Williams Syndrome and Severe OSA?!
Managing Cardiac Dysfunction in the MRI Suite

Kelly A. Machovec, MD, MPH
Warwick A. Ames, MBBS, FRCA
Duke University Hospital, Durham, North Carolina

Case Summary

An 18 month old male with documented Williams Syndrome (WS) requires anesthesia for a magnetic resonance imaging (MRI) study of the brain to evaluate central sleep apnea. A recent transthoracic echocardiogram shows supravalvular aortic and pulmonic stenosis. Our discussion will begin with Williams Syndrome - the signs and symptoms, risk of sudden death, and relationship of myocardial oxygen supply and demand to achieve hemodynamic stability. Participants will consider options for sedation and general anesthesia, with attention paid to the challenges of anesthetizing and monitoring a cardiac patient in the MRI suite. Further, we will incorporate the problem of sleep apnea into patient management. We will address assessment of sleep apnea severity in a pediatric patient in the absence of a sleep study, and how the cardiopulmonary affects of sleep apnea may impact the hemodynamic profile of patients with WS. This problem based learning discussion will require participants to formulate an anesthetic plan for this patient having both noninvasive (MRI) and invasive (e.g. orthopedic) procedures. Formulation of a postoperative care plan will be included.

Goals and Objectives

1. Describe the features of Williams Syndrome
2. Discuss the myocardial oxygen supply and demand relationship in patients with Williams Syndrome
3. Identify methods to assess obstructive sleep apnea in children in the absence of a formal sleep study
4. Discuss how severe obstructive sleep apnea may impact anesthetic management of a patient with Williams Syndrome
5. Modify anesthetic plan for patient with above pathophysiology requiring an invasive versus noninvasive surgical procedure

Discussion Outline

An 18 month old male with Williams Syndrome presents for magnetic resonance imaging of the brain to evaluate central sleep apnea. He had previously undergone a polysomnogram that demonstrated an apnea-hyponea index of 24, nadir oxygen saturation of 83%, and a respiratory arousal index of 10.

Preoperative Evaluation
Williams Syndrome

- What is Williams Syndrome?

- What are the signs and symptoms of Williams Syndrome?
- What diagnostic studies do you want? EKG? TEE? Cardiac catherization?
- What are the described anesthetic implications of Williams Syndrome?

Obstructive Sleep Apnea

- How could you evaluate OSA in a child? How does it differ from OSA in an adult?
- What is a polysomnogram? What information does it provide?
- How do you interpret the results of this child's polysomnogram? How does OSA affect your anesthetic management?
- What is central apnea?

Procedures in MRI

- What are the unique challenges that are involved with providing anesthesia in an MRI suite? What supplies do you require in MRI before anesthetizing this patient? Will you do this case alone or with a colleague?
- Will you have someone in the room with the patient during the MRI, or will they sit outside the room? What is the risk of magnetic radiation to a provider in the room with the scanner?

After discussion of the above issues, we will provide additional patient history. He recently had an electrocardiogram showing sinus rhythm at a rate of 120 beats per minute. Transesophageal echocardiography revealed biventricular hypertrophy with normal systolic function and no valvular abnormalities. Cardiac catherization reveals mild bilateral branch pulmonary artery stenosis, supravalvular aortic stenosis with a gradient of 50 mm Hg across the obstruction, and no coronary ostial anomalies.

- How will you provide anesthesia for this patient for MRI? Will you do sedation or general anesthesia? If you chose general anesthesia will you utilize an endotracheal tube or an LMA? How will your plan change if the patient has a difficult airway?
- Do you want to establish intravenous access pre-induction?
- Where will you perform the induction? What equipment do you need?
- What are your anesthetic goals at induction? What medications will you use?
- What are your hemodynamic goals? Describe factors that influence the balance between myocardial oxygen supply and demand. How will you manipulate this balance?
- Discuss the monitors you will employ for this procedure.

After discussion of the above issues, the patient will proceed with the MRI under sedation. The patient is sedated and the scan begins. You must deepen the sedation at the start of the scan due to patient movement. After several minutes, the patient is hypoventilating and the pulse oximeter reads 92%. The group will decide if this case will proceed under general anesthesia or sedation. The patient is successfully sedated and the procedure begins. Five minutes into the MRI, the end tidal carbon dioxide level decreases from 36 to 22 over 5 exhaled breaths. The pulse oximeter reading decreases from 98% to 90%.

- What is your differential diagnosis?
- How will you assess this patient?

The scanning process pauses so you can enter the room and assess the patient. At this time, end tidal carbon dioxide has fallen to 10 mm Hg and the pulse oximeter is not displaying a number; there is a poor plethysmography tracing. Blood pressure by non-invasive cuff is 52/30 mm Hg. EKG shows sinus bradycardia with a rate of 58 beats per minute. (We will provide an EKG rhythm strip showing sinus bradycardia with ST segment changes.)

- What is your next step?

The patient is having a cardiac arrest. The next section will guide the participants through a discussion of Pediatric Advanced Life Support.

- What medications will you administer? What actions are dictated by PALS protocol?
- Do you want any additional monitoring modalities?
- Will you resuscitate the patient in the MRI scanning room or move to another location?

The child is successfully resuscitated from the cardiac arrest. We move on to discuss post-operative management.

- Where will this child recover from anesthesia? Would your plan change if this had been an uncomplicated MRI?

We will modify the above scenario so that instead of an MRI, this child was scheduled for unilateral femoral osteotomy for hip dysplasia.

- What is your anesthetic plan? Could you perform a regional or neuraxial anesthetic with sedation? Will you place an arterial line?
- Discuss the options for post-operative pain control.
- Where will he recover from anesthesia? Will you admit him to the pediatric intensive care unit for monitoring?

Case Discussion

Williams Syndrome is a congenital disease due to deletion of the elastin gene on chromosome 7. Loss of the elastin protein in the media of large arteries results in a phenotype described as an "elastin arteriopathy": hypertrophied smooth muscle cells, increased collagen, and obstructive intimal lesions[1]. These arterial changes are present in the aorta, pulmonary arteries, and the renal and mesenteric arteries[1]. Physiologically, reduced elastin decreases arterial distensibility, producing widened pulse pressure and decreased diastolic coronary blood flow. Deletion of genes near the elastin locus is

responsible for the non-vascular phenotypic characteristics of Williams Syndrome, including characteristic facies, mental retardation, transient neonatal hypercalcemia, hyperacusis, renal abnormalities, and joint laxity[2].

The obstructive intimal lesions present in Williams Syndrome create supravalvular aortic and pulmonic stenosis; the pulmonic stenosis is often diffuse. Biventricular hypertrophy develops in response to these stenoses. In addition, the coronary arteries are abnormal due to two processes[3]. First, the right and/or left aortic valve leaflets adhere to the tissue above the coronary ostium, creating a mechanical obstruction to blood flow. Second, the left ventricular pressure produced in response to the supravalvular stenosis subject the coronary arteries to chronic high pressures, resulting in tortuosity, accelerated atherosclerosis and aneurysmal change[4].

Current literature includes many case reports describing sudden death during anesthesia in patients with Williams Syndrome[1,4]. Bradycardia and hypotension are frequent harbingers of cardiac arrest, which may be resistant to resuscitation. The anesthesiologist must balance myocardial oxygen supply and demand to prevent ischemia. Determinants of oxygen demand include heart rate, contractility, and wall tension, with slower rates, reduced contractility and reduced wall tension minimizing demand. Determinants of oxygen supply include heart rate, arterial blood oxygen content, and coronary perfusion pressure (aortic pressure minus left ventricular end diastolic pressure). Dysrhythmias can be disastrous as they may decrease diastolic filling time. Obstructed coronary vessels will exacerbate any imbalance in supply and demand.

Obstructive sleep apnea (OSA) is characterized by periodic, partial, or complete obstruction in the upper airway during sleep. The American Society of Anesthesiologists recently published updated practice guidelines for the perioperative management of patients with OSA, highlighting the differences between children and adults, the pathophysiology, diagnostic criteria and the anesthetic management[5]. The presence of OSA may complicate the cardiac pathology of a patient with Williams syndrome by contributing to right ventricular hypertrophy[6,7]. Equally in a scenario of critical oxygen supply and demand, the potential for apnea becomes increasingly important.

The anesthetic goals in caring for a patient with Williams syndrome include maintenance of sinus rhythm, avoidance of myocardial depression, maintenance of euvolemia, high systemic vascular resistance, and avoidance of increases in pulmonary vascular resistance. Judicious use of vagolytic agents and avoidance of catecholamine release is advisable. Considerations in obstructive sleep apnea include avoidance of respiratory depression and maintaining adequate ventilation and oxygenation. Many combinations of agents can be safely used to achieve the above hemodynamic goals. Dexmedetomidine in particular would provide adequate sedation for MRI without compromising ventilation[8]; the mild bradycardia and hypotension often encountered would likely be well tolerated.

Anesthetizing a patient with cardiac or respiratory pathology is challenging in off-site locations, particularly in the magnetic resonance imaging (MRI) suite. Standard

American Society of Anesthesiologists monitoring may be employed with modifications. Electrocardiogram monitoring with ST segment analysis would alert the provider to myocardial ischemia; however, accurate lead placement may interfere with the image quality, and ST segment interpretation may be unreliable due to the high magnetic field[9].[10] Although unlikely necessary for MRI, arterial pressure monitoring would be challenging if required. Temperature should be monitored, as hyperthermia may lead to tachycardia and negative effect on myocardial oxygen supply and demand balance. Further, ventilation must be closely monitored particularly if sedation is employed. Even with a provider in the room, it is difficult to judge the adequacy of ventilation in a small child who is completely inside the machine. End tidal carbon dioxide monitoring is possible with specialized nasal cannulae, but the waveform may be variable.

Importantly, the anesthesia team must prepare to evacuate the patient in case of an emergency. The ASA emphasizes that in the event of a cardiac arrest, the patient should be removed from the MRI scanner and transported to a safe location in close proximity to the scanner for resuscitation. All resuscitation equipment (including airway equipment, suction, and a code cart) and personnel should be available at that location[10].

Care for a child with Williams Syndrome should occur in a setting with full resuscitation capability, including ECMO, and a specialized team of physicians and support staff who are comfortable with the associated cardiac physiology. The care team should prepare for post-operative intensive care unit admission should the need arise.

References

1. Burch TM, McGowan FX, Jr., Kussman BD, Powell AJ, DiNardo JA. Congenital supravalvular aortic stenosis and sudden death associated with anesthesia: what's the mystery? *Anesthesia and analgesia.* Dec 2008;107(6):1848-1854.

2. Lashkari A, Smith AK, Graham JM, Jr. Williams-Beuren syndrome: an update and review for the primary physician. *Clinical pediatrics.* Apr 1999;38(4):189-208.

3. Practice Guidelines for blood component therapy: A report by the American Society of Anesthesiologists Task Force on Blood Component Therapy. *Anesthesiology.* Mar 1996;84(3):732-747.

4. Horowitz PE, Akhtar S, Wulff JA, Al Fadley F, Al Halees Z. Coronary artery disease and anesthesia-related death in children with Williams syndrome. *Journal of cardiothoracic and vascular anesthesia.* Dec 2002;16(6):739-741.

5. American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep a. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. *Anesthesiology.* Feb 2014;120(2):268-286.

6. Schwengel DA, Sterni LM, Tunkel DE, Heitmiller ES. Perioperative management of children with obstructive sleep apnea. *Anesthesia and analgesia.* Jul 2009;109(1):60-75.

7. Chan JY, Li AM, Au CT, et al. Cardiac remodelling and dysfunction in children with obstructive sleep apnoea: a community based study. *Thorax.* Mar 2009;64(3):233-239.
8. Mason KP, Zurakowski D, Zgleszewski SE, et al. High dose dexmedetomidine as the sole sedative for pediatric MRI. *Paediatric anaesthesia.* May 2008;18(5):403-411.
9. Andrzejowski J, Mundy J. Anaesthesia for MRI angiography in a patient with Williams syndrome. *Anaesthesia.* Jan 2000;55(1):97-98.
10. Practice advisory on anesthetic care for magnetic resonance imaging: a report by the Society of Anesthesiologists Task Force on Anesthetic Care for Magnetic Resonance Imaging. *Anesthesiology.* Mar 2009;110(3):459-479.