CASE REPORT

LETHAL FUNGAL AORTITIS IN SURGICALLY CORRECTED SUPRAVALVULAR AORTIC STENOSIS IN A CHILD WITH WILLIAMS SYNDROME

Ayesha Butt[1], Naela Ashraf[2], Khuzaima Tariq[2], Muneer Amanullah[2]

[1]Yale School of Medicine, New Haven, CT-USA, [2]Liaquat National Hospital, Karachi-Pakistan

Williams syndrome (WS), is a multisystem disorder occurring in 1 in 10,000 live births with supravalvular aortic stenosis (SVAS) being the most common cardiovascular manifestation. We present the case of a 2.5 years old male, a known case of WS who presented with cognitive delay, a history of right-sided stroke and left hemiplegia. Echocardiography revealed severe SVAS with a gradient of 105 mmHg. The diameter of the Sino tubular junction was 4 mm. Computerized tomography angiogram showed diffuse stenosis of ascending aorta with intraluminal thrombus. At surgery, the ascending aorta was augmented with autologous pericardial patches and end-to-end anastomosis of the proximal and distal aorta completed the reconstruction. The patient was discharged in a stable condition. He presented 6 weeks post-op with a pulsating pseudoaneurysm through the sternal wound. Emergency surgery with the removal of fungal vegetation and reconstruction of the ascending aorta was performed. He expired due to fungal sepsis a week later.

Keywords: Williams-beuren syndrome; Supra valvular aortic stenosis; Infectious aortitis

Citation: Butt A, Ashraf N, Tariq K, Amanullah M. Lethal fungal aortitis in surgically corrected supravalvular aortic stenosis in a child with Williams syndrome. J Ayub Med Coll Abbottabad 2023;35(2):320–3.

DOI: 10.55519/JAMC-02-10055

INTRODUCTION

Williams syndrome (WS), also known as Williams-Beuren syndrome, is a multisystem disorder occurring in 1 in 10,000 live births and includes cardiovascular, skeletal and renal anomalies, dysmorphic facies and intellectual disability.[1] It is caused by a microdeletion of chromosome 7q11.23, which includes the elastin (ELN) gene. Deletion of one of the ELN alleles, resulting in hemizygosity of ELN, begets a myriad of cardiovascular (CVS) anomalies. Supravalvular aortic stenosis (SVAS), and pulmonary artery stenosis (PAS) are the two most common structural CVS abnormalities and are the leading cause of mortality in WS.[2]

Supravalvular aortic stenosis is the rarest cause of left ventricular outflow tract obstruction (LVOTO) and only 8–14% of paediatric congenital aortic stenosis (AS) cases are attributed to SVAS. There are two main types of SVAS in WS: discrete (type I, 75% of cases) with an isolated, hourglass-shaped narrowing at the sino tubular junction (STJ) or diffuse (type II) with a diffuse, long-segment stenosis of the ascending aorta. SVAS afflicts 45–70% of children with WS and mandates surgery in up to 30%. Surgical correction is targeted towards expanding the STJ, the aortic root and rectifying any additional stenoses and yields excellent results.[3]

One of the rare post-operative complications is the formation of a pseudoaneurysm. The chances of infection are high in pre-existing aneurysm. This infection can become life-threatening as there is high risk of rupture and possibility of widespread sepsis. Emergency surgery is required when these complications are feared and is directed towards removal of infected material and reconstruction of the aorta.[4] Herein, we present our experience with surgical correction of life threatening SVAS in a child with Williams syndrome with a history of stroke who had a SVAS with a peak pressure gradient of 105 mmHg and diffuse stenosis of ascending aorta with an intraluminal thrombus. The follow-up is also discussed where he presented with lethal fungal aortitis and a pseudoaneurysm through the sternum.

CASE REPORT

A two and half years old male, with a known case of Williams Syndrome, presented to our institute for surgical treatment of SVAS. The child had a cognitive delay and a history of right sided stroke resulting in left hemiplegia 3 months prior to presentation. He also had a hospital admission due to sepsis a month before the presentation. Upon examination, the child had elfin facies. He weighed 9 kg, had a body surface area of 0.45m², heart rate of 102 beats/minute, respiratory rate of 22/minute, blood pressure of 124/67 mmHg and oxygen saturation of 91%. The rest of his physical examination confirmed left-sided hemiplegia. No murmur was appreciated on auscultation.

Echocardiography revealed severe supravalvular aortic stenosis, with a peak pressure gradient of 105 mmHg and a mean pressure gradient of 65 mm Hg. A large echogenic mass, measuring 24 mm by 13 mm, was seen within the ascending aorta. Mild bilateral pulmonary artery branch stenosis (peak pressure gradient 20 mmHg), mild left ventricular hypertrophy and moderate pericardial effusion (9.4 mm anteriorly and 5.2 mm at apex) were also demonstrated. Aortic annular diameter was 10 mm, diameter of the sinuses of valsalva was 14 mm and the

sinotubular junction measured 4 mm. Left ventricular ejection fraction (LVEF) was 69%.

Computerized tomography angiogram (CTA) chest delineated circumferential but asymmetric and irregular wall thickening of ascending aorta, extending from the aortic root till mid aortic arch (Figure-1). The maximum wall thickness was 3.5 mm. Moreover, an intraluminal non occluding thrombus was seen and the minimum patent diameter of the ascending aorta was 4 mm. There was sparing of the origins of the coronary arteries. Aneurysmal dilatation of the proximal arch, demonstrating the presence of a pseudo thrombus was also noted. The maximum diameter of the pseudoaneurysm was 14.4 mm with the patent lumen measuring 12.2 mm. Circumferential thickening with mild to moderate luminal narrowing of major branches of the pulmonary artery with extension along its second-order branches was seen. The patient had an erythrocyte sedimentation rate (ESR) of 66 mm/hour (reference range: 0–25). Other laboratory investigations, including the coagulation profile, were within normal limits. The patient was stratified as high risk for surgery. A median sternotomy followed by thymectomy and pericardiotomy, heparinization and single stage venous cannulation was performed. The aorta was cannulated at the aortic arch level and cardiopulmonary bypass (CPB) was initiated. The aorta was clamped and opened transversely and cardioplegia was given directly into the coronary ostia. The aorta was full of thrombus due to stasis as a result of the severely stenosed ascending aorta. The aorta was transacted, cleared of all thrombi and the thickened portions of the aortic wall were excised down to the aortic sinuses and the ascending aorta was augmented with autologous pericardial patches. End-to-end anastomosis of the reconstructed proximal and distal aorta completed the reconstruction. The left heart was de-aired and cross clamp was removed. Transoesophageal echocardiography (TEE) revealed no gradient in the aorta and the patient was taken off CPB with minimal inotropic support. Total CPB time and aortic cross-clamp time were 118 and 68 minutes, respectively.

Post-operative echocardiogram showed no significant dilatation of ascending aorta, aortic arch or descending aorta. No significant pressure gradient was seen across ascending aorta, arch of the aorta or descending aorta. LVEF was 64%. The patient was discharged on the 9th post-op day in stable condition on aspirin and anti-failure therapy. He presented 6 weeks post-op to the ER with a pulsating mass eroding through the sternal wound. An emergency and life-threatening consent was obtained, and the patient was taken to the surgery where after heparinization right carotid artery and right Internal jugular vein were cannulated. CPB was established and the patient was cooled to 22 °C. During cooling, the sternotomy was performed. The pericardial cavity was full of bloody effusion. The pseudoaneurysm was originating from the ascending aortic wall on the opening the aorta and was found to be full of fleshy vegetation extending from the aortic valve to the arch. The wall of the aorta was eroded. After the removal of the vegetation and necrotic aortic wall, the aorta was reconstructed using the bovine pericardial patch. The patient was rewarmed, and CBP was discontinued with minimal inotropic support. The neck vessels were reconstructed, and the chest was kept open. The vegetations were sent for culture and heavy growth of *Candida albicans* was reported. The chest was closed the next day and by the second post-op day, the patient was off inotropes and had a GCS of 15/15. He remained stable but then developed signs of sepsis and expired a week later due to fungal sepsis.

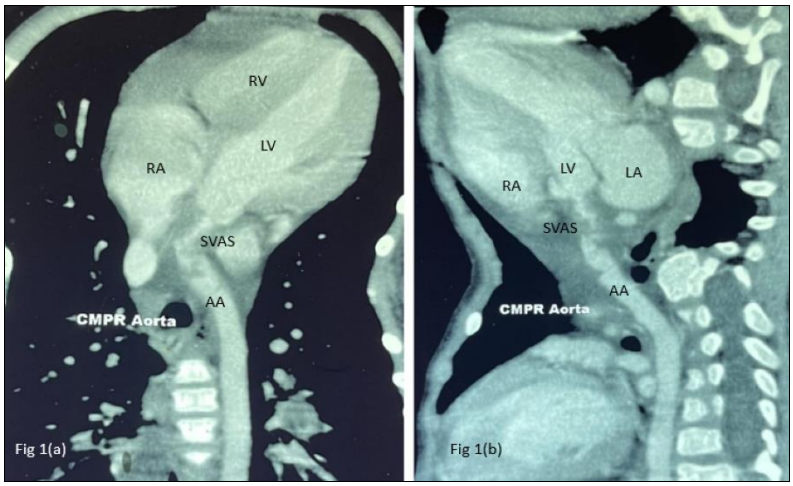

Figure-1: Computerized tomography angiogram (CTA) shows long segment SVAS present with thick wall, intraluminal thrombus and 4 mm patent lumen

1(a) coronal section. 1(b) sagittal section

RV: Right Ventricle. RA: Right Atrium. LV: Left Ventricle. LA: Left Atrium. SVAS: Supravalvular Aortic Stenosis. AA: Ascending Aorta. CMPR Aorta: Curved Multiplanar Reconstruction of aorta

DISCUSSION

WS is classified as a general arteriopathy predominantly affecting medium and large-size arteries.[5] Cardiovascular abnormalities in WS stem from hemizygosity of ELN gene and are the most common cause of death in WS. Recent studies have delineated that inadequate circumferential growth as opposed to vascular smooth muscle cell proliferation is the primary reason for aortic stenosis in the context of elastin haploinsufficiency. This represents a major shift in understanding the pathophysiology of this disease.[2,6]

Williams syndrome has a kaleidoscope of manifestations. The typical facial features seen in WS, often referred to as elfin facies in literature, include broad forehead; periorbital fullness; a stellate pattern of the irises; a flattened nasal bridge with an upturned nose; a long philtrum and full lips; high, rounded cheeks; and a pointed chin. Patients with WS have an exuberant personality, often referred to as cocktail personality and are loquacious despite having a mean IQ of 50–60.[1]

Supravalvular aortic stenosis and PAS are seen in 45% and 60% of WS patients presenting during the first year of life, respectively and in 45% and 40% of WS patients, respectively who present later.[2] There are more than one associated cardiac anomaly present in 75% of patients with SVAS.[1] These include coronary artery stenosis, bicuspid aortic valve, ventricular septal defect, mitral valve prolapses and regurgitation. Although there are many risk factors for stroke present in WS e.g., hypertension, cardiac disease and arterial stenosis, there are only a few case reports about cerebrovascular disease in Williams syndrome.[7] Our patient suffered a cerebrovascular accident (CVA) at two years of age, resulting in left hemiplegia.

Echocardiography with Doppler has a high sensitivity for the diagnosis of SVAS but it does not sufficiently describe the anatomy of the lesion. Whereas cardiac catheterization with angiography is capable of defining the anatomy in detail, magnetic resonance imaging (MRI) and multidetector CT-scanning have the benefit of being less invasive and carrying fewer risks while delineating the anatomy adequately.[8] Hence, echocardiography and CT angiogram were employed in our patient.

Medical therapies to ameliorate CVS symptoms in WS have predominantly been helpful only in the treatment of hypertension, which occurs in 40–50% of WS patients.[9] Surgery remains the mainstay of treatment for SVAS and has been reported to herald excellent outcomes. Different surgical techniques have been described which mostly vary according to the number of Valsalva sinuses that are augmented by patch repair. The most commonly employed techniques include single patch repair, two sinus augmentation with an inverted Y patch and three patch techniques. The first two are asymmetrical while the third is a symmetrical technique.

The surgical correction for SVAS has metamorphosed remarkably over time. Originally, McGoon *et al*. elaborated upon the one-patch autoplasty technique, which ameliorated the stenotic aortic area with patch extension into the non-coronary sinus of Valsalva. This was succeeded by the Doty technique involving an inverted Y-shaped incision being made across the supravalvular-constricting ring and into the right coronary and non-coronary sinuses of Valsalva, followed by the insertion of a pantaloon-shaped Dacron patch.[10] Following this, Brom presented a three-patch repair of all three aortic sinuses, restoring the original geometry of the aortic root. Later, several innovations to eliminate patch material in this technique have been proposed.[11]

A recent study found no difference in outcomes for symmetrical (Brom's three-patch technique or slide aortoplasty) versus asymmetrical (single patch or inverted Y-shaped patch) techniques. We used Doty technique in our patient. A study of patients with SVAS (41% with Williams syndrome), demonstrated the survival for SVAS surgery as 90±7% at 5 years and 82± 10% at 20 years.[12]

The formation of a thrombus in the ascending aorta is a rare but highly deleterious finding that has been sporadically reported. The existence of a thrombus in a location so close to the carotid arteries is a harbinger for embolization leading to CVA, in addition to peripheral embolic events. Hence, it carries a high risk for mortality and morbidity.[13]

Infectious thoracic aortitis is a rare, but life-threatening situation. Mycotic aneurysm is an extreme presentation of aortitis which usually develops on a pre-existing aneurysm. Despite the name mycotic, many cases are associated with bacterial aetiology and very few are fungal.[4] The number of reported cases has increased due to the increasing number of surgical aortic repairs performed. There may be multiple factors associated such as hematogenous seeding, local translocation, iatrogenic complication or fistula formation from oesophagus or bronchial tree. Most of the patients have widespread sepsis at the time of presentation. This makes the management and surgery challenging and there is significant mortality reported even after the surgery.[14]

Emergency surgery is indicated in impending rupture or widespread sepsis. The main surgical management involves resection of the infected aorta and subsequent reconstruction. In-situ graft reconstruction is the most recommended method.[15]

CONCLUSION

SVAS is the most common cardiac manifestation in Williams syndrome. Surgery is the mainstay of treatment. While surgery usually has an excellent outcome, the risk of complications remains. One of the rare but serious complications with high mortality is an infected pseudoaneurysm and aortitis which warrant emergent treatment.

REFERENCES

1. Collins RT 2nd. Cardiovascular disease in Williams syndrome. Circulation 2013;127(21):2125–34.
2. Collins RT 2nd. Cardiovascular disease in Williams syndrome. Curr Opin Pediatr 2018;30(5):609–15.
3. Wu FY, Mondal A, Pedro J, Gauvreau K, Emani SM, Baird CW, *et al*. Long-term surgical prognosis of primary supravalvular aortic stenosis repair. Ann Thorac Surg 2019;108(4):1202–9.
4. Lopes RJ, Almeida J, Dias PJ, Pinho P, Maciel MJ. Infectious thoracic aortitis: a literature review. Clin Cardiol 2009;32(9):488–90.
5. Szaflik K, Kaźmierczak P, Moll JJ, Moll JA. Severe Congenital Obstruction of the Left Main Coronary Artery Coexisting With Supravalvular Aortic Stenosis in Williams Syndrome:A Dangerous Association. World J Pediatr Congenit Heart Surg 2016;7(2):216–9.
6. Jiao Y, Li G, Korneva A, Caulk AW, Qin L, Bersi MR, *et al*. Deficient Circumferential Growth Is the Primary Determinant of Aortic Obstruction Attributable to Partial Elastin Deficiency. Arterioscler Thromb Vasc Biol 2017;37(5):930–41.
7. Wint DP, Butman JA, Masdeu JC, Meyer-Lindenberg A, Mervis CB, Sarpal D, *et al*. Intracranial Arteries in Individuals with the Elastin Gene Hemideletion of Williams Syndrome. Am J Neuroradiol 2014;35(1):90–4.
8. Zamani H, Babazadeh K, Fattahi S, Mokhtari-Esbuie F. Williams-Beuren's Syndrome: A Case Report. Case Rep Med 2012;2012:585726.
9. Owens EA, Jie L, Reyes BAS, Van Bockstaele EJ, Osei-Owusu P. Elastin insufficiency causes hypertension, structural defects and abnormal remodelling of renal vascular signaling. Kidney Int 2017;92(5):1100–18.
10. Bakhtiary F, Amer M, Etz CD, Dähnert I, Wilhelm Mohr F, Bellinghausen W, *et al*. Mid-term outcome after surgical repair of congenital supravalvular aortic stenosis by extended aortoplasty. Interact Cardiovasc Thorac Surg 2013;17(4):688–90.
11. Mongé MC, Eltayeb OM, Costello JM, Johnson JT, Popescu AR, Rigsby CK, *et al*. Brom Aortoplasty for Supravalvular Aortic Stenosis. World J Pediatr Congenit Heart Surg 2018;9(2):139–46.
12. Deo SV, Burkhart HM, Schaff HV, Li Z, Stensrud PE, Olson TM, *et al*. Late outcomes for surgical repair of supravalvar aortic stenosis. Ann Thorac Surg 2012;94(3):854–9.
13. Soo A, Marley D, McGrath-Soo L, Herron B, Parissis H. Ascending aorta thrombus: a diagnostic and treatment dilemma. Asian Cardiovasc Thorac Ann 2014;22(6):731–3.
14. Kahlberg A, Melissano G, Tshomba Y, Leopardi M, Chiesa R. Strategies to treat thoracic aortitis and infected aortic grafts. J Cardiovasc Surg (Torino) 2015;56(2):269–80.
15. Wein M, Bartel T, Kabatnik M, Sadony V, Dirsch O, Erbel R. Rapid progression of bacterial aortitis to an ascending aortic mycotic aneurysm documented by transesophageal echocardiography. J Am Soc Echocardiogr 2001;14(6):646–9.

Submitted: August 30, 2021	*Revised: November 4, 2021*	*Accepted: March 23, 2022*

Address for Correspondence:

Muneer Amanullah, H. No. 492, DOHS Phase-1, Malir Cantt Karachi-Pakistan
Cell: +92 307 222 1813
Email: muneer.amanullah18@gmail.com