CASE REPORT

Williams syndrome associated with complete atrioventricular septal defect

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Williams syndrome is a genetic disorder associated with characteristic facies, supravalvar aortic stenosis, peripheral pulmonary stenosis, mental retardation, hypertension, premature aging of skin, and congenital cardiac defects. Many cardiac defects such as bicuspid aortic valve, mitral valve regurgitation, coarctation of the aorta, and ventricular or atrial septal defects are linked to the syndrome. Complete atrioventricular septal defect has rarely been associated with Williams syndrome and only one necropsy case has been reported in the literature. The long term follow up of Williams syndrome associated with complete atrioventricular septal defect is reported. During a 10 year follow up period, the pressure gradient in the ascending aorta did not increase despite narrowing of the ascending aorta as identified on an aortogram.

Williams syndrome is a genetic disorder that occurs in 1 in 20 000–50 000 live births. It is also a developmental disorder involving the vascular system, the connective tissue, and the central nervous system and associated with cardiac anomalies. Herein we report a rare case of Williams syndrome associated with complete atrioventricular septal defect.

CASE REPORT

A 13 year old girl was admitted to our hospital for the postoperative examination. She had undergone repair of cardiac defects in our hospital when she was 3 years old. She was born at 42 weeks of gestation weighing 2200 g. She had a characteristic face with elfin features and mental retardation. On admission for surgical repair, systolic ejection murmur and mitral regurgitant murmur were heard. The second heart sound was fixedly split and the pulmonary second sound was accentuated. A chest x-ray showed an increased cardiothoracic ratio of 0.63 and an increased pulmonary vasculature. An ECG showed left axis deviation and right ventricular hypertrophy.

Right ventricular pressure was high at 94/0 mm Hg. The main pulmonary arteriogram showed supravalvar, branch, and peripheral stenoses (fig 1). The left ventriculogram showed goose neck sign (fig 2). An aortogram showed supravalvar aortic stenosis but there was no pressure gradient in the ascending aorta (fig 2). The diagnosis of Williams syndrome with associated complete atrioventricular septal defect was based on her characteristic face, supravalvar aortic stenosis, and goose neck sign on the left ventriculogram. The complete atrioventricular septal defect was repaired with the two patch method and the main pulmonary artery was enlarged with a bovine pericardial patch to relieve the supravalvar pulmonary stenosis. The postoperative pressure measured immediately after complete cardiac repair had decreased from the preoperative high right ventricular pressure of 90/0 mm Hg to 60/0 mm Hg as a result of the decreased systolic pressure in the main pulmonary artery. However, the systolic pressure of the right and left pulmonary arteries did not change because the peripheral pulmonary stenosis could not be corrected because of anatomical restrictions. There was also no pressure gradient in the ascending aorta. Postoperative cardiac catheterisation, performed in this admission 10 years after surgical repair of the cardiac defect, showed that the right ventricular pressure was 62/0 mm Hg, which had not changed from the previous postoperative study. There was also no pressure gradient in the ascending aorta. Before the second admission, fluorescence in situ hybridisation analysis detected the hybridisation signal on only one chromosome 7 in this patient.

DISCUSSION

Williams and colleagues reported on four patients with the triad of characteristic facies, mental retardation, and supravalvar aortic stenosis in 1961. Features of this disorder are congenital heart disease, hypertension, premature aging of the
skin, dysmorphic facial features, infantile hypercalcaemia, a
gregarious personality, and mental retardation. Subsequently,
Beuren and colleagues noted the frequent association of per-
ipheral pulmonary stenosis. Occasionally, Williams syndrome
is associated with other congenital abnormalities such as
bicuspid aortic valve, mitral valve regurgitation, coarctation of
the aorta, and ventricular or atrial septal defects. Jones and
colleagues evaluated 19 patients with Williams syndrome and
found five with pulmonary stenosis, two with ventricular sep-
tal defect, two with atrial septal defect, and one with valvar
aortic stenosis. Extracardiac defects other than supravalvar
aortic stenosis were three instances of peripheral pulmonary
stenosis, three of aortic hypoplasia, and two of mesenteric and
celiac artery stenosis. Mitral valve disease rarely accompa-
nied Williams syndrome. Becker and colleagues reported
mitral valve thickening in three cases of supravalvar aortic
stenosis. Akcoral and associates reported that mitral valve
prolapse was accompanied by supravalvar aortic stenosis in
only four cases, including their reported case. Mitral regurgi-
tation was rarely accompanied by supravalvar aortic stenosis
syndrome or Williams syndrome. Hanya and colleagues
reported on a necropsy case of supravalvar aortic stenosis
associated with complete atrioventricular septal defect, to our
knowledge for the first time in the literature. They also
reported no pressure gradient in the ascending aorta, as in our
case. They considered that no pressure gradient in the ascend-
ing aorta was due to a left to right shunt that was produced by
the complete atrioventricular septal defect. However, in
contrast to Hanya’s report, in our case 10 years after complete
repair there was also no pressure gradient in the ascending
aorta despite dissolution of the intracardiac shunt after com-
plete repair.

Genetic study of Williams syndrome discovered complete
deletion of the elastin gene on chromosome 7. Complete
atrioventricular septal defect was often associated with
Down’s syndrome, but it sometime occurs alone without
trisomy 21. Although the vast majority of patients with the
clinical features of Down’s syndrome have complete trisomy
21, in a minority portions of chromosome 21 are duplicated.
Molecular and cytogenetic mapping of small duplication has
suggested that the atrioventricular septal defect critical region
maps to a 4–5 Mb interval at 21q22.1-qter. Inoue and
colleagues introduced a human chromosome 21 into mouse
embryonic stem cells. Differentiation into cardiomyocytes was
delayed in the embryonic stem cells with an entire human
chromosome 21. However, when a human chromosome with
deletion at 21q22.1 was transferred, cardiomyocyte differenti-
tation was normal. From a genetic viewpoint, the cause of
solitary complete atrioventricular septal defect without
Down’s syndrome is not understood. In the present study,
Williams syndrome seems to be associated with complete
atrioventricular septal defect by chance because the affected
genetic site of Williams syndrome is different from that of
Down’s syndrome. To our knowledge, this is the first descrip-
tion in the literature of a long follow up period of Williams
syndrome associated with complete atrioventricular septal
defect. During 10 years’ follow up, the pressure gradient in
the ascending aorta did not increase despite the narrowing of
the ascending aorta seen on the aortogram.

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