

Severe aortic obstruction in Williams-Beuren syndrome – a short case series

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Abstract

Williams-Beuren syndrome is a multisystem disorder caused by the deletion of multiple genes on chromosome 7.

Many patients are identified through the presence of dysmorphic features and associated cardiac abnormalities.

We report two cases demonstrating supravalvular aortic stenosis (a common feature of Williams syndrome) and coarctation of the aorta on computed tomography (CT) aortogram.

Introduction

Williams-Beuren syndrome is a complex developmental disorder characterised by congenital heart and vascular disease, mental retardation, a characteristic learning profile, a hypersocial personality and infantile hypercalcaemia. Its prevalence has been estimated to range from 1:13 700 to 1:25 000 live births.¹ This syndrome is associated with a microdeletion in the chromosomal region 7q11.23, encompassing the elastin gene. Confirmation of this syndrome can be made by detecting elastin hemizygosity by fluorescence *in situ* hybridisation (FISH).¹⁻³ Reports suggest that this microdeletion of the elastin gene is responsible for the typical vasculopathy of the Williams syndrome, namely supravalvular aortic stenosis (SVAS) and pulmonary artery stenosis.^{2,3}

Cardiovascular abnormalities occur in approximately 80% of reported cases, with SVAS being the most common cardiac anomaly, present in 64% of patients.¹ Other cardiopathies include pulmonary artery stenosis, aortic hypoplasia, coarctation of the aorta, mitral valve prolapse, and septal defects.¹ Imaging plays an important role in demonstrating these vascular disorders. Magnetic resonance (MR) and computed tomography (CT) angiography with three-dimensional (3D) reconstruction provides excellent visualisation of the ascending aorta and aortic arch and should be used to delineate the extent of SVAS and other arteriopathies.⁴

Case reports

Patient 1 was a 3-month-old female infant referred by a general practitioner for an incidental murmur. On clinical examination, the child was acyanotic and had the typical facies of Williams-Beuren syndrome. The systolic blood pressure readings in the right upper limb compared with the right leg showed a gradient of 40 mmHg. In addition there was cardiomegaly and a systolic murmur was heard. Hence a clinical diagnosis of aortic stenosis and a coarctation of the aorta were suspected.

On echocardiography, there was a hypertrophied left ventricle, with a hypoplastic aortic valve annulus (diameter 7 - 8 mm), with bilateral peripheral pulmonary stenosis. The chest X-ray revealed an enlarged left ventricle and there was no evidence of cardiac failure. CT aortogram with 3D reformats confirmed supravalvular aortic narrowing, coarctation of the aorta just distal to the left subclavian artery (long segment 6 mm) as well as coarctation distally of the descending aorta (Figs 1 a & b,

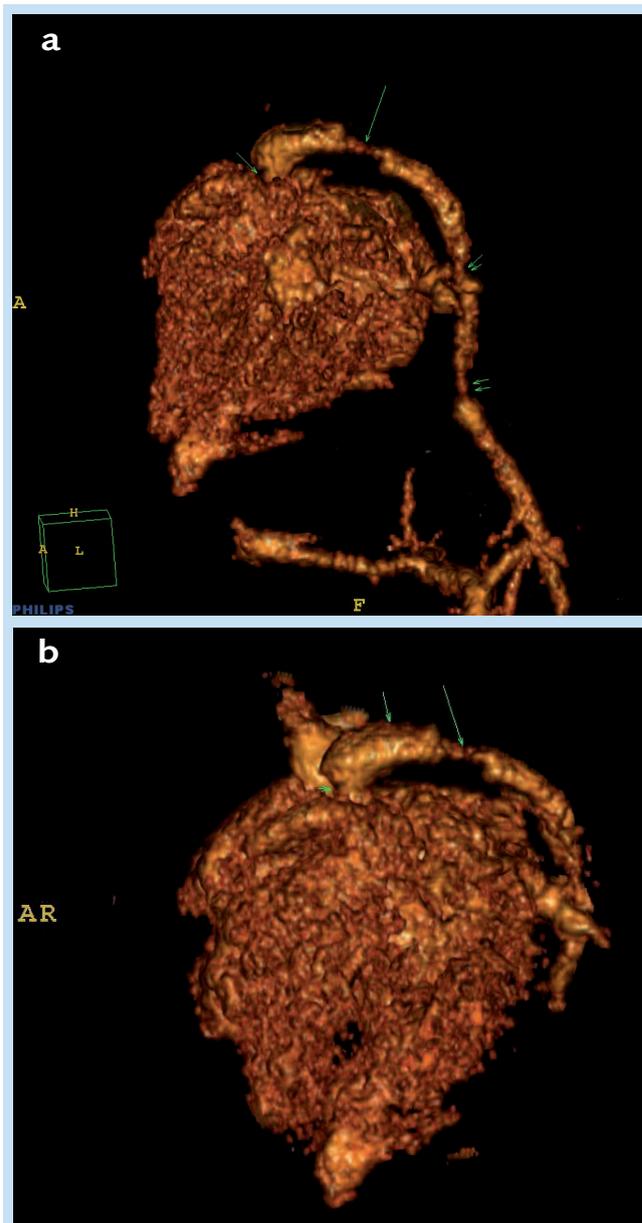


Fig. 1 (a) 3D CT aortogram AP view demonstrating supravalvular aortic stenosis at the level of the sinotubular junction (short arrow), coarctation of the aorta distal to the left subclavian (long arrow), coarctation distally of the descending abdominal aorta (double arrows). (b) Lateral 3D CT aortogram showing poststenotic dilatation of the aorta (short arrows) and coarctation of the aorta (long arrow).



Fig. 2. Sagittal maximum intensity projection image (arrows) depicting coarctation of the aorta.

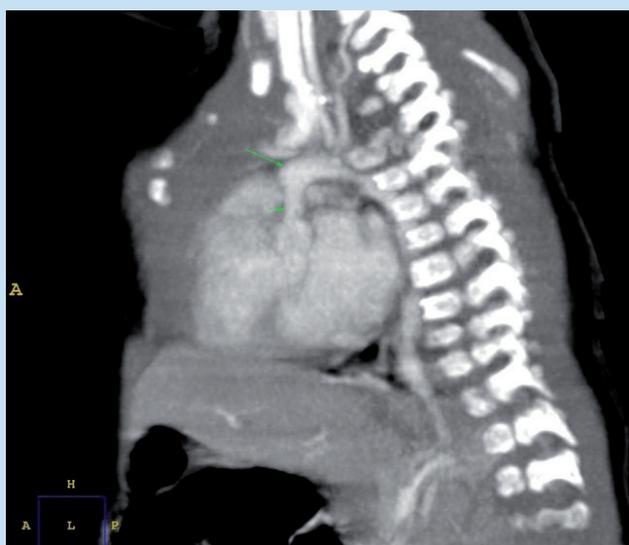


Fig. 3. Sagittal MIP image – demonstrating SVAS (short arrow) and poststenotic dilatation (long arrow).

2 & 3). It also showed an absent renogram on the left (confirmed absent left kidney on ultrasound).

Patient 2 was seen initially as a 3-month-old female with an incidental murmur, dysmorphic features and clinical features of immunosuppression. The patient was however lost to follow-up until 2 years of age when she was again referred for a cardiac assessment. On examination the child was very friendly and approachable, but was clearly dysmorphic. She was acyanotic with a systolic blood pressure of 110 mmHg in the right upper limb. All the pulses were easily felt and of normal volume.

Echocardiography showed mild supra-aortic narrowing. The aortic valve annulus was normal. In addition there was mild bilateral branch pulmonary stenosis.

The chest X-ray revealed a normal heart size and no features of cardiac failure.

CT aortogram with multiplanar reformats (MPR) confirmed severe SVAS, however the rest of the abdominal aorta and its branches were normal (Fig. 4). In comparison to patient 1, both kidneys were present and normal. Genetic (FISH) analysis on both patients showed the 7q11.23 chromosomal deletion, confirming the diagnosis of Williams-Beuren syndrome.

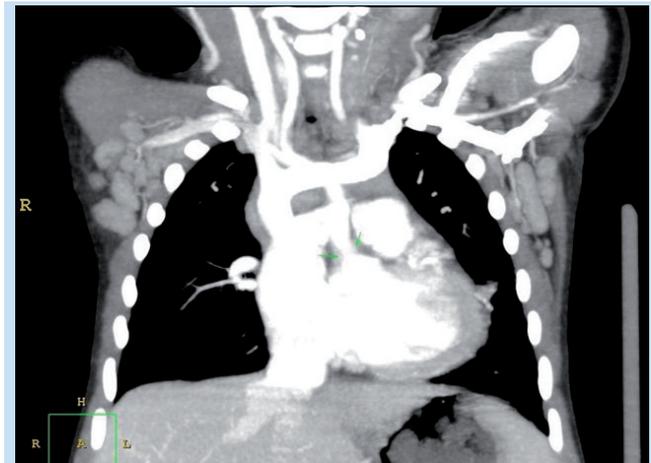


Fig. 4. Coronal MIP image – arrows depicting the localised area of narrowing visible above the aortic sinuses. The origins of the brachiocephalic vessels are normal.

Discussion

The Williams-Beuren syndrome, a rare congenital anomaly involving the vascular system, connective tissue, and central nervous system, was initially described by Williams *et al.* in 1961, and then by Beuren in 1962.⁵

Aside from the common vascular anomalies found in this syndrome, other organ systems are also affected. Renal anomalies are present in up to 17% of cases; these anomalies may be cystic, with hydro-nephrosis, agenesis, hypoplasia, reflux, diverticula, nephrocalcinosis and ischaemia.⁵ In our patient 1, CT findings revealed an absent left renogram, consistent with agenesis.

Other abnormalities described include cerebral vessel stenosis, coronary artery stenosis and myocardial infarction, diverticular disease, rectal prolapse, hypercalcaemia, hypercalciuria and hypothyroidism. Intracardiac abnormalities are less common but include ventricular septal defects and rarely mitral insufficiency.⁵

The distinctive facial appearance of patients with Williams-Beuren syndrome is characterised by hypertelorism, saddle nose, excessive periorbital tissue, thick lips, full open mouth, stellate iris pattern and dental abnormalities (Figs 5 a-c). These patients are almost always communicative and sociable. In our cases we observed facial and behavioural characteristics of this syndrome.

The diagnosis of SVAS and other vasculopathies of the Williams-Beuren syndrome can be made by multiple imaging modalities. The defining feature of this malformation is an aortic narrowing at the level of the sinotubular junction, but in some cases there is narrowing of the entire abdominal aorta and arch branches (see Fig. 1). MRI and CT



Fig. 5. Photographs demonstrating distinctive facial appearances of Williams-Beuren syndrome: (a) stellate irises, (b) microdontia – widely spaced teeth, (c) malocclusion.

aortography provide excellent visualisation of the abdominal aorta and aortic arch and should therefore be used to delineate the extent of SVAS. It can also demonstrate the degree and extent of coarctation and collateral formation. In coarctation of the aorta, characteristic rib notching is often present on chest X-ray or CT scan and is indicative of extensive arterial collateral formation bypassing the area of coarctation; a characteristic '3' sign is often also seen on chest X-ray.⁴ Rib notching is rare in the first 5 years of life; the CT scan of patient 1 revealed multiple areas of aortic coarctation without rib notching and collateral formation.

MRI is potentially the most comprehensive cardiac and vascular imaging modality available without the use of ionising radiation or contrast media. Paediatric patients usually require general anaesthesia. Both our patients had severe aortic stenosis and were regarded as high anaesthetic risk for sudden death, therefore CT aortography was chosen as the modality of choice.

The vascular abnormalities in Williams-Beuren syndrome must be distinguished from other congenital or acquired arteriopathies such as fibromuscular dysplasia or Takayasu's arteritis, respectively. The results of a previous study by Kim *et al.*, show that with time pulmonary artery stenosis tends to improve and SVAS to progress.^{2,6} SVAS often presents in childhood, and if not corrected by surgery can lead to heart failure and death.³ Case reports of sudden death in patients with Williams-Beuren syndrome date back to when the first cases were published in 1961.⁷ The majority of sudden death cases have been associated with myocardial infarction.⁷ As a result of the severity of the SVAS and coarctations, patient 1 died shortly after. Patient 2 is awaiting surgery.

Surgical treatment of supravalvular stenosis is by resection of the obstructed segment. Surgical enlargement of the narrowed sinotubu-

lar region and adjacent ascending aorta is recommended if symptoms (angina, dyspnoea, syncope) or a mean pressure gradient of > 50 mmHg are present.⁴ Coarctation of the aorta is treated with either percutaneous transluminal angioplasty with or without endovascular stent placement or surgery. Surgery comprises reconstruction of the aorta with resection of the stenotic segment, interposition of grafts or aorta-aortic bypasses or enlargement with patches.

Conclusion

Arteriopathy in Williams-Beuren syndrome is generalised and may involve any artery of the body, caused by elastin deficiency, and is the most common cause of morbidity and mortality. Both CT and MRI assist in operative planning and to visualise the extent of the disease. A detailed cardiac evaluation must be performed in all patients demonstrating the characteristic features of Williams syndrome because of the high frequency of cardiovascular anomalies and sudden death.

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