CLINICAL VIGNETTE

Noonan Syndrome and Anesthesia

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Introduction

Noonan syndrome, an autosomal dominant disorder with heterogeneous phenotypic expression, was first described by Jacqueline Noonan in 1963.[1] The most common manifestations include pulmonic stenosis, short stature, low-set ears, and wide-set eyes. Due to a gain of function mutation in the RAS/MAPK signaling pathway,[2] its clinical presentations reflect the diverse downstream ramifications of this overactivation.

The ramifications include cerebrovascular malformations, abnormal pigmentation, auditory defects, lymphatic dysplasia, hematological abnormalities associated with coagulopathy, and intellectual disabilities. Noonan syndrome affects an estimated 1 in 1000-2500 individuals, and is the second most common syndromic congenital heart disease (CHD) trailing only Down syndrome.[3]

Case Presentation

A 51-year-old female with Noonan syndrome complicated by congenital pulmonic valve stenosis, status post valvotomy and infundibulotomy at age 4, was evaluated for a colonoscopy under monitored anesthesia care (MAC) for a history of chronic rectal bleeding. Her other medical history included mild-intermittent asthma and a history of pregnancy related congestive heart failure.

During pre-operative anesthesia assessment, patient reported no recent lower extremity edema, fatigue, orthopnea, or paroxysmal nocturnal dyspnea. Her electrocardiogram showed normal sinus rhythm with no ischemic changes, and a right superior axis deviation. Her echocardiogram was essentially unchanged from her prior study with EF of 60-65%, moderate pulmonary regurgitation, mild pulmonic stenosis, and mild mitral regurgitation with mild left atrial dilation. Due to her residual pulmonic stenosis and regurgitation in the setting of Noonan syndrome, the patient was further evaluated with a cardiac MRI, which showed findings consistent with the previous TTE studies.

On the day of the scheduled colonoscopy, patient was placed on standard anesthesia monitors (EKG, non-invasive blood pressure cuff, pulse oximetry, capnography) and given supplemental oxygen via face mask. She underwent monitored anesthesia care with intravenous propofol and maintained spontaneous ventilation with a patent airway. The patient

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tolerated the procedure well with stable vital signs and discharged home in stable condition without event.

Discussion

Noonan syndrome, given its highly pleomorphic clinical patterns, can be associated with numerous potential risks in patients undergoing anesthesia care. Our patient was spared the severe cardiac manifestations that would otherwise place her at higher risk for anesthetic complications. Fortunately, her pulmonic stenosis was surgically addressed early in childhood. Her residual pulmonic stenosis and regurgitation were not functionally limiting, and the lack of ischemic changes on ECG as well as the lack of anginal symptoms on her history were reassuring.

The patient’s mild congestive heart failure symptoms during pregnancy have been reported in other pregnant patients with Noonan syndrome.[4] During the first and second trimesters of pregnancy, the peripheral vascular resistance (PVR) falls, with recovery occurring by the postpartum period.[5] Decreased PVR leads to decreased venous return to the right heart and consequent impairment of left ventricular output in a pregnant patient with pulmonic stenosis. This increases risk for procedures that cause sympathectomy such as epidural anesthetics.[6]

While the patient tolerated MAC anesthesia well, the diagnosis of Noonan syndrome, particularly in the pediatric population, warrants careful pre-operative evaluation for the array of cardiovascular, skeletal, hematological, and neurological manifestations.

From a cardiovascular standpoint, the most common pathology in Noonan syndrome is pulmonic stenosis, but numerous other cardiac abnormalities may be present. A retrospective case series of 293 patients with Noonan syndrome, identified pulmonic stenosis (57%), ASD (32%), hypertrophic cardiomyopathy (16%), and VSD (12%) with less than 10% having patent ductus arteriosus, mitral valve prolapse, bicuspid aortic valve, aortic root dilation or aortic coarctation. Many such pathologies occurred in combination.[7]

Grading of pulmonic stenosis is based on transthoracic echocardiography with Doppler, by measuring the velocity across the right ventricular outflow tract obstruction and deriving the transvalvular gradient pressure. A peak gradient of <36mmHg

is mild, 36-64mmHg is moderate, and >65mmHg is severe, with management additionally guided by associated patient symptoms.[8]

Intraoperatively, pulmonic stenosis, especially in conjunction with right ventricular hypertrophy, requires special attention in the setting of increased preload and the need for adequate pulmonary perfusion. Conditions that may increase right-sided heart pressures such as hypoxia, elevated peak airway pressures or hypercarbia should be avoided.[9] Intraoperative monitoring of systemic vascular resistance and mean arterial pressure with central lines and arterial lines may be indicated for severe pulmonic stenosis. The condition may be further complicated with intra-atrial or intraventricular defects, with intracardiac shunting, which can lead to paradoxical embolism.

Noncardiac manifestations of Noonan syndrome may also impact care. Abnormal triangular shaped facies could hinder bag mask ventilation. Structural airway abnormalities may may increase difficulty of laryngoscopy. Pectus deformities are present in an estimated 70% of Noonan syndrome[10] and can compromise lung capacities, potentially causing impaired spontaneous or mechanical ventilation.

Noonan syndrome patients are at elevated risk for coagulopathy secondary to thrombocytopenia, monocytosis, or myeloproliferative disease and should be screened for history of easy bruising or bleeding. Laboratory assessment of complete blood count and coagulation studies may be considered.

In conclusion, while the potential complications arising from Noonan syndrome are multiple, an individualized plan based on the specific cardiovascular, pulmonary, musculoskeletal, and hematological disease processes will enable anesthesiologists to provide safer patient care.

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