Case Report

Cardiac Arrest after Induction of Anesthesia in a 2-month-old Infant with Undiagnosed Williams Syndrome

Abstract

A 2-month-old male infant presented for elective repair of inguinal hernias. His preoperative medical history and physical examination were unremarkable. During induction of anesthesia, the infant sustained an adverse cardiac event. The event was characterized by tachycardia, hypotension, and massive ST-segment elevation. Despite vigorous resuscitation, spontaneous hemodynamic stability could not be achieved and extracorporeal membrane oxygenation was required. A transthoracic echocardiogram revealed severe hypoplasia of the ascending aorta. As effective cardiac function did not recover and there was evidence of diffuse ischemic brain injury, life support was withdrawn. Genetic testing performed postoperatively was definitive for Williams syndrome.

Keywords: *Anesthesia, cardiac arrest, induction, pediatric, Williams syndrome*

Julie D Dunlap, Morton C Green, Aali M Shah, Brandon T Kibby, Deborah F Billmire[1]

Departments of Clinical Anaesthesia and [1]Surgery, Riley Hospital for Children, Indianapolis, IN 46202-5200, USA

Introduction

Williams syndrome is a multisystem genetic disorder caused by a hemizygous deletion in the long arm of chromosome 7 in the region 7q11.23. Loss of one of the *ELN* genes from this chromosome band results in a deficiency of elastin.[1,2] Congenital cardiac defects are common in children with Williams syndrome. These defects include supravalvular aortic stenosis (SVAS), pulmonary artery stenosis, and coronary arterial ostial stenosis.[3,4] Fusion of the aortic valve leaflets to the aortic wall can produce functional coronary artery stenosis and reduce cardiac blood flow. Stenoses of the abdominal aorta, renal arteries, and intracranial arteries can also occur. Reduced elastin in the large arteries causes increased arterial stiffness that promotes early-onset hypertension.[5] Arterial elasticity is important to cardiac mechanics as energy is stored in the arterial wall during systole and released during diastole. This effect promotes cardiac efficiency, improves peripheral blood flow, reduces left ventricular afterload, and increases coronary blood flow.[6,7] Elastin deficiency in the myocardium may directly reduce cardiac performance.[8,9]

Noncardiovascular features of Williams syndrome include elfin facies, growth retardation, endocrine dysfunction, and pulmonary emphysema.[10] The risk of sudden death from cardiomyopathy is 25–100 times greater than the normal population.[11]

The risk of an adverse cardiac event during anesthesia may be as high as 11%.[12] Focused specialty care may significantly reduce that risk if the diagnosis of Williams syndrome is known before anesthesia.[13] We report a case of cardiac arrest in a 2-month-old infant with undiagnosed Williams syndrome.

Written permission from the patient's mother and approval from the Indiana University Institutional Review Board for the publication of case report were obtained.

Case Report

The patient was a term, 2-month-old male weighing 4.8 kgs, who presented for the elective repair of inguinal hernia. The medical history was unremarkable, and no cardiac murmurs were detected during routine pediatric examinations. Preoperative vital signs were: temperature 36.6°C, heart rate 154/min, blood pressure 107/59, respiratory rate 44/min, and arterial oxygen saturation 100% (room air). No cardiac murmurs were heard.

Anesthesia was induced with sevoflurane in oxygen to a maximum sevoflurane

How to cite this article: Dunlap JD, Green MC, Shah AM, Kibby BT, Billmire DF. Cardiac arrest after induction of anesthesia in a 2-month-old infant with undiagnosed Williams syndrome. Ann Card Anaesth 2019;22:210-2.

Address for correspondence:
Dr. Julie D Dunlap, Riley Hospital for Children, Room 2820, 705 Riley Hospital Drive, Indianapolis, IN 46202-5200, USA.
E-mail: jdunlap2@iuhealth.org

Access this article online

Website: www.annals.in

DOI: 10.4103/aca.ACA_38_18

Quick Response Code:

concentration of 8%, and an intravenous catheter was inserted. Propofol (2 mg/kg intravenous) was administered, and the trachea was intubated with a 3.0 mm internal diameter cuffed tracheal tube. The inspired concentration of sevoflurane was reduced to 3% immediately after intubation. Heart rate at that time was 146 bpm and systolic blood pressure was between 70 and 80 mmHg. Five minutes after intubation, there was a significant change in the electrocardiogram that appeared to be a wide QRS complex tachycardia. As the systolic blood pressure decreased to 58/26, resuscitation was initiated with chest compressions, and repeated doses of epinephrine and sodium bicarbonate. Although epinephrine boluses transiently increased systolic blood pressure but subsequently, it became very low (30-40 mmHg to immeasurable. Over 20 min, nine doses of epinephrine (2–10 μg/kg), four doses of sodium bicarbonate (2–5 mEq/kg), one dose of calcium gluconate (5 mg/kg), one dose of magnesium sulfate (30 mg/kg), and one electrical countershock were administered, and an epinephrine infusion at 50 μg/kg/min was initiated. It became evident that the change in the QRS pattern was actually secondary to massive elevation of the ST segment. Despite aggressive resuscitation efforts, spontaneous circulation could not be restored. Extracorporeal membrane oxygenation (ECMO) was established within 1 h of the arrest, and the patient was transferred to the Intensive Care Unit (ICU). A transthoracic echocardiogram showed moderate-to-severe decreased left ventricular function and a diffusely hypoplastic (4.5 mm, normal 7.5–9 mm[14]) and thickened ascending aorta. The aortic valve was tri-leaflet and normal. Over the next 48 h in the ICU, while on ECMO, the infant suffered a series of seizures. Serial echocardiograms showed no improvement in cardiac function, and cranial computed tomography demonstrated diffuse hypoxic-ischemic injury. Life support was withdrawn. Cytogenetic analysis with fluorescence *in situ* hybridization was positive for deletion in the Williams syndrome critical region. One chromosome showed signals for ELN, LIMK1, and D7S613. These signals were absent in the other chromosome 7.

Discussion

The increased risk of anesthesia for patients with Williams syndrome has been reported by several sources.[15-21] Patients at highest risk are those with SVAS when a decrease in diastolic blood pressure reduces coronary blood flow, leading to myocardial ischemia. Recommendations for anesthesia are similar to those for adults with ischemic heart disease.[22-24] These recommendations include maintenance of cardiac preload, myocardial contractility, and systemic vascular resistance (SVR) directed at optimization of coronary blood flow. Although the recommendations for administering an anesthetic that minimizes a reduction of diastolic blood pressure and maintains coronary blood flow are logical, the situation in patients with Williams syndrome may be more complex than that of adult patients with coronary artery disease. Reduced compliance of the aorta due to elastin deficiency in Williams patients can cause marginal blood flow to the subendocardium under normal physiologic conditions. Endocardial perfusion could be further compromised by the effects of anesthetics that are usually well tolerated by normal infants. This may explain the rapidity with which severe hypotension occurs during anesthesia and the poor response to resuscitation in Williams patients. There may be electrophysiologic mechanisms for cardiac arrest such as ventricular dysrhythmia secondary to prolongation of the Q-T interval.[25] Prolongation of the Q-T interval in patients with Williams syndrome resembles the increase in Q-T interval of patients with ischemic heart disease.

The diagnosis of Williams syndrome in an infant can be difficult as many of the signs of the disease are not present at an early age. Williams patients with SVAS and a cardiac murmur are typically diagnosed at 1–1.5 years of age. Detection, however, may be delayed until 4–5 years of age if SVAS is not present.[26] The cardiovascular pathology of our patient was atypical and different from other reported cases. Most patients with Williams syndrome have SVAS with or without coronary artery anomalies. Our patient had a severely hypoplastic aorta without detectable coronary stenosis and no cardiac murmur. The only preoperative clue may have been the elevated systolic blood pressure of 107 mmHg. Accurate measurement of blood pressure in a young infant, however, is influenced by many variables, and systolic blood pressure of 107 mmHg does not generally cause concern.[27]

We can only speculate as to the mechanism of the cardiac arrest in our patient. Sevoflurane and propofol both decrease (SVR) and sevoflurane is known to increase the Q-T interval.[28-31] Although the infant tolerated the induction with sevoflurane, a further decrease in SVR caused by propofol could have reduced myocardial blood flow. This is the youngest reported patient with undiagnosed Williams syndrome who suffered a cardiac arrest during anesthesia and underscores the increased risk of anesthesia for these patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's mother has given his consent for his images and other clinical information to be reported in the journal. The patient's mother understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Merla G, Brunetti-Pierri N, Micale L, Fusco C. Copy number variants at Williams-Beuren syndrome 7q11.23 region. Hum Genet 2010;128:3-26.
2. Heinz A, Huertas AC, Schräder CU, Pankau R, Gosch A, Schmelzer CE, *et al.* Elastins from patients with Williams-Beuren syndrome and healthy individuals differ on the molecular level. Am J Med Genet A 2016;170:1832-42.
3. Yuan SM. Congenital heart defects in Williams syndrome. Turk J Pediatr 2017;59:225-32.
4. van Pelt NC, Wilson NJ, Lear G. Severe coronary artery disease in the absence of supravalvular stenosis in a patient with Williams syndrome. Pediatr Cardiol 2005;26:665-7.
5. Osei-Owusu P, Knutsen RH, Kozel BA, Dietrich HH, Blumer KJ, Mecham RP, *et al.* Altered reactivity of resistance vasculature contributes to hypertension in elastin insufficiency. Am J Physiol Heart Circ Physiol 2014;306:H654-66.
6. Collins RT 2nd. Cardiovascular disease in Williams syndrome. Circulation 2013;127:2125-34.
7. Belz GG. Elastic properties and Windkessel function of the human aorta. Cardiovasc Drugs Ther 1995;9:73-83.
8. Jöbsis PD, Ashikaga H, Wen H, Rothstein EC, Horvath KA, McVeigh ER, *et al.* The visceral pericardium: Macromolecular structure and contribution to passive mechanical properties of the left ventricle. Am J Physiol Heart Circ Physiol 2007;293:H3379-87.
9. Mizuno T, Yau TM, Weisel RD, Kiani CG, Li RK. Elastin stabilizes an infarct and preserves ventricular function. Circulation 2005;112:I81-8.
10. Pober BR. Williams-Beuren syndrome. N Engl J Med 2010;362:239-52.
11. Wessel A, Gravenhorst V, Buchhorn R, Gosch A, Partsch CJ, Pankau R, *et al.* Risk of sudden death in the Williams-Beuren syndrome. Am J Med Genet A 2004;127A:234-7.
12. Olsen M, Fahy CJ, Costi DA, Kelly AJ, Burgoyne LL. Anaesthesia-related haemodynamic complications in Williams syndrome patients: A review of one institution's experience. Anaesth Intensive Care 2014;42:619-24.
13. Brown ML, Nasr VG, Toohey R, DiNardo JA. Williams syndrome and anesthesia for non-cardiac surgery: High risk can be mitigated with appropriate planning. Pediatr Cardiol 2018;39:1123-8.
14. Kampmann C, Wiethoff CM, Wenzel A, Stolz G, Betancor M, Wippermann CF, *et al.* Normal values of M mode echocardiographic measurements of more than 2000 healthy infants and children in central Europe. Heart 2000;83:667-72.
15. Horowitz PE, Akhtar S, Wulff JA, Al Fadley F, Al Halees Z. Coronary artery disease and anesthesia-related death in children with Williams syndrome. J Cardiothorac Vasc Anesth 2002;16:739-41.
16. Monfared A, Messner A. Death following tonsillectomy in a child with Williams syndrome. Int J Pediatr Otorhinolaryngol 2006;70:1133-5.
17. Pham PP, Moller JH, Hills C, Larson V, Pyles L. Cardiac catheterization and operative outcomes from a multicenter consortium for children with Williams syndrome. Pediatr Cardiol 2009;30:9-14.
18. Hornik CP, Collins RT 2nd, Jaquiss RD, Jacobs JP, Jacobs ML, Pasquali SK, *et al.* Adverse cardiac events in children with Williams syndrome undergoing cardiovascular surgery: An analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database. J Thorac Cardiovasc Surg 2015;149:1516-220.
19. Medley J, Russo P, Tobias JD. Perioperative care of the patient with Williams syndrome. Paediatr Anaesth 2005;15:243-7.
20. Gupta P, Tobias JD, Goyal S, Miller MD, Melendez E, Noviski N, *et al.* Sudden cardiac death under anesthesia in pediatric patient with Williams syndrome: A case report and review of literature. Ann Card Anaesth 2010;13:44-8.
21. Latham GJ, Ross FJ, Eisses MJ, Richards MJ, Geiduschek JM, Joffe DC, *et al.* Perioperative morbidity in children with elastin arteriopathy. Paediatr Anaesth 2016;26:926-35.
22. Collins Ii RT, Collins MG, Schmitz ML, Hamrick JT. Peri-procedural risk stratification and management of patients with Williams syndrome. Congenit Heart Dis 2017;12:133-42.
23. Matisoff AJ, Olivieri L, Schwartz JM, Deutsch N. Risk assessment and anesthetic management of patients with Williams syndrome: A comprehensive review. Paediatr Anaesth 2015;25:1207-15.
24. 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? Anesth Analg 2008;107:1848-54.
25. Collins RT 2nd, Aziz PF, Gleason MM, Kaplan PB, Shah MJ. Abnormalities of cardiac repolarization in Williams syndrome. Am J Cardiol 2010;106:1029-33.
26. Huang L, Sadler L, O'Riordan MA, Robin NH. Delay in diagnosis of Williams syndrome. Clin Pediatr (Phila) 2002;41:257-61.
27. Park MK, Menard SM. Normative oscillometric blood pressure values in the first 5 years in an office setting. Am J Dis Child 1989;143:860-4.
28. Kassam SI, Lu C, Buckley N, Lee RM. The mechanisms of propofol-induced vascular relaxation and modulation by perivascular adipose tissue and endothelium. Anesth Analg 2011;112:1339-45.
29. Chang KS, Davis RF. Propofol produces endothelium-independent vasodilation and may act as a Ca2+ channel blocker. Anesth Analg 1993;76:24-32.
30. Wodey E, Pladys P, Copin C, Lucas MM, Chaumont A, Carre P, *et al.* Comparative hemodynamic depression of sevoflurane versus halothane in infants: An echocardiographic study. Anesthesiology 1997;87:795-800.
31. Kleinsasser A, Kuenszberg E, Loeckinger A, Keller C, Hoermann C, Lindner KH, *et al.* Sevoflurane, but not propofol, significantly prolongs the Q-T interval. Anesth Analg 2000;90:25-7.