

A rare cardiovascular finding in two cases with Williams syndrome: recurrent coarctation of aorta

Williams sendromlu iki olguda nadir bir kardiyovasküler bulgu: Tekrarlayan aort koarktasyonu

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ABSTRACT

Williams syndrome is a genetic disorder caused by multiple gene deletions on chromosome 7. The majority of the cases is sporadic and has typical facial appearance, cardiac anomalies and mental retardation. Cardiovascular anomalies are present in about 80% of the cases, most frequently supraaortic stenosis and pulmonary arterial stenosis. In this article, we report two pediatric cases with a rapidly progressive form of aortic coarctation, each of whom required two surgeries and two percutaneous balloon dilatations within the first five months of life.

Keywords: Child; recurrent aort coarctation; Williams syndrome.

ÖZ

Williams sendromu 7. kromozomda çoklu gen delesyonu sonucunda oluşan genetik bir bozukluktur. Olguların çoğu sporadiktir ve tipik yüz görünümü, kardiyak anomaliler ve mental retardasyon mevcuttur. En sık supraaortik darlığı ve pulmoner arteriyel darlık olmak üzere, olguların yaklaşık %80'inde kardiyovasküler anomaliler görülmektedir. Bu yazıda yaşamın ilk beş ayında iki kere cerrahi ve iki kere perkütan balon dilatasyonu gerekli olan, aort koarktasyonunun hızlı ilerleyen formu görülen iki pediatrik olgu sunuldu.

Anahtar sözcükler: Çocuk; tekrarlayan aort koarktasyonu; Williams sendromu.

Williams syndrome is a rare genetic disorder seen in 1 per 20.000 to 50.000 live births.^[1,2] The disease is typically characterized by dysmorphic facial features, cardiovascular disorders, hypertension, growth retardation, infantile hypercalcemia, behavioral problems, cocktail personality, and varying degrees of mental retardation.^[3] The genetic defect is on one of the 28 genes located in the q11.23 region of chromosome 7.^[4,5] Elastin gene mutation causes proliferation of the smooth muscle cells and fibroblasts and reduces arterial flexibility with irregular arrangement of short elastic fibers.^[6] The major pathological signs of the disease include thickening, fibrosis, and luminal stenosis of the media

and intima of great arteries.^[1,7] The most common cardiac problems are supraaortic stenosis and peripheral pulmonary stenosis.^[5] In this article, we present two pediatric cases with a rare cardiac problem of Williams syndrome: aortic coarctation and recoarctation.

CASE REPORT

Case 1- A five-day-old baby presented to our clinic with murmur on cardiac examination. On physical examination, micrognathia, wide mouth, full lips, long philtrum, short flat nose, hypertelorism, and periorbital edema were noted. Grade 1/4 systolic murmur was heard on the left of the sternum and femoral pulses



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were unable to be palpated on cardiovascular system examination. Other system examination findings were normal. Electrocardiogram also showed normal findings. Mild narrowing of the right and left pulmonary arteries (25-27 mmHg), significant aortic coarctation, and normal left ventricular function were detected by echocardiography. Genetic analysis (fluorescence *in situ* hybridization method) confirmed the diagnosis by detection of the deletion of chromosome 7q11.23. Balloon dilation angioplasty was performed at the site of coarctation; however, the intervention was unsuccessful with no significant change in the gradient (53 mmHg and 47 mmHg before and after the procedure, respectively) and diameter (2.8 mm and 3.2 mm before and after the procedure, respectively) (Figure 1). The patient was operated using an end-to-end anastomosis technique for coarctation, when he was 5.5 months old. The coarctation area was open with no evidence of antegrade diastolic run-off by echocardiography before discharge. At the first visit, one month after surgery, recoarctation (gradient between the ascending and descending aorta was 90 mmHg) was detected and balloon dilation angioplasty was performed and failed to decrease the gradient. At 10 months of age, the patient was reoperated with subclavian flap aortoplasty technique for recoarctation. During the next six months, restenosis was not detected in the coarctation area and the patient was followed in a good overall condition.

Case 2– A four-month-old girl was examined in another clinic due to growth retardation and



Figure 1. An unsuccessful balloon dilation angioplasty image of our first case.

balloon dilation angioplasty was performed for aortic coarctation. She was referred to our clinic for surgery, as angioplasty failed. On physical examination, micrognathia, wide mouth, full lips, long philtrum, short flat nose, hypertelorism, and periorbital edema were noted. Grade 1/4 systolic murmur was heard on the left of the sternum, while all other system examination findings were normal. Mild-to-moderate narrowing of the left pulmonary artery (60 mmHg), mild stenosis of the mitral valve, and significant aortic coarctation were detected by echocardiography. Left ventricular function was normal. Genetic analysis (fluorescence *in situ* hybridization method) confirmed the diagnosis by detection of the deletion on chromosome 7q11.23.

The patient was operated by end-to-end anastomosis technique for aortic coarctation, when she was seven months old. Echocardiographic findings of the patient before discharge showed mild residual coarctation. At the first visit, one month after surgery, recoarctation (gradient between ascending and descending aorta increased from 60 to 100 mmHg) was detected and balloon dilation angioplasty performed decrease the gradient failed. Therefore, the patient was reoperated with subclavian flap aortoplasty technique for recoarctation, when she was 11 months old. During the follow-up visit, one year after re-do surgery, her overall condition was good without residual coarctation.

DISCUSSION

Cardiovascular system involvement which accounts for approximately 80% of cases with Williams syndrome is the leading cause of morbidity and mortality.^[8] The most common cardiac pathologies are supravalvular aortic stenosis and peripheral pulmonary stenosis.^[8-10] Collins et al.^[7] reported that peripheral pulmonary stenosis and supravalvular aortic stenosis were seen in 62% and 57% of 129 patients with Williams syndrome, respectively. Other cardiac findings include bicuspid aortic valve, aortic regurgitation, mitral valve prolapse, mitral regurgitation, ventricular septal defect, atrial septal defect, coarctation of the aorta, atrioventricular septal defect, the anomalous left coronary artery from the pulmonary artery (ALCAPA), and tetralogy of Fallot (TOF).^[2,3,5,6] Both of our cases had peripheral pulmonary stenosis which did not require surgical intervention and were non-progressive. One of them had mild mitral stenosis, as well.

Although large vessel occlusion was seen in 20% of patients, there were no patients with coarctation of

the aorta according to the review study on Williams syndrome published in 2001 by the American Academy of Pediatrics.^[11] The frequency of aortic coarctation in patients with Williams syndrome was reported to be 18% by Collins et al.^[5] According to the published data, although coarctation of the aorta in patients with Williams syndrome is rare, recoarctation may be more common in this patient population.^[10]

In a study including patients with coarctation of the aorta, Collins et al.^[5] performed surgery to four patients (18%) balloon dilation angioplasty to three patients. Coarctation recurred in all of the patients undergoing balloon angioplasty and only one patient undergoing surgery. In another study, Del Pasqua et al.^[2] reported that re-coarctation developed in one of five patients who underwent surgery. Similarly, balloon angioplasty either before or after surgery was unsuccessful in our cases. Briefly recoarctation was seen shortly after the surgery (within the first month) and reoperation was performed.

In Williams syndrome, elastin gene mutation causes proliferation of the smooth muscle cells and fibroblasts, reduces arterial flexibility with irregular arrangement of short elastic fibers, leading to luminal stenosis by medial thickening of the muscular layer of the great arteries.^[6-7,12] Development of coarctation of the aorta in Williams syndrome can be explained by this pathophysiology. There is a limited number of cases reported in the literature with renarrowing within a short time after surgery or balloon dilation angioplasty.^[12,13] However, data on the underlying mechanism of recurrence of coarctation immediately after intervention are still scarce.

Furthermore, it can be challenging to decide the repair process of aortic coarctation before surgery in patients with Williams syndrome. A surgeon can decide the technique according to the thickness of the length of the medial layer of coarctation of the aorta during surgery. To date, there are reported cases in whom the left subclavian artery flap and allograft patch aortoplasty techniques were applied.^[12-14] In a case report, Arrington et al.^[13] showed that coarctation was repaired by pulmonary allograft patch method due to severe diffuse medial thickening of the thoracic aorta and its branches during surgery. On the other hand, in our cases, surgeons preferred an end-to-end anastomosis technique in the initial surgery due to the short segment coarctation areas. However, the left subclavian artery flap method was preferred for the second operations due to the long segment coarctation areas. The recoarctation operations of the cases with

Williams syndrome should be performed by more aggressive methods.

In conclusion, although coarctation of the aorta is rare in Williams syndrome, there is high risk of recurrence after surgery or balloon angioplasty. Therefore, patients with Williams syndrome should be closely followed after treatment of aortic coarctation and more aggressive surgical procedures should be considered, where applicable.

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