Anesthetic Management of a Child With Noonan's Syndrome and Idiopathic Hypertrophic Subaortic Stenosis

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Noonan's syndrome is a relatively rare hereditary disorder characterized by abnormalities of the facial, cardiovascular, and skeletal systems (1,2). There has been only one case report describing a patient with Noonan's syndrome in which the patient underwent a cesarean section under regional anesthesia (3). In this report we describe the preoperative evaluation and anesthetic management of a child with Noonan's syndrome complicated by idiopathic hypertrophic subaortic stenosis (IHSS), a lesion not typically associated with this syndrome.

Case Report

A 7-yr-old girl was admitted for elective cholecystectomy because of repeated episodes of cholecystitis secondary to cholelithiasis. The diagnosis of Noonan's syndrome was made when she was 18 mo of age. At that time she was admitted with facial abnormalities that included hypertelorism, bilateral epicanthal folds, antimongolian palpebral slant, ptosis, micrognathia, flattening of the midface, low-set ears, and high palatal arch. Chromosomal studies showed her to be genotype 46XX. She exhibited moderate developmental delay, pronounced webbing of the neck, widely spaced nipples, mild lordosis, lower leg edema, short stature, and IHSS. Two years before this admission for surgery, she had complained of fatigue. An echocardiogram performed at that time demonstrated IHSS with a small ventricular septal defect. She had been clinically controlled with 12.5 mg/day of atenolol given orally. The patient had undergone no previous anesthetic. The family history was unremarkable for anesthetic complications or other congenital abnormalities.

Physical examination revealed an alert, cooperative girl who weighed 22 kg (45th percentile for age), and whose height was 93 cm (below third percentile for age). Arterial blood pressure was 100/60 mm Hg, heart rate was 86 beats/min, and respiratory rate was 24 breaths/min. Echocardiogram, performed with sedation and as a nonstressed study, revealed a hypertrophied septum (1.8 cm thick) with concentric hypertrophy of a small hyperkinetic left ventricle. A small high ventricular septal defect and mild left atrial enlargement were noted. There was also muscular subaortic stenosis with a 15 mm Hg subaortic gradient and mild mitral regurgitation. The electrocardiogram was suggestive of left atrial enlargement and left ventricular hypertrophy.

Preoperative analysis of arterial blood gases showed pHa = 7.39, $Paco_2$ = 41 mm Hg, and Pao_2 = 64 mm Hg breathing room air. Evaluation of her airway demonstrated a high palatal arch, moderate degree of micrognathia, dental malocclusion, and a webbed neck. Radiologic studies showed a mild degree of kyphoscoliosis (15°) and lordosis but a normal cervical spine. Hemoglobin was 12.4 g/dL, and serum electrolytes, creatinine, glucose, aspartate transaminase (serum glutamic oxaloacetic transaminase), alanine transaminase (serum glutamic pyruvic transaminase), and alkaline phosphatase were within normal limits.

A fiberoptic laryngoscope as well as a variety of laryngoscope blades were prepared. The patient was orally premedicated with atenolol (12.5 mg) and diazepam (5 mg) 2 h before induction of anesthesia. Before establishing intravenous access, 4 mg of midazolam was administered intranasally. The child readily accepted a 22-gauge intravenous catheter in her left arm after 10 min.

After application of electrocardiograph leads, pulse oximeter (oxygen saturation [Spo_2] = 95%), and noninvasive blood pressure monitors, anesthesia was induced with halothane, nitrous oxide, and oxygen via a face mask. Controlled ventilation was begun, and a right radial arterial catheter was then inserted for continuous monitoring of blood pressure and arterial blood gas tensions if needed. A mild tachycardia of 110 beats/min was controlled with three bolus doses of

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200 μg/kg of esmolol followed by a continuous infusion of esmolol before laryngoscopy. The heart rate returned to preoperative levels of 80–90 beats/min. Paralysis was provided by vecuronium (0.1 mg IV). Three attempts to directly visualize the glottis using a laryngoscope blade were unsuccessful. Endotracheal intubation was finally accomplished by passage of a 3.3-mm Rüsch introducer-stylet into the trachea as a guide followed by the insertion of a 5.0-mm internal diameter, uncuffed endotracheal tube inserted over the introducer. During the attempts at endotracheal intubation, blood pressure, Spo_2, and heart rate remained at preinduction levels. Anesthesia was maintained with a mixture of 0.5%–1.0% halothane, oxygen, and air and a continuous infusion of 0.4–0.8 $\mu g \cdot kg^{-1} \cdot h^{-1}$ of sufentanil, 100–300 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of esmolol, and 0.05–0.10 $mg \cdot kg^{-1} \cdot h^{-1}$ of vecuronium. Antibiotic prophylaxis was with ampicillin and gentamicin administered intravenously. Ventilation was controlled to achieve an end-tidal CO_2 of 35–40 mm Hg, and the Spo_2 was maintained between 90% and 100%. Intravenous fluids were initially 20 mL/kg of lactated Ringer's solution followed by aggressive replacement of losses during the intraoperative course. A total of 750 mL of fluid was administered intravenously during the 180-min operation. The estimated blood loss was 30 mL. Reversal of residual paralysis was accomplished with the intravenous administration of 0.2 mg of glycopyrrolate and 1.5 mg of neostigmine. The trachea was successfully extubated during deep general anesthesia. During the immediate postoperative period, the heart rate and arterial blood pressure were maintained within normal limits using a continuous infusion of esmolol. Subsequently, β-adrenergic blockade was maintained by intravenous propranolol followed by oral atenolol. The patient was discharged 3 days after an uneventful recovery.

Discussion

Noonan's syndrome is an increasingly recognized but relatively rare clinical entity that presents with various congenital anomalies. The syndrome has been recognized in phenotypic males who have certain anomalies that also occur in females with Turner's syndrome. Both males and females have normal karyotypes (1,2).

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 pectus 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 (1). The association of Noonan's syndrome with IHSS has been previously described (4). 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.

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, as encountered in our patient, is based on the redundant thick webbed neck, micrognathia, and high arched palate, as well as other described facial abnormalities (3). Regional anesthesia was excluded in our patient because it was believed that the associated vasodilation might increase the subaortic gradient and further compromise the patient's cardiac output. Furthermore, the child's moderate mental retardation and potential combativeness, coupled with probable technical difficulties associated with the short stature, kyphoscoliosis, and lordosis, made regional anesthesia impractical and potentially dangerous. An awake oral or nasal intubation might have been technically impractical in a struggling child as well as probably difficult due to the described facial abnormalities. Furthermore, the detrimental effects of tachycardia might again compromise cardiac output.

The decision to use a slow inhalation induction followed by controlled ventilation was made after discussion with the parents. A fiberoptic intubation set was available in the event of a failed intubation by direct laryngoscopy. Endotracheal intubation was successfully accomplished using a conventional laryngoscope and introducer.

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. 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 (5). If the odontoid process is hypoplastic, the atlas (C1) may dislocate anteriorly and may cause spinal cord compression (3,5).

Congenital heart disease is a common component of Noonan's syndrome. Pulmonic valve stenosis was encountered in all patients in one series (6), and in 30%–50% of patients in another study (7). Coarctation of the aorta and aortic stenosis were present in 25%–40% of patients with Noonan's syndrome in the

same reports (6,7). Eccentric hypertrophy, affecting the superior portion of the anterior wall, the septum, or the diaphragmatic portion of the left ventricle, and progressive obstructive cardiomyopathy have been reported previously in association with Noonan's syndrome (5,7). The eccentric hypertrophy frequently is nonobstructive and asymptomatic.

The patient we describe is one of the rare cases in whom the hypertrophy became obstructive and symptomatic (5). A hemodynamically insignificant ventricular septal defect (diagnosed by echocardiogram despite absence of characteristic murmur) was an additional incidental finding in this patient. The degree of dynamic obstruction in IHSS varies with the rate of ejection of blood and the volume of the left ventricle. Obstruction is increased by tachycardia, increased contractility, arterial vasodilation, and decreased preload (8–11). The anesthetic goals therefore include maintenance of appropriate intravascular volume while avoiding direct or reflex increases in contractility or heart rate.

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. Intravenous access and maintenance of adequate preload were accomplished after premedication. Fluid (20 mL/kg) was given just before induction to increase preload. Laryngoscopy was attempted only after achieving deep levels of inhalational anesthesia and the administration of esmolol. This was to prevent catecholamine release or increases in sympathetic nervous system activity and tachycardia, which might otherwise have increased the subaortic pressure gradient (8).

The respiratory system is often compromised in patients with Noonan's syndrome because of the "shield-shaped" chest, pectus deformity, kyphoscoliosis, and short stature (1,2). 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. In this case it was decided to insert an arterial catheter for continuous monitoring of blood pressure as well as arterial blood gases if necessary. The low preoperative Pao_2 value obtained breathing room air was considered to be most likely due to right-to-left shunting via the ventricular septal defect, which increases when the child cries in response to arterial puncture. Because the degree of kyphoscoliosis was mild, an increased (A-a) CO_2 gradient was thought to be unlikely. Ventilation was adjusted according to the monitored end-tidal CO_2.

The patient with Noonan's syndrome may also have a variety of orthopedic abnormalities (1,2) that should be considered in planning the anesthetic. 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).

In summary, patients with Noonan's syndrome may have a variety of anomalies, some of which present challenging anesthetic dilemmas. Preoperative evaluation should include a thorough evaluation of the airway and cardiovascular system. The anesthetic plan should consider the above anomalies and be designed to prevent further complications. Inhalation induction of anesthesia allows airway control and maintenance of a low left ventricular outflow pressure gradient. Halothane and β-adrenergic blockers are useful and well tolerated in most patients with IHSS. Adequate administration of intravenous fluid is advisable to prevent increases in the subaortic gradient.

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