CASE REPORT

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A Treatable Eisenmenger

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Abstract

Williams-Beuren syndrome, commonly known as Williams syndrome (WS) is a rare genetic condition. It presents with distinct facial appearance, cardiovascular anomalies, a characteristic neurodevelopmental and behavioural profile. It involves elastin gene deletion at chromosome 7. We present a case that had peripheral pulmonary artery stenosis with WS. Patient presented to our emergency and a detailed clinical examination suggested this diagnosis, which was later confirmed by further radiological and genetic testing. Patient was successfully treated for the cardiovascular lesions and discharged home.

Case report

A seven-year-old male child presented to emergency with complaints of diffuse abdominal pain, dull in nature and associated with constipation since 3 days. He did not have any history of fever, vomiting or any drug intake. On examination, the child had tachycardia and no tenderness in abdomen. He was given laxative and he passed hard stools, relieving the pain. On detailed history the family, told that he also had occasional shortness of breath since last few years. He was worked-up in other hospitals of New Delhi and a diagnosis of idiopathic pulmonary artery hypertension (PAH) was formed. At the time of presentation in our hospital, he was being treated for PAH. With the history in consideration, the patient was re-examined. On cardiovascular examination, it was observed that there was a palpable second heart sound without thrill in left second intercostal space parasternally. An ejection systolic murmur of grade 3/6, which increased with inspiration, was also heard in the same area. On careful auscultation of the back, ejection systolic murmurs of grade 2/6 were audible at bilateral inferior angle of both scapulae, which were increasing with inspiration. These murmurs were not fitting with the diagnosis of idiopathic PAH.

In the interim, blood investigations revealed high total calcium levels and ultrasound of the abdomen showed few small renal stones in left kidney. These findings made us re-assess the entire case once again. It was noticed that the child's facial features (Fig. 1a) and his dentition (Fig. 1b) were not normal. With all these findings, a diagnosis of Williams Syndrome (WS) was strongly suspected. Echocardiography revealed dilated right atrium and ventricle with turbulence of blood flow in distal pulmonary arteries. Paediatric cardiologist also reviewed the case and computed tomography (CT) pulmonary angiography was performed. It revealed multiple focal areas of stenosis and post-stenotic dilatations in segmental and subsegmental branches of both pulmonary arteries (Fig. 2). On intervention angiography, difference in gradients of pre-stenotic and post-stenotic segments of pulmonary arteries were established, suggestive of pulmonary artery stenosis (PAS). In the same sitting, balloon dilatation of left pulmonary artery was done. The patient was discharged in a stable condition after the procedure. Meanwhile, sample sent for

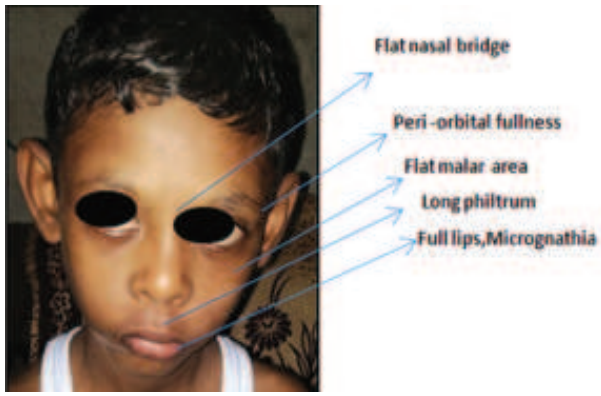

Fig. 1a: *Showing abnormal facial features of the patient.*

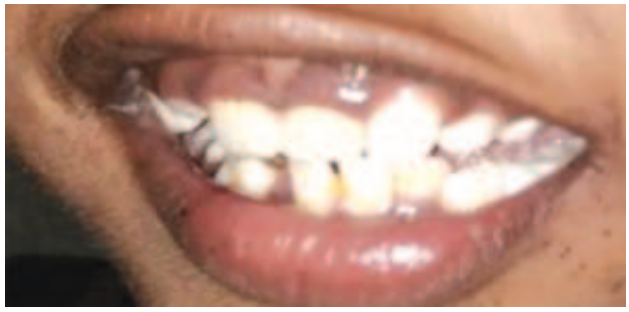

Fig. 1b: *Dental malocclusion in the same patient.*

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fluorescence in situ hybridisation (FISH) also confirmed genetic mutation of WS (Fig. 3). After 1.5 months, the patient was readmitted for balloon dilatation of right pulmonary artery. The patient was later discharged with advice for regular follow-up in paediatric cardiology outpatient department.

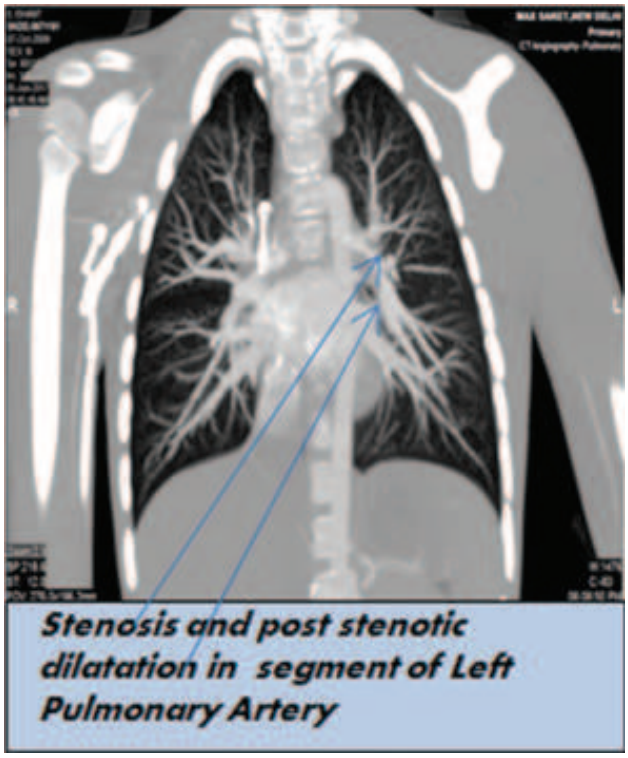

Fig. 2: *Showing CT angiography of the patient.*

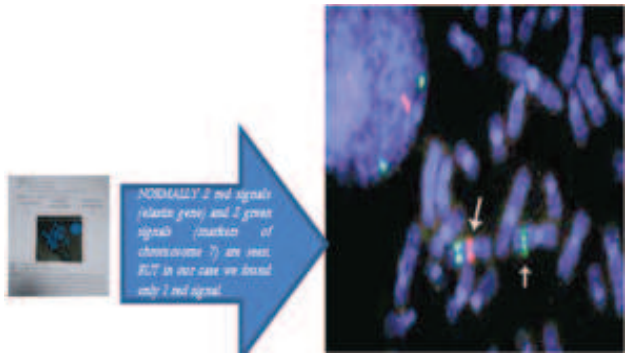

Fig. 3: *showing FISH confirmed genetic mutation of WS.*

Discussion

WS is a rare genetic disorder with an incidence of 1 per 7,500 - 20,000 births. Most of the cases are sporadic. However, in 25% of cases, one parent is found to have an inversion of chromosome 7[1]. Though it is equally prevalent among males and females, an earlier presentation of cardiovascular disease with greater severity may be observed in males[2,3].

Also known as contiguous gene deletion syndrome, in view of deletion at chromosome 7 involving a region that spans more than 28 genes[4,5,6], the cardiovascular findings and facial dysmorphology in WS are attributed to the connective tissue pathology due to elastin gene haploinsufficiency (loss of 1 of 2 copies)[7,8]. Though WS children are born full-term, microcephaly maybe observed in one-third of them[9].

Appearance of face in WS may include short upturned nose, flat nasal bridge, long philtrum, flat malar area, wide mouth, full lips, dental malocclusion, widely spaced teeth, micrognathia and periorbital fullness. Most of these features were present in the reported case (Figs. 1a and 1b). Cardiovascular findings include supravalvular aortic stenosis (SVAS), PAS and mitral valve regurgitation[10]. SVAS is the most common cardiac lesion in WS and it tends to progress in severity with the age of the patient[11]. PAS is the second most common lesion in WS and its natural history is one of improvement with age[11], but in our case the patient required intervention for this lesion.

Other findings include strabismus, cataract, sensorineural hearing loss, hoarse voice, joint hyperelasticity, contractures, kyphoscoloisis or lordosis. An incidental finding of hypercalcaemia in a child may also hint towards the diagnosis of WS. Echocardiography and CT angiography are the non-intervention modalities to detect cardiac and major vessels abnormalities. Intervention angiography of WS patient can be both a diagnostic and therapeutic procedure, as was in this case.

The American Academy of Paediatrics (AAP) had suggested a scoring system based on a study of 107 WS confirmed cases[12]. It is based on 7 items-growth, behaviour, development, facial features, cardiovascular problems, connective tissue abnormality and calcium studies. If the total score is less than 3, a diagnosis of WS is unlikely. But if it is 3 or more, FISH should be done. Our patient had a score of 12. In FISH, green signals are markers of chromosome 7 and red signals are markers of elastin gene in chromosome 7. In normal population, 2 red and 2 green signals are seen. In patients with WS (and also in our case), 2 green signals and only 1 red signal are observed. Intervention angiography and balloon dilatation in two separate settings, for PAS, were the therapeutic procedures done in our case, which relieved the child of the cardiac defects in WS.

We conclude from this case report that a detailed history and complete clinical examination for any case of PAH is a vital step. It may point to an underlying clinical diagnosis. Peripheral PAS should always be ruled-out before labelling the case as idiopathic PAH. Though peripheral branch PAS

usually resolves spontaneously, it may sometimes require therapeutic intervention.

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