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Case Report

William's syndrome with mitral valve disease

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A 1½-year-old child was brought to pediatric OPD for delayed development. He had characteristic elfin like face with flat bulbous nasal bridge, upturned nose, full lips, wide mouth and long filtrum (Fig. 1). He was apparently asymptomatic and had no history of breathlessness or feeding difficulties. Child was active and playful. Examination revealed normal anthropometric parameters with weight of 14 kg and height 98 cm. Child was able to stand with support and could speak monosyllables only. There was difference in radial pulse volume in both arms, right being stronger than left, systolic blood pressure in right arm was 104/64 mmHg and in left arm 90/60 mmHg thus there was a difference of 14 mm with higher pressure in right arm. Auscultation revealed an ejection systolic grade IV/VI murmur in left parasternal and right infraclavicular area. There was grade III/VI pan systolic murmur heard in left axilla and left infrascapular region. Echocardiography revealed presence of supravalvular hourglass type

aortic stenosis with gradient of 100 mmHg while aortic valve was normal. Both pulmonary arteries were stenosed at origin and had gradient of 40 mm each. Severe mitral valve regurgitation was also present with mitral valve prolapse involving tip of anterior mitral leaflet. Examination of eyes revealed stellate-shaped pigmentation of anterior iris radiating out from papillary area. His hearing was normal. Neurological examination revealed normal tone and reflexes in all the limbs.

Karyotyping demonstrated normal 46 XY chromosome. FISH probe when hybridized to the metaphase showed one green signal on 7q22 i.e. control region but the critical region 7q11 involving elastin gene (ELN)-specific probe is deleted, a specific finding of William's syndrome (Fig. 2). The other normal chromosome shows both 7q11 in red and 7q22 in green. Ultrasonography of abdomen confirmed normal size and location of both kidneys. Renal vascular Doppler also showed normal flow velocity in both renal arteries. Serum calcium levels and thyroid function tests were normal.

Cardiac catheterization was performed to demonstrate exact size and extent of supravalvular region of aorta so as to plan surgical management in this child. Angiogram performed with injection of contrast into ascending aorta demonstrated tubular type of supravalvular aortic stenosis involving 14 mm of ascending aorta (Fig. 3). Pressure gradient of 100 mmHg was recorded in the narrowed segment of aorta. Right ventricular pressure was 60 mmHg with gradient of 40 mm across the stenosed segments. Bilateral branch pulmonary stenosis present at origin was demonstrated by selective injection into main pulmonary artery (Fig. 4). Patient

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Fig. 1 – Child with classical facial appearance of William's syndrome.

underwent surgery where supravulvular aortic enlargement and pulmonary arterioplasty was done with bovine pericardium. Mitral valve annuloplasty was also performed with a strip of bovine pericardium. Patient is recovering well and is under follow-up.

Fig. 2 – The figure shows one green signal on the deleted chromosome and one red and one green signal on the normal chromosome.

Discussion

William's syndrome is a rare congenital developmental disorder named after JCP Williams in 1961. Alois J. Beuren in 1962 reported association of typical facies and pulmonary artery branch stenosis with this syndrome.¹ It is a complex genetic syndrome comprising developmental abnormalities with short stature, craniofacial dysmorphic features and cardiac anomalies. Children are hypersociable and have some mental retardation. The reported incidence of cardiovascular anomalies is variable. Supravulvular aortic stenosis is the classic abnormality associated with 37–73% of cases of William's syndrome. Pulmonary artery stenosis is also relatively common.² Association of mitral valve disease is not well defined. In a series 37% of cases with William's syndrome had mitral valve prolapse while only one case had mitral insufficiency.³ In another large series of patient's with William's syndrome mitral valve disease was reported in only 12 out of 53 patients of which 9 had severe regurgitation.⁴ Hemizygosity at the elastin gene locus on chromosome 7q11.23 has been demonstrated to be the cause of vascular lesions in this syndrome. The deletion of the elastin gene leads to a reduced elastin content in the media of developing vessels, which may lead to recurrent injury and fibrosis. The reduced vascular inelasticity may also result in increased hemodynamic stress, leading to changes such as smooth muscle proliferation, fibrosis and luminal narrowing. The medial hypertrophy is responsible for the supravulvular stenosis and other arteries as pulmonary, carotid and coronary arteries seen in William's syndrome.⁵

Fig. 3 – Aortic root angiogram showing tubular supravulvular aortic stenosis.

Fig. 4 – Angiogram depicting bilateral pulmonary artery branch stenosis at osteum.

Our patient had classical facies of William's syndrome with confirmed diagnosis by FISH. This patient is of special significance as he had several cardiac manifestations together as severe supravalvular aortic stenosis, bilateral pulmonary artery branch stenosis and very rarely described severe mitral valve regurgitation. Cardiovascular complications are the

major cause of death in these patients particularly when they have biventricular outflow obstruction.⁶ Though the patient was asymptomatic inspite of multiple cardiac lesions early corrective surgery was performed for all cardiac lesions. Child is under follow-up and has good prognosis. He requires close follow-up for blood pressure, thyroid functions, serum calcium levels and growth parameters as these patients are known to have hypertension, features of hypothyroidism and higher calcium levels.

Conflicts of interest

All authors have none to declare.

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