

A rare case of discrete aortic coarctation in Williams-Beuren syndrome. Diagnostic and therapeutic considerations

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Abstract

Williams-Beuren syndrome (WBS) is a genetic disorder caused by elastin gene deletions, and is characterized by cardiovascular malformations, primarily including supravalvular aortic stenosis and peripheral pulmonary stenosis. We report a case of a neonate who developed severe discrete aortic coarctation, underwent multiple surgical interventions, and was subsequently diagnosed with WBS. Severe discrete aortic coarctation is a rare event in WBS newborns. An abnormally thick aortic wall is present in these patients and is the basis of the failure of the classical approach towards coarctation repair, which consists of end-to-end anastomosis as first surgical choice. Our case, and a very few similar previously documented cases, have all demonstrated recoarctation, which only aortic patch implantation was able to successfully repair. In light of this, we would also like to underline the importance of early WBS diagnosis. Therefore, even in mild syndromic phenotype such as low birth weight or facial dysmorphism that raise the suspicion of a genetic syndrome, it is advisable to perform fluorescent *in situ* hybridization analysis rather than merely karyotypic one.

Introduction

Williams-Beuren syndrome (WBS) is a congenital multisystem developmental disorder found in 1:10000 live births. The genetic defect involves gene microdeletions on chromosome 7q11.23 including the

ELN gene encoding elastin. Williams-Beuren syndrome phenotype includes a wide spectrum of congenital malformations with cardiovascular disorders representing the most worrisome ones. Other main features include central nervous system and connective tissue involvement, mainly with characteristic elfin face, mental and growth retardation and hypercalcemia.^{1,2}

Structural cardiac abnormalities occur in 80% of WBS patients, among which supravalvular aortic stenosis (SVAS) and peripheral pulmonary stenosis (PPS) being the most prevalent, with 75% and 40% respectively. However, other arteriopathies (principally coronary, renal and mesenteric) have also been described playing an important role in morbidity and early mortality. In addition, the elastin insufficiency give rise to stenosis of the thoracic aorta (STA), in which there must be a distinction between a long-segment narrowing of the thoracic aorta, and a discrete coarctation.^{3,4}

We report a case of a newborn with atypical presentation and delayed diagnosis of WBS, who developed a severe discrete aortic coarctation (CoA), which is a rare finding in WBS patients (less than 1%),⁴ and underwent multiple surgical interventions.

Based on our case and few other previously documented cases,⁴⁻⁶ we noted a particular clinical course in these patients, and unlike previously done, we suggest here an alternative primary approach in the treatment of such rare cases.

Case Report

The patient is a full-term Caucasian baby-girl born (2.4 kg) by cesarean section due to intrauterine growth restriction (IUGR). At birth the baby showed signs of breathing difficulties that required n-CPAP ventilation and several hours of oxygen therapy. She was discharged in good general conditions 5 days later. *Ex-post facto*, mild facial dysmorphism was present at birth but was being overlooked.

At 1 month, physical examination revealed a 3/6 harsh systolic murmur, decreased palpable bilateral femoral pulses and elevated blood pressure with gradient of 40 mmHg between her upper and lower limb. Echocardiography showed mild pulmonary trunk flow acceleration, no SVAS, but moderate systolic flow acceleration over the aortic isthmus coincident with mild CoA. No evidence of left ventricular hypertrophy (LVH) and closed ductus arteriosus.

Due to progressive deterioration in her hemodynamic status, at 2 months a surgery via left thoracotomy was performed, including resection of the coarctated region and end-to-end anastomosis. During the operation the surgeon reported a particularly abnormal aortic wall thickening. In light of this finding, the presence of mild facial dysmorphism and IUGR, a karyotype analysis was eventually performed and came back negative for Turner syndrome.

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Echocardiography 2 weeks post surgery demonstrated only mild systolic flow acceleration.

However, reevaluation one month after surgery revealed severe recoarctation with elevated pressure gradient, as well as LVH and systemic hypertension. Initially, the patient underwent an unsuccessful transcatheter balloon expansion, and a subsequent aortic arch enlargement by a CorMatrix patch was performed via median sternotomy and cardiopulmonary bypass. In addition, antihypertensive therapy was administered with Propranolol and Captopril. Given the recoarctation and the negativity for Turner syndrome, we first suspected WBS, which was confirmed by fluorescence *in situ* hybridization (FISH) analysis. At 4 months, 27 days after surgery, pressure gradient has normalized. Antihypertensive therapy was gradually interrupted.

Echocardiography follow-up at 12 months demonstrated no LVH and no residual coarctation. The baby-girl is feeding well and progressively growing.

Discussion

Two substantial matters merit our attention. The first one concerns the late diagnosis of WBS in neonates not presenting normally. Our patient was born only with low weight and a mild facial dysmorphism. She had neither SVAS nor PPS, and other characteristics of WBS such as hypercalcemia were not present. Nonetheless, upon presentation of CoA we did think of a genetic syndromic association, but mistakenly considered only karyotype analysis. The first message is therefore; when coarctation is associated with mild syndromic phenotype (*i.e.* IUGR; mild facial dysmorphism) we suggest carrying out early FISH analysis rather than only karyotype screening.

The second issue worth mentioning is the therapeutic approach in these patients. It has been clearly demonstrated by the case presented here, and by all the few other previously documented cases,⁴⁻⁶ that the best hemodynamic and clinical outcomes were achieved by means of aortic enlargement with a patch. A patch implantation is the surgeon's first choice when it comes to long-segment thoracic aorta stenosis, and we believe however that this should also be the first choice in cases of discrete CoA in patients affected with WBS.

The reason of failure of both, end-to-end anastomosis and balloon dilation is the consequence of an irregular elastic fibers arrangement of the vessel wall, caused by the elastin mutation with a particularly abnormal aortic wall thickening, which was also evident in many other aortic surgeries of WBS babies.³⁻⁶ Under these circumstances one can argue that CoA in WBS should be distinguished from the clas-

sic form of coarctation and as such, requires different initial surgical approach.

Conclusions

In conclusion, based on these evidences, and due to the histopathologic morphology of the aortic wall,⁵ which dramatically increases the risk of early recoarctation, we believe that in the presence of discrete coarctation, an early diagnosis of WBS is critical. Even though it is a very rare event, we should keep in mind the possibility of having a non-chromosomal syndrome such as WBS, and thus performing FISH analysis instead of a karyotypic one whenever a syndromic clinical picture is suspected. For the least, upon encountering an abnormally thick aortic wall during first intervention, we strongly advise the cardiac surgeon, to bear in mind that this finding is compatible with WBS, and consider aortic patch implantation rather than end-to-end anastomosis. The abnormal aortic wall in WBS patients is unable to sustain the anastomosis and recoarctation occurred in each of the documented cases. Only a patch implantation has proven to be a successful solution for coarctation in WBS babies. Taking all this into account may save the baby the pain and the risk of undergoing multiple interventions, as well as lower the medical costs of such avoidable scenario.

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