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Anesthetic care during spinal fusion in a patient with Williams syndrome

M. Gross[1], D. P. Martin[2,3], W. Samora[4], J. Klamar[4], J. D. Tobias[2,3]

[1]Ohio University Heritage College of Osteopathic Medicine, Dublin, Ohio, USA
[2]Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital, Columbus, Ohio, USA
[3]Department of Anesthesiology & Pain Medicine, The Ohio State University, Columbus, Ohio, USA
[4]Department of Orthopedic Surgery, Nationwide Children's Hospital and The Ohio State University, USA Columbus, Ohio

Corresponding author: M. Gross, Ohio University Heritage College of Osteopathic Medicine, Dublin, Ohio, USA
Email: mg975311@ohio.edu

Keypoints

1. Williams syndrome is a complex genetic disorder with cardiovascular, renal, endocrine, gastrointestinal, and central nervous system involvement.
2. Structural cardiovascular abnormalities, most commonly supravalvular aortic stenosis, occur in 80% of patients with Williams syndrome.
3. Sudden death related to stenosis of the coronary ostia or the coronary arteries may occur with coronary ischemia resulting in perioperative cardiac arrest.
4. Perioperative goals include preservation of sinus rhythm, avoidance of tachycardia, maintenance of adequate diastolic blood pressure to ensure coronary perfusion, and control of factors that determine myocardial oxygen consumption (systemic vascular resistance, preload, and contractility).

Abstract

Williams syndrome, also known as Williams-Beuren syndrome, was originally described in 1961. Patients with Williams syndrome have several distinguishing characteristics, including dysmorphic facies, cognitive dysfunction, hypercalcemia in infancy, and distinctive emotional and behavioral traits. This complex genetic syndrome results from a microdeletion on chromosome 7 that involves approximately 28 genes including the elastin gene (ELN). This deletion of ELN has been linked to many of the common connective tissue manifestations of Williams syndrome including the characteristic cardiovascular structural abnormalities. The associated orthopedic involvement including scoliosis and kyphosis frequently requires surgical intervention. We present a 12-year-old adolescent with Williams syndrome requiring anesthetic care for a posterior spinal fusion. Associated organ system involvement and its perioperative impact are discussed.

Keywords

Williams syndrome, elastin, supravalvular aortic stenosis, anesthesia

Introduction

Williams syndrome (WS), also known as Williams-Beuren syndrome, was originally described by Williams, Barrat-Boyes, and Lowe in 1961.[1] WS affects multiple organ systems and has several distinguishing characteristics, including dysmorphic facies, cognitive dysfunction, hypercalcemia in infancy, and distinctive emotional and behavioral traits. Unique congenital cardiovascular malformations include supravalvular aortic and pulmonary stenosis (SVAS).[2,3] This complex genetic disorder is

estimated to occur in approximately 1 in 10,000 live births, resulting from a microdeletion on chromosome 7.[2,4,5] The chromosome 7q11.23 deletion involves a region of approximately 28 genes including the elastin gene (ELN).[5] The deletion of ELN has been linked to many of the common connective tissue manifestations of Williams syndrome.[3] Cardiovascular structural abnormalities are present in up to 80% of Williams syndrome patients and are the most common cause of death.[2,6] During the perioperative setting, coronary artery stenosis has been frequently documented as a major contributor to sudden death in patients with WS.[7-10] The associated orthopedic involvement including scoliosis and kyphosis frequently requires surgical intervention and the multisystem involvement of WS poses a significant risk in the perioperative care for these patients. We present a 13-year-old adolescent with WS requiring anesthetic care during a posterior spinal fusion. Potential end-organ involvement is reviewed and its perioperative impact discussed.

Case report

Preparation of this case report followed the guidelines of the Institutional Review of Nationwide Children's Hospital (Columbus, Ohio). A 12-year-old, 52-kilogram adolescent female with Williams syndrome presented for posterior spinal fusion for treatment of thoracolumbar levoscoliosis. The diagnosis of Williams syndrome was confirmed by genetic testing at 3 months of age following a high clinical suspicion due to characteristic facies. Additional past medical history and comorbid conditions included mild supravalvular aortic stenosis, mild aortic regurgitation, Chiari malformation type 1 (surgically corrected), syrinx of the spinal cord, developmental delay, conductive hearing loss, and ADHD. Past surgical history included intradural Chiari decompression at age 9 years and an aborted posterior spinal fusion 1-2 months prior due to loss of motor evoked potentials (MEPs) after adding traction weight. Of note, anesthetic care during that procedure included anesthetic induction with propofol and maintenance anesthesia with desflurane and remifentanil according to our usual intraoperative protocol (see discussion for a review of anesthetic care during MEP monitoring).[11]

This patient was hospitalized for 2 months to undergo a 3-stage procedure including halo application with traction followed by posterior spinal fusion of the T3-L3 vertebrae. For the purpose of this paper, we will focus on the third or final procedure which included the completion of the posterior spinal fusion and removal of the halo. Inpatient medications at the time of surgery included acetaminophen (640 mg by mouth every 6 hours as needed), oxycodone (5 mg by mouth every 4 hours as needed), docusate sodium (40 mg by mouth every 12 hours), ondansetron (4 mg IV every 8 hours as needed), diazepam (5 mg by mouth every 6 hours as needed), dextromethorphan (30 mg by mouth at bedtime), and melatonin (5 mg at bedtime as needed). Home medications included aripiprazole (1 mg by mouth every day) and methylphenidate (20 mg by mouth every day). These two medications were held the day of surgery. Physical examination revealed a well appearing, normocephalic adolescent female with a Mallampati class II airway with normal dentition. The cardiorespiratory examination was normal. The patient was ambulatory; however, when in bed, there was a halo in place with 35 pounds of traction. Preoperative laboratory evaluation including complete blood count, electrolytes, renal function, and coagulation function were normal. A recent electrocardiogram was normal, and an echocardiogram demonstrated mild supravalvular aortic stenosis and mild aortic regurgitation, unchanged from previous echocardiograms. A series of radiographs of the spine over a period of 5 years showed progressive thoracic levoscoliosis, with a maximum angle of 90 degrees. The patient was held *nil per os* for 8 hours prior to surgery and was transferred to the operating room with 35 pounds of traction applied where routine American Society of Anesthesiologists' monitors were applied. Prior to the induction of anesthesia, midazolam (2 mg) was administered intravenously through a pre-existing 22 gauge intravenous cannula which was in the right median cubital vein. Anesthesia was induced

with intravenous propofol (100 mg) and fentanyl (50 µg). Bag-valve-mask ventilation was provided without difficulty. Endotracheal intubation with a 6.0 mm cuffed endotracheal tube was facilitated by the administration of intravenous rocuronium (20 mg). After anesthetic induction and endotracheal intubation, two large bore peripheral intravenous cannulas and an arterial line were placed using ultrasound guidance. Total intravenous anesthesia with propofol and remifentanil was chosen for this procedure rather than our usual practice of desflurane-remifentanil due to her recent aborted surgery in which MEPs were unable to be obtained.[11] Propofol was started at 150 µg/kg/min and titrated to maintain the bispectral index (BIS) at 50-60. Methadone (5 mg) was administered intravenously followed by remifentanil, starting at 0.2 µg/kg/min and titrated to maintain the mean arterial pressure (MAP) at 55-65 mmHg. Baseline neurophysiological monitoring including motor evoked potentials (MEP) and somatosensory evoked potentials (SSEP) were obtained. The patient was turned and positioned prone. Traction was maintained after turning prone. Tranexamic acid (50 mg/kg bolus dose followed by an infusion at 5 mg/kg/hr) was administered intraoperatively to prevent fibrinolysis and to limit blood loss. Intraoperative cell salvage was used with the return of 150 mL of salvaged and washed blood to limit the need for allogeneic blood products. No allogenic packed red blood cells were administered. The surgical procedure was completed in 5 hours 35 minutes with an estimated blood loss of 400 mL. Acetaminophen (670 mg) and incremental doses of hydromorphone were administered intravenously to provide postoperative analgesia. Following the administration of sugammadex (100 mg), the patient's trachea was extubated, and she was transferred to the post-anesthesia care unit (PACU) and then the cardiothoracic intensive care unit (CTICU). Postoperative analgesia was provided by hydromorphone delivered by patient or nurse-controlled analgesia with intermittent acetaminophen. Intravenous ketorolac was started on postoperative day 1. Her postoperative hemoglobin remained stable at 9.1-9.3 g/dL. Her postoperative course was unremarkable, and she was discharged to the inpatient ward on postoperative day 1 and discharged to home on postoperative day 5.

Discussion

As with any anesthetic encounter, effective perioperative care begins with a preoperative evaluation with a medication review, identification of the end-organ impact of the primary disease process, review of associated comorbid conditions, and a consideration of the implications of the intended surgical procedure. The multisystem involvement associated with Williams syndrome raises many considerations for the anesthetic management of this patient population.

Of primary concern is the cardiovascular pathology including both congenital heart defects such as SVAS and acquired lesions of the coronary arteries. The most frequent anatomic abnormalities of the cardiovascular system in patients with Williams syndrome include supravalvular aortic stenosis (45%), peripheral pulmonary stenosis (37%), mitral valve prolapse (15%), aortic coarctation (14%), ventricular septal defect (13%), and supravalvular pulmonary stenosis (12%). The ELN deletion may result in stenotic lesions of other large arterial vessels including the carotid and renal arteries.[13,14] These peripheral stenotic lesions may progress leading to additional end-organ effects including hypertension, renal insufficiency, and cerebral ischemic events.

During the perioperative period, sudden death related to coronary ischemia and an imbalance of myocardial oxygen delivery and demand has been reported.[2,6-10] Primary involvement of the coronary arteries or severe biventricular outflow obstruction may lead to sudden death. Outflow obstruction results in hypertrophy and increased end diastolic pressure which increase myocardial oxygen demands. Abnormalities of coronary blood flow may result from either primary anatomical obstruction of the coronary ostia or more distal lesions with stenosis of the coronary arteries. In the setting of SVAS, obstruction of a coronary orifice may be the result of distortion of the aortic leaflets with adherence of the left or right coronary

cusp to the wall of the aorta immediately above the ostia. High pre-stenotic pressure can be transmitted to the coronary arteries, resulting in dysplasia, intimal fibrosis and muscular hypertrophy, leading to narrowing of the coronaries arteries. Regardless of the specific lesion, the mechanism for sudden death is myocardial ischemia, decreased cardiac output, and ventricular arrhythmias. Given these concerns, the preoperative work-up should include a history to elicit signs and symptoms of myocardial ischemia including chest pain, physical examination, and echocardiogram. Although not part of our clinical practice, preoperative coronary angiography for all patients with Williams syndrome requiring anesthetic care has even been suggested.[15]

Given the potential for arrhythmias, a preoperative electrocardiogram (ECG) should be obtained. Holter monitoring may be indicated if there are concerns regarding arrhythmias or in patients with a prolonged QT interval.[16] Anesthetic considerations for patients with prolonged QTc interval include avoidance of potential factors that may further prolong the QT interval including an increase in sympathetic tone, hypothermia, electrolyte abnormalities (hypokalemia, hypomagnesemia, and hypocalcemia), and specific attention to choice of medications. A usual reference for the anesthesia provider regarding the effects of medications on the QT interval is WWW.QTDRUGS.ORG.

During the perioperative period, control of factors that affect myocardial oxygen consumption and delivery including heart rate, left ventricular end-diastolic pressure, diastolic blood pressure, and afterload may limit the incidence of coronary ischemia. Despite such care, sudden death remains a significant risk during anesthetic care for patients with Williams syndrome. Given such concerns, our intraoperative care included continuous blood pressure monitoring with an invasive arterial cannula and continuous ECG monitoring with both inferior and anterior leads (5 lead ECG). Intraoperative goals included control of heart rate and maintenance of diastolic blood pressure at preoperative values. We chose to provide postoperative care of our patient in the CTICU with continuous monitoring of blood pressure and a five lead ECG to provide a means of early identification of coronary ischemia or hemodynamic instability.

Craniofacial involvement in Williams syndrome may also impact perioperative care.[17] Difficult mask ventilation and endotracheal intubation must be anticipated due to mandibular hypoplasia, flattened midface, wide mouth, dental malocclusion, and poor dentition which are often seen in these patients.[3,17] Although we were able to successfully accomplish endotracheal intubation using direct laryngoscopy without significant difficulties, the ability to accomplish adequate bag-valve mask ventilation should be demonstrated prior to the administration of neuromuscular blocking agents. Additionally, the appropriate equipment for dealing with the difficult airway should be readily available including indirect laryngoscopy tools.[18]

Additional end-organ involvement may include the central nervous system (CNS), renal involvement, the gastrointestinal tract, and endocrinopathies. CNS involvement includes developmental delay, visuospatial deficits, and seizures. Gastrointestinal involvement varies from gastrointestinal reflux (GER) and chronic abdominal pain. Issues during infancy may include poor feeding, repeated bouts of emesis, and failure to thrive. Early in infancy endocrine concerns including hypercalcemia predominate, but these issues generally subside during the toddler and later years.[19] Hypercalcemia may result in chronic hypercalciuria with stone formation or nephrocalcinosis and worsen GI symptoms including GER and abdominal pain. Subclinical hypothyroidism is noted in up to 15-30% of patients with Williams syndrome.[20] Evaluation of thyroid function is indicated even in the absence of overt clinical signs. Renal involvement with chronic renal insufficiency and hypertension may be the result of hypercalcemia-induced nephrocalcinosis and renovascular hypertension. Renal structural abnormalities include renal aplasia, horseshoe kidney and renal cysts. Preoperative evaluation of renal function (serum

electrolytes, blood urea nitrogen, and creatinine) and a urinalysis are suggested prior to anesthetic care.

Additional perioperative considerations, not specific to Williams syndrome, include the potential for respiratory involvement due to scoliosis and the anesthetic needs to facilitate neurophysiological monitoring. Scoliosis can cause restrictive lung disease, the degree of which may correlate with the severity of the curve.[21] Associated CNS involvement and poor upper airway control with impaired cough effort may further compromise postoperative respiratory function. Preoperative assessment with questions regarding a history of recurrent pneumonia or swallowing problems may identify at risk patients. Preoperative preparation should include aggressive treatment of respiratory infections and a plan to ensure adequate postoperative pulmonary clearance techniques including incentive spirometry or cough-assist. Residual effects of anesthetic agents and neuromuscular blocking medications may impact upper airway control and postoperative respiratory function. Short acting agents whose effects dissipate rapidly should be considered.

Spinal cord injury and resultant neurological deficits are recognized risks during posterior spinal fusion. Neurophysiological monitoring with somatosensory evoked potentials (SSEPs) and MEPs are routinely used to decrease the incidence of neurological deficits.[22] When neurophysiological monitoring is used, specific attention must be directed toward the anesthetic regimen to ensure that adequate MEPs and SSEPs can be obtained. In our patient, given previous concerns, neurophysiological monitoring was facilitated by total intravenous anesthesia.[23]

Williams syndrome is a complex genetic disorder resulting from a microdeletion of the elastin gene. Distinguishing characteristics include dysmorphic facies, cognitive dysfunction, hypercalcemia in infancy, structural cardiovascular and coronary artery involvement, and distinctive emotional and behavioral traits. The multi-organ involvement poses several concerns during the perioperative period (Table 1). Even with appropriate preparation and perioperative care, intraoperative mortality may occur. Of primary concern is control of the myocardial oxygen supply-demand ratio with preservation of sinus rhythm, avoidance of tachycardia, and control of systemic vascular resistance, preload, and contractility.[24]

Table 1. Perioperative considerations of Williams syndrome

1. Cardiovascular involvement
    a. Structural cardiac disease, most commonly supravalvular aortic stenosis
    b. Coronary artery involvement with coronary ischemia
    c. Arrhythmias including prolonged QT interval
2. Difficult bag-valve-mask ventilation and endotracheal intubation
    a. Mandibular hypoplasia
    b. Flattened midface
    c. Poor dentition and dental malocclusion
3. Renal involvement
    a. Hypercalciuria with nephrocalcinosis or nephrolithiasis
    b. Renal insufficiency
    c. Renal artery stenosis and renovascular hypertension
    d. Renal structural abnormalities including renal aplasia, horseshoe kidney, and renal cysts
4. Endocrine involvement
    a. Hypothyroidism
    b. Hypercalcemia
5. Gastrointestinal involvement
    a. Gastrointestinal reflux
    b. Chronic abdominal pain
    c. Failure to thrive, poor feeding, and repeated bouts of emesis in infancy
6. Central nervous involvement
    a. Developmental delay
    b. Visuo-spatial deficits
    c. Seizures
    d. Impaired upper airway control and cough effort
    e. Hypotonia

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