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As effective cardiac function did not recover and there was evidence of diffuse ischemic brain injury, life support was withdrawn.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

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. 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. 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. 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. Elastin deficiency in the myocardium may directly reduce cardiac performance.

Noncardiovascular features of Williams syndrome include elfin facies, growth retardation, endocrine dysfunction, and pulmonary emphysema. The risk of sudden death from cardiomyopathy is 25–100 times greater than the normal population. The risk of an adverse cardiac event during anesthesia may be as high as 11%. Focused specialty care may significantly reduce that risk if the diagnosis of Williams syndrome is known before anesthesia. We report a case of cardiac arrest in a 2-month-old infant with undiagnosed Williams syndrome.

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 concentration. 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.
Cardiac arrest in infant with Williams syndrome

Prolongation of the Q‑T interval in patients [28‑31] [25] [26]

These recommendations include [14]

Patients [27]

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recommendations for administering an anesthetic that

optimization of coronary blood flow. Although the

and systemic vascular resistance (SVR) directed at

maintenance of cardiac preload, myocardial contractility,

heart disease.

anesthesia are similar to those for adults with ischemic

diastolic blood pressure reduces coronary blood flow,

at highest risk are those with SV AS when a decrease in

became evident that the change in the QRS pattern was

Despite aggressive resuscitation efforts, spontaneous

became a significant change in the electrocardiogram

Discussion

The increased risk of anesthesia for patients with Williams

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.

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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 vascular smooth muscle 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 2005;212:2125-34.

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 infract and preserves ventricular function. Circulation 2005;112:1811-8.

10. Pober BR. Williams-Beuren syndrome. N Engl J Med 2010;362:239-52.

11. Mizuno T, Yau TM, Weisel RD, Kiani CG, Li RK. Elastin stabilizes an infract and preserves ventricular function. Circulation 2005;112:1811-8.

12. Olsen M, Fahy CJ, Costi DA, Kelly AJ, Burgoine 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, Toohy 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 Hales Z. Coronary artery disease and anesthesia-related death in children with Williams syndrome. J Cardiothorac Vase Anesth 2002;16:739-41.