

Diffuse hypoplasia of the aortic arch and isthmus in a patient with Williams syndrome

Williams sendromu olan bir hastada arkus aorta ve isthmusun yaygın hipoplazisi

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Summary– Williams syndrome is a rare neurodevelopmental disorder characterized by mental retardation, growth deficiency, hypercalcemia, cardiac defects, and a distinctive facial appearance. Cardiovascular abnormalities are present in approximately 80% of Williams syndrome patients. Surgical treatment is generally performed for supra-avalvular aortic stenosis, aortic coarctation, pulmonary artery stenosis, or ventricular septal defect. In rare cases, diffuse hypoplasia of the aortic arch with a normal left ventricular outflow tract and ascending aorta may be diagnosed in early childhood. Described herein is the case of a 16-month-old female with Williams syndrome and diffuse hypoplasia of the aortic arch and isthmus, and concomitant pulmonary stenosis and a ventricular septal defect. The patient underwent a successful surgical repair of the aortic arch with a modified pericardial patch technique.

Williams syndrome is a rare neurodevelopmental disorder characterized by mental retardation, skeletal abnormalities, endocrine disorders, and cardiovascular anomalies. The prevalence of Williams syndrome is estimated at 1 in 8000 live births.^[1-6] The cardiovascular anomalies are due to underlying elastin arteriopathy affecting the great vessels in approximately 80% of patients.^[6] In neonates and children with Williams syndrome, cardiovascular anomalies generally include supra-avalvular aortic stenosis, aortic coarctation, pulmonary artery stenosis, subaortic stenosis, or patent ductus arteriosus.^[1-6] However, in

Özet– Williams sendromu mental gerilik, büyüme geriliği, hiperkalsemi, kalp defektleri ve tipik yüz görünümü ile kendini gösteren nadir bir nörolojik gelişme bozukluğudur. Williams sendromlu hastaların yaklaşık %80'inde kardiyovasküler anomaliler görülmektedir. Cerrahi girişim genellikle supra-avalvuler aort stenozu, aort koarktasyonu, pulmoner arter stenozu ve ventriküler septal defekt sebebiyle yapılır. Buna rağmen, sol ventrikül çıkım yolu ve çıkan aortanın normal olduğu nadir olgularda aort yayının yaygın hipoplazisi erken çocukluk döneminde teşhis edilebilir. Bu yazıda, Williams sendromu, yaygın aort yayı hipoplazisi ile eşzamanlı ventriküler septal defekt ve pulmoner stenoz olan 16 aylık kız hastayı sunuyoruz. Hastada aort yayının modifiye perikart yaması tekniğiyle cerrahi tamiri başarıyla yapılmıştır.

rare cases, diffuse aortic arch hypoplasia with a normal left ventricular outflow tract and ascending aorta may be diagnosed in early childhood.

Herein, a case of hypoplasia of the aortic arch and isthmus in a child with Williams syndrome is described with a focus on the surgical management with a modified patch repair.

CASE REPORT

A 16-month-old female with Williams syndrome was referred to the hospital. On admission, the patient was

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asymptomatic and had no cyanosis. Blood pressure was 160/62 mmHg on the right upper extremity, but peripheral pulses on both femoral arteries were weak on palpation. Cardiac auscultation revealed a 3/6 grade systolic murmur on the left parasternal area. Transthoracic echocardiography indicated a ventricular septal defect, stenosis of the right pulmonary artery, and hypoplasia of the aortic arch and isthmus. The left and right ventricular outflow tracts were normal. The diameters (z scores) of the ascending aorta, aortic arch, isthmus, and descending aorta were 7.5 mm (+0.92), 6.0 mm (-3.47), 2.5 mm (-9.24), and 6.2 mm (-0.72), respectively. Conventional angiography confirmed hypoplasia of the aortic arch and isthmus (Fig. 1). Blood pressure measured in the ascending and descending aorta was 148/58 mmHg and 122/54 mmHg, respectively. Surgery was planned to repair the aortic hypoplasia and concomitant intracardiac anomalies.

The operation was performed under cardiopulmonary bypass. Simultaneous monitoring of the right radial and femoral arteries was established. Near-infrared spectroscopy was used to monitor cerebral perfusion. After sternotomy and thymectomy, an autologous pericardial patch was prepared and treated with 2% glutaraldehyde. Surgical exploration confirmed hypoplasia of the aortic arch and isthmus. Before establishment of cardiopulmonary bypass, a modified pericardial patch had been prepared using a modified technique for arch reconstruction.^[4] Following systemic heparinization, cardiopulmonary bypass was established with a 5-mm Gore-Tex graft (W.L. Gore & Associates, Inc., Newark, DE, USA) that was anastomosed to the brachiocephalic artery and cannulation of both vena cavae. The aortic arch, isthmus,

and supra-aortic branches were mobilized (Fig. 2). The stenotic segment of the isthmus was exposed. At 28°C, the aorta was clamped distally to the brachiocephalic artery and distally to the isthmus. At this stage, the heart was beating and pump flow was lowered to maintain arterial pressure at approximately 40 mmHg. Aortotomy incision was extended from the proximal aortic arch toward the proximal descending aorta, where the aortic wall character was more normal. The arch reconstruction with a modified patch was performed with 7/0 Prolene (Ethicon, Inc., Somerville, NJ, USA) sutures beginning at the normal descending aorta toward the proximal aortic arch. When the suture line of the patch (Fig. 3) was close to the clamp on the aortic arch, selective cerebral perfusion was

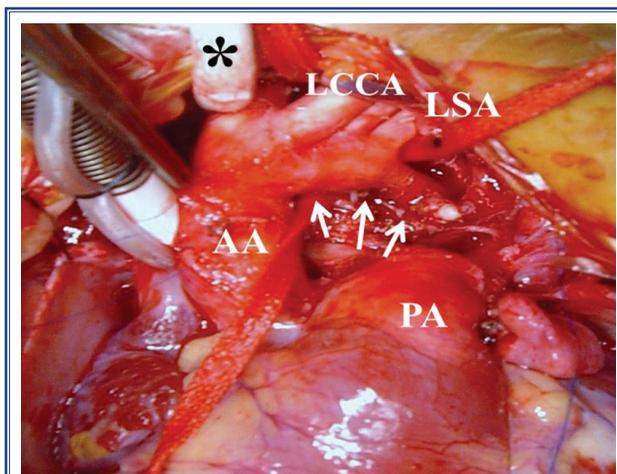


Figure 2. Operative view demonstrating hypoplasia of the aortic arch and isthmus (arrows).

AA: Ascending aorta; LCCA: Left common carotid artery; LSA: Left subclavian artery; PA: Pulmonary artery; *: Graft through the brachiocephalic artery.

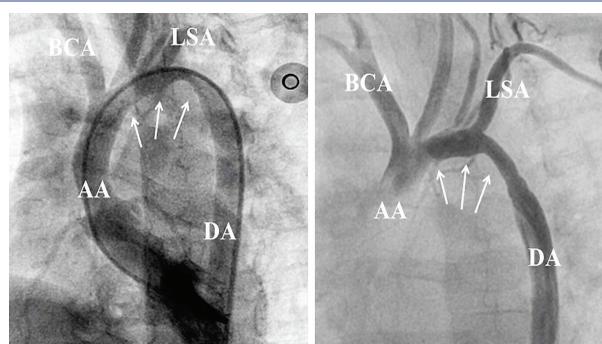
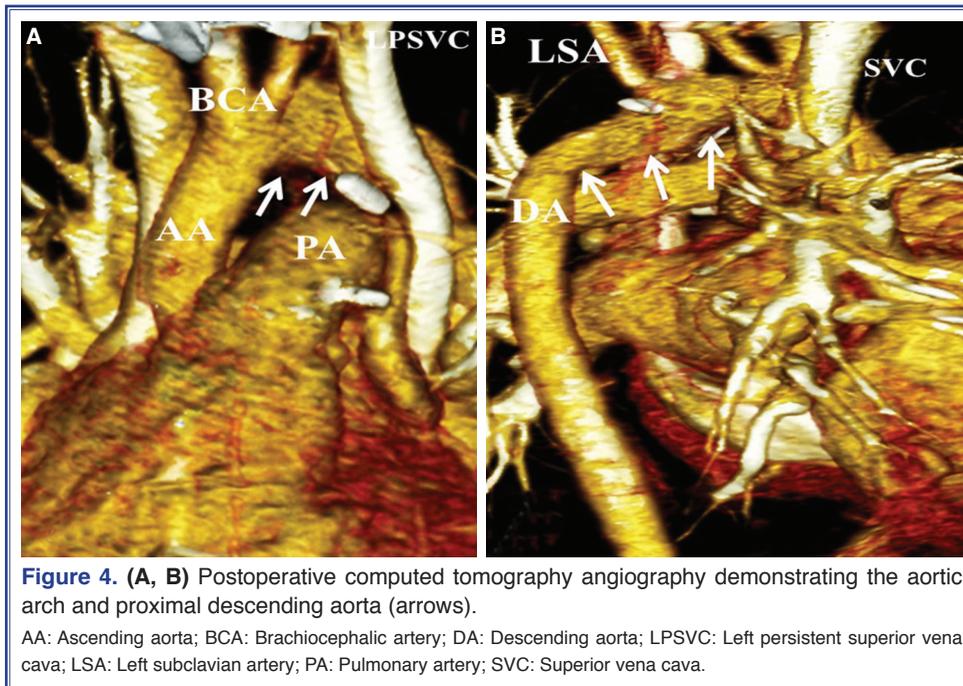


Figure 1. Angiogram demonstrating hypoplasia of the aortic arch and isthmus (arrows).

AA: Ascending aorta; BCA: Brachiocephalic artery; DA: Descending aorta; LSA: Left subclavian artery.



Figure 3. Pericardial patch.



initiated. The reconstruction was extended toward the distal ascending aorta. After reconstruction of the whole aortic arch, cerebral perfusion stopped and systemic perfusion was re-started. The ventricular septal defect was repaired with a pericardial patch through a right atriotomy incision. The area of pulmonary artery stenosis was reconstructed using a pericardial patch. The patient was weaned from cardiopulmonary bypass uneventfully. Cardiopulmonary bypass, aortic clamping, and cerebral perfusion times were 180, 76, and 25 minutes, respectively. Following reconstruction, there was no residual gradient between the right radial and femoral arteries.

In the postoperative period, peripheral pulses were palpable, and hypertension was controlled with propranolol. Transthoracic echocardiography indicated a normal aortic arch without residual stenosis. The patient was discharged on postoperative day 12, uneventfully.

At 6-month follow-up, she was asymptomatic and well. Computerized tomography angiography revealed that the aortic arch was patent without aneurysm or stenosis (Fig. 4).

DISCUSSION

Williams syndrome is a rare neurodevelopmental disorder with specific phenotypic characteristics and

cardiac abnormalities. Patients present with varying degrees of mental retardation, dysmorphic face (elfin face), growth deficiency, and hypercalcemia. Genetic studies have demonstrated that Williams syndrome is caused by a deletion of about 26 genes from the long arm of chromosome 7.^[1-3] Specifically, underlying elastin arteriopathy, due to a microdeletion of chromosomal region 7q11.23, leads to a varying degree of aortic wall anomalies in almost half of the patients in infancy.^[3] In the differential diagnosis, other syndromes with diagnostic facial characteristics, such as Down syndrome, Noonan syndrome, Shone syndrome, Kabuki syndrome, or Turner syndrome should be excluded using genetic analysis. Anatomically, the proximal ascending aorta, the left ventricular outflow tract, and the aortic isthmus are frequently involved in Williams syndrome patients. However, diffuse hypoplasia of the aortic arch is rare.^[2] The life expectancy of Williams syndrome patients depends upon the degree and management of cardiac and other associated anomalies.

Cardiovascular disease of medium and large arteries is the hallmark of Williams syndrome. Cardiovascular abnormalities are diagnosed in approximately 80% of patients.^[6] Aortic wall anomalies present with discrete stenosis or diffuse hypoplasia. This may develop in the ascending aorta, isthmus, and rarely, the aortic arch. While supravalvular aortic stenosis is

the most common indication for surgery in children with Williams syndrome, aortic coarctation is a well-known indication in infants.^[3] Specifically, arch hypoplasia and/or multi-level aortic obstruction are associated with worse outcomes.^[1-3] Aortic hypoplasia leads to increasing arterial resistance, which can cause high blood pressure, cardiac hypertrophy, and cardiac failure. Therefore, early repair of aortic wall anomalies avoids associated morbidities and mortality in later age.

The cardiovascular manifestation of patients with Williams syndrome has been reported in previous studies.^[3,7,8] In children with Williams syndrome, it has been reported in the literature that supravalvular aortic stenosis is seen with an incidence of between 56% and 73%.^[3,7,8] Most have local stenosis at the level of the proximal ascending aorta, but in rare cases, a diffuse type with extensive aortic involvement is seen. Other cardiac anomalies include ventricular septal defects; patent ductus arteriosus; stenosis of other arteries, such as the carotid, cerebral, coronary, brachiocephalic or subclavian artery; and coarctation of the aorta.^[7] The incidence of pulmonary stenosis varies between 13% and 83% in the reports.^[3,7,8] But, the ratio of isolated hypoplasia of the aortic arch is not clear. In a review conducted by Pober et al.,^[8] the combined prevalence of severe diffuse hypoplasia of the aorta was 2%. Therefore, the diagnosis of diffuse hypoplasia of the aortic arch is among the unusual presentations in Williams syndrome.

Clinically, aortic arch anomalies can be diagnosed incidentally in patients with ventricular septal defect, stenosis of the pulmonary artery, or patent ductus arteriosus, as occurred in our patient. However, in the event of severe stenosis of the left or right ventricular outflow tract and coarctation, patients present very early in infancy with symptoms of heart failure and pulmonary congestion.^[3,7,8] And, if there is a severe decrease in cardiac output and systemic perfusion, metabolic acidosis and organ failure may adversely affect the outcome of patients. Eronen et al.^[3] noted that cardiovascular symptoms were evident at birth in 47% of 75 patients. On admission, a transthoracic echocardiography examination is valuable in the assessment of aortic arch hypoplasia and associated cardiac anomalies. Conventional angiography, computed tomography, and magnetic resonance imaging provide additional data on the anatomical presentation and the

extension of aortic arch pathologies. Conventional angiography was performed in our case. It showed diffuse hypoplasia of the aortic arch and stenosis of the isthmus, as well as a pressure gradient between the upper and lower extremities. The surgical strategy of reconstruction was, therefore, defined preoperatively.

The management of aortic hypoplasia in Williams syndrome patients is performed with the reconstruction of stenotic segments using pericardial patches. Previous studies have reported that the outcome of aortic arch repair is favorable and safe in children.^[3,7,8-10] Technically, an extended or end-to-end coarctation repair through a thoracotomy incision may be preferred in a case of isolated coarctation of the aorta. In intracardiac pathologies, the surgical correction is made concomitantly. In cases with coarctation or renal artery stenosis, treatment of hypertension is necessary and percutaneous interventions may be preferred. However, the surgical approach to aortic arch hypoplasia and associated intracardiac anomalies is a median sternotomy incision. In such cases, the aortic arch, the proximal descending aorta, and the supra-aortic branches are mobilized. Pulmonary autograft, pulmonary allograft, homograft patches, or composite aortoplasty techniques can be used for arch reconstruction.^[10] During reconstruction, systemic perfusion can be established either via direct innominate artery cannulation or re-routing of the cannula in the aorta. Because the aortic clamps are placed distal to the brachiocephalic artery, reconstruction of the distal arch and isthmus can be performed while the heart is beating. Cardiac arrest may be necessary to complete the repair of the proximal aortic arch as well as associated cardiac pathologies. Nevertheless, if the coronary arteries are involved, the risk of myocardial dysfunction may be increased.

In our patient, a glutaraldehyde-treated autologous pericardial patch was used. This patch was composed according to a technique described by Gargiulo et al.^[4] Although bovine pericardium was used by the authors, our experience has shown that the use of an autologous pericardial patch was feasible for aortic arch reconstruction. We have used this technique uneventfully in more than 10 patients with aortic arch hypoplasia within the last 4 years.

In conclusion, we present an unusual presentation of Williams syndrome with hypoplasia of the aortic arch and associated cardiac anomalies. In this patient,

hypoplasia of the arch was associated with stenosis of the aortic isthmus, and this increased the extent of the aortic disease. In the management of such cases, an autologous pericardial patch is an alternative for reconstruction of the aortic arch and isthmus.

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