be 96/51 and SpO2 98%.On auscultation of the heart a systolic murmur 2/6 was heard at pulmonary and aortic area. On auscultation of the lungs the respiratory sound was normal.There wasn't history of allergic reactions.

From his preoperative investigations the hemoglobin level, the serum electrolytes, creatinine, glucose, aspartate transaminase (serum glutamic oxaloacetic transaminase), alanine transaminase (serum glutamic pyruvate transaminase), and alkaline phosphatase were within the normal limits. The routine coagulation tests were normal (PT, INR and aPTT), as the number of his platelets. Also, he had no history of easy bruising or excessive bleeding with minor trauma.

The preoperative evaluation of his airway demonstrated, moderate degree of micrognathia, dental malocclusion, high palatal arch, a slightly webbed neck with moderate neck extension and limited mouth opening. The Mallampatti score was 3.

Unfortunately, we haven't advised any premedication before surgery and when the child arrived in the operation theater wasn't very cooperative and especially during the dissociation from his father. Nevertheless, a peripheral venous access was secured without difficulty using a 20G cannula. On patient's arrival in the operating room, non-invasive monitoring (pulse oximeter, electrocardiographic monitor, blood pressure cuff) was established. His blood pressure was 100/70 mmHg, his heart rate was 90 beat/min, and oxygen saturation was 98%. Before induction to anesthesia oxygen was given via to face mask.The patient was given 1mg midazolam.Induction of anesthesia was performed in the supine position by using propofol (total dose of 80mg) and fentanyl (50μg) incrementally. After establishing successful bag mask ventilation, rocuronium 15 mg was administered to facilitate tracheal intubation.

The patient was intubated with a 4.5 mm internal diameter cuffed oral endotracheal tube following a Cormack Lehane grade II view on laryngoscopy. He had the short, hypoplastic and rounded shaped epiglottis that covered the vocal cord, and was visible only the inferior border of the commissure fissure. The tracheal tube was smoothly carried into the trachea and its position confirmed by auscultation of the lungs and capnography. Resuscitation and difficult airway cart was kept ready. The patient was ventilated with an air/oxygen mixture (FiO2 40%), tidal volume 220 (10ml/Kg) and respiratory rate 22. After induction, the patient remained cardiovascular stable throughout the procedure and anesthesia was maintained with sevoflurane (1 minimum alveolar concentra-

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tion). End-tidal carbon dioxide tension was maintained at 37-39 mmHg. During the perioperative period, his heart rate ranged from 80-100 beats/min and his systolic and diastolic blood pressure varied from 100 to 109 mmHg and from 55 to 60 mmHg, respectively. The oxygen saturation was maintained at 99-100%. The surgery lasted 60 minutes, the estimated amount of blood loss was 10 ml and a total of 200 ml of Ringer's Lactate was administered intravenously during surgery. For postoperative pain control, we administered paracetamol 400mg IV as a loading dose. The residual neuromuscular blockade was reversed with sugammadex 100mg I.V at the end of the surgery and the patient recovered consciousness 5 minutes later. After extubation, the patient was removed to PACU (post anesthetic care unit) for continuous hemodynamic and respiratory monitoring for 60 minutes. During this period, the heart rate, the blood pressure and respiratory frequency were maintained within normal limits. The rest of the post-operative period in the ward was uneventful. Patient was discharged 24 hours after the surgery.

DISCUSSION

Studies on the Noonan syndrome had been first conducted in 1963 by Jaqueline Noonan (pediatric cardiologist of the University of Kentucky), who noticed a heart defect (stenosis of the pulmonary valve) associated in most of the cases to common physical characteristics such as short height, hypertelorism, low junction of the ears, and deformed thorax and face in some of her patients. The first description of the syndrome, however, was probably made in 1883 by Kobylinski. Initially the Noonan syndrome was mistaken for the Turner syndrome for the similarity in the physical characteristics. The karyotype of Noonan syndrome is normal.The characteristics distinguishing it from Turner's syndrome include karyotype analysis, gender distribution (Noonan syndrome only in women),and fertility, the site of the cardiac lesion, the facial appearance and the presence of mental retardation[5,6].

Subsequently, studies conducted by Tartaglia allowed to identify the gene responsible for the Noonan syndrome, which is located on the long arm of the chromosome 12 (12q24.1). Later, other studies highlighted the genetic heterogeneity of the condition. The gene PTPN11 situated on chromosome 12q24 could be responsible for such syndrome. It codifies the protein SHP-2, crucial for transferring the intracellular signal that regulates some developmental processes, amongst them the formation of the semilunar valves of the heart. In order to test this hypothesis they have screened this gene, searching for possible mutations, first in familiar cases and subsequently in sporadic cases[5,6].

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Although currently the diagnosis is exclusively based on clinical criteria, the discovery of the mutation of gene PTPN11 in about 50% of the patients affected by the syndrome might lead to a better understanding of the pathogenetic mechanisms that determine some of the phenotypes of the syndrome and, probably, will enable in the future a laboratory test for confirming the diagnosis or the pre-birth diagnosis. The syndrome affects various ethnic groups[5,6].

The clinical picture of Noonan's syndrome consists of short stature, webbing of the neck, flattening of the mid-face, hypertelorism, ptosis, epicanthal folds, antimongolian palpebral slant, micrognathia, ear abnormalities, and a "shield-shaped' sternal deformity that gives the illusion of widely separated nipples. In addition, most patients have pedus carinatum or excavatum, cubitus valgus, and frequently, congenital heart disease. The most common congenital lesion is pulmonic stenosis either alone or in combination with a septal defect, usually atrial[7].

Mental retardation, usually mild, is a frequent feature of the syndrome. Renal and skeletal anomalies have also been described. The inheritance may be familial, autosomal dominant, or sporadic, but no chromosome abnormality has yet been found[7].

The anesthetic considerations and potential problems of the patient with Noonan's syndrome include the possibility of a difficult airway, impairment of cardiopulmonary function, and issues associated with mental retardation and short stature. The potential for airway difficulties in Noonan's syndrome is based on the redundant thick webbed neck, micrognathia, and high arched palate, as well as other described facial abnormalities. Awake intubation (oral or nasal might be technically impractical in a shrugging child as well, as probably difficult due to the described facial abnormalities[8,9].

In our caselocal anesthesia with mild sedation was excluded because of the mental retardation and difficulty in cooperation and also the difficulties of the operation (multiple teeth extraction). So general anesthesia with endotracheal intubation was one way and that was successfully accomplished using a conventional laryngoscope and a soft introducer (bouggie).

A cervical spine radiograph is advisable in patients with significant short stature before attempting manipulation of the neck. This is to exclude atlantoaxial instability, otherwise, cervical cord compression may result. In our case there wasn’t significant short stature, so we didn’t ask for a cervical spine radiograph. Although we are unaware of reports of cervical instability associated with Noonan's syndrome, odontoid dysplasia with atlantoaxial instability occurs frequently in syndromes affecting the axial skeleton. If the odontoid process is hypo-

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plastic, the atlas may dislocate anteriorly and may cause spinal cord compression[8].

Congenital heart disease is a common component of Noonan's syndrome. Pulmonic valve stenosis was encountered in all patients in one seriesand in 30%-50% of patients in another study. Coarctation of the aorta and aortic stenosis were present in 25%-40% of patients with Noonan's syndrome in the same reports. Eccentric hypertrophy, affecting the superior portion of the anterior wall, the septum, or the diaphragmatic portion of the left ventricle, and progressive obstructive cardiomyopathy has been reported previously in association with Noonan's syndrome**.** The eccentric hypertrophy frequently is non-obstructive and asymptomatic[10,11].The child in our case report had an annually cardiological evaluation throughout childhood and he didn't require any medications for his cardiac function after the valvuloplasty and the surgical intervention to close the atrial septal defect, when he was 12 months old.A hemodynamically insignificant ventricular septal defect (diagnosed by echocardiogram despite absence of characteristic murmur) was an additional finding in this patient. The anesthetic goals include maintenance of appropriate intravascular volume while avoiding direct or reflex increases in contractility or heart rate. The detrimental effects of tachycardia might compromise cardiac output.

Children and/or mentally retarded patients present the problems of intravenous access and smooth induction to a deep level of general anesthesia, both desirable conditions for induction in these patients. Laryngoscopy was attempted only after achieving deep levels of anesthesia. This was to prevent catecholamine release or increases in sympathetic nervous system activity and tachycardia.

The respiratory system is often compromised in patients with Noonan's syndrome because of the "shield-shaped' chest, pectus deformity, kyphoscoliosis, and short stature. Preoperative evaluation should include chest roentgenogram, arterial blood gas determinations, and/or pulmonary function studies in these patients. This assessment may be helpful in predicting the need for postoperative ventilation, intraoperative monitoring and management. Ventilation was adjusted according to the monitored end-tidal CO_2[1,8].

The patient with Noonan's syndrome may also have a variety of orthopedic abnormalities that should be considered in planning the anesthetic procedure. In addition to kyphoscoliosis and short stature, patients may exhibit cubitum valgum, clinodactyly, and vertebral anomalies that may affect positioning, protection of pressure points with padding, intravenous access, and choice of anesthetic technique (regional versus general anesthesia)[1,8].

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The differential diagnosis of the child with Noonan syndrome is considerable. It is important to exclude Turner's syndrome and other chromosomal abnormalities for example trisomy 8p, trisomy 22mocaicism. Other syndromes that combine facial changes with short stature or cardiac abnormalities may be confused with Noonan syndrome for example Williams or Aarskog's syndrome. Both of these syndromes are well defined and recognition of the full phenotype of Noonan syndrome should readily allow accurate discrimination between them. Two other syndromes have been differentiated from Noonan syndrome based on specific ectodermal changes. The association of multiple lentigines with pulmonary stenosis and deafness led to the description of leopard syndrome[12,13].

CONCLUSION

The syndrome has a reported incidence of 1 in 1000 to 1 in 2500 live births and so it isn't a very rare condition. Children or adolescents with short stature, facial abnormalities and cardiovascular defects should be evaluated for this syndrome. Preoperative evaluation should include a thorough evaluation of the airway and cardiovascular system. Intraoperatively we must be prepared for a difficult airway and avoid the sympathetic nervous system activation. The whole anesthetic management should consider all the above anomalies and be designed to prevent further complications. Intense monitoring should be continued in the postoperative period to avoid the anticipated surgical and anesthetic adverse effects and ensure a successful outcome.

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Author Disclosures:

Authors Kolonia K, Papadonta ME, Sarakatsianou Ch, Variadis D, Georgopoulou S have no conflicts of interest or financial ties to disclose.

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