Persistent great artery dilatation in Beals syndrome: A novel finding

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ABSTRACT

We report a unique case of dilated aortic root and pulmonary artery in an infant with clinical features consistent with Beals syndrome confirmed to have fibrillin-2 mutation. This case highlights a novel finding of main pulmonary artery dilatation that has not been previously reported with Beals syndrome or fibrillin-2 mutation. In addition, the importance of serial echocardiography and consideration of medical management is discussed.

Keywords: Beals syndrome, dilated great arteries, fibrillin-2 mutation

INTRODUCTION

Fibrillin-2 mutation can be seen in Beals syndrome, a rare autosomal dominant connective tissue disorder characterized by arachnodactyly, scoliosis, facial abnormalities, and crumpled appearance of the top of the ear.[1] The true incidence of this connective tissue disorder is unknown and difficult to estimate due to overlap with the clinical diagnostic features of Marfan syndrome. Initially, the absence of associated cardiac anomalies was thought to differentiate Beals from Marfan syndrome. Cardiac defects have now been reported with Beals syndrome including patent ductus arteriosus, atrial septal defects, mitral valve prolapse, ventricular septal defects, and one report of spontaneously resolving neonatal cardiomyopathy.[1,2] Aortic root dilatation may occur in patients with fibrillin-2 mutation and may persist into childhood in those with associated Marfanoid features.[3] However, cases of Beals syndrome with dilatation of both great arteries and the implications for medical management have not been previously reported.

CASE REPORT

Cardiac evaluation was requested for a full-term newborn with clubbed feet and long bones on fetal anatomy ultrasound. She was found to have dysmorphic facies, long bones, contractures of the feet and hands, and frontal bossing. She had a reportedly normal echocardiogram in the newborn nursery though specific measurements of the arteries and valves were not recorded.

At 1 week of life, genetic testing revealed a *de novo* splice site fibrillin-2 mutation with the c. 3725-2delA pathogenic variant confirming the suspected diagnosis of Beals syndrome. An echocardiogram performed at 3 months of age was notable for a patent foramen ovale, mild tricuspid valve prolapse without regurgitation, a mildly dilated aortic root at 1.56 cm (*Z* score +4.3), and an ascending aorta at the upper limits of normal at 1.16 cm (*Z* score: +1.8) [Figure 1]. The aortic valve was trileaflet with a dilated annulus of 1.05 cm (*Z* score: +3.1) without regurgitation or stenosis. The main pulmonary artery was also measured at the upper limits of normal at 1.16 cm (*Z* score: +1.9). Biventricular size and systolic function were normal. In consult with a cardiogeneticist, filamen-A testing was recommended, and atenolol was initiated for the dilated ascending aorta.

Repeat echocardiogram 1 month later found persistently dilated aortic root at 1.59 cm (*Z* score: +4.4) and ascending aorta at the upper limits of normal at 1.19 cm (*Z* score: +1.9). The main pulmonary artery was also borderline dilated (*Z* score: +1.9). Her extracardiac course included bilateral lower extremity cast placement

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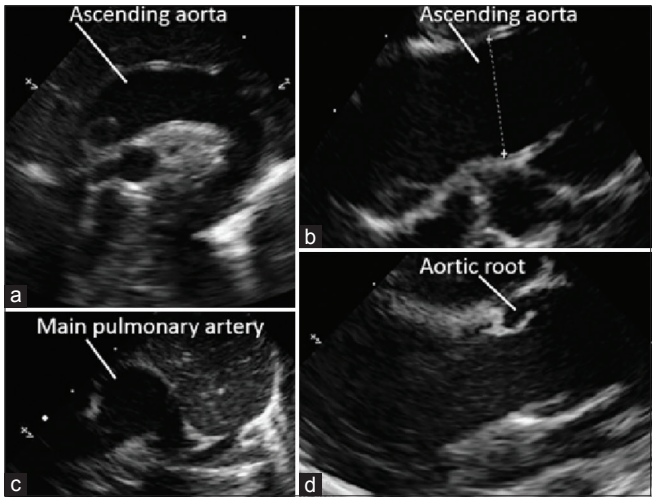

Figure 1: Transthoracic echocardiogram demonstrating dilated (a and b) ascending aorta, (c) main pulmonary artery and (d) aortic root at 3 months of age

for club feet, G-tube insertion for failure to thrive, and tracheostomy for tracheobronchomalacia.

Further outpatient cardiology follow-up at 9 months of age demonstrated further progression of the dilatation of the aortic root at 1.85 cm (*Z* score: +4.9), ascending aorta at 1.42 cm (*Z* score: +2.6), and main pulmonary artery at 1.51 cm (*Z* score: +2.2) [Figure 2]. Due to wheezing symptoms, her atenolol was discontinued, and she was started on losartan for persistent aortic root dilatation in consult with the cardiogeneticist. She continues to follow with cardiology for surveillance echocardiograms.

DISCUSSION

While there are reports of dilated aortic root with fibrillin-2 mutation, there are limited reports of this finding in Beals syndrome[3] and none with dilatation of both the ascending aorta and main pulmonary artery. Studies suggest that fibrillin-2 is involved in the initial assembly of the aortic matrix and overlaps with fibrillin-1 in aortic development.[4] Aortic root dilatation is a known finding in Marfan syndrome, which results from a mutation in the fibrillin-1 gene.[5] However, there are additional reports of aortic root dilatation with fibrillin-2 mutation, particularly in patients with bicuspid aortic valves.[5,6] One study reported aortic root dilatation in a patient with fibrillin-2 mutation and clinical features of both congenital contractural arachnodactyly and Marfan syndrome persisting through 5 years of age.[7] The finding of aortic root dilatation in our patient with Beals syndrome and confirmed fibrillin-2 mutation is unique because the extracardiac findings typically associated with Loeys–Dietz and Marfan syndromes are absent in our patient. In addition to the absence of vascular findings and skeletal malformations typical of

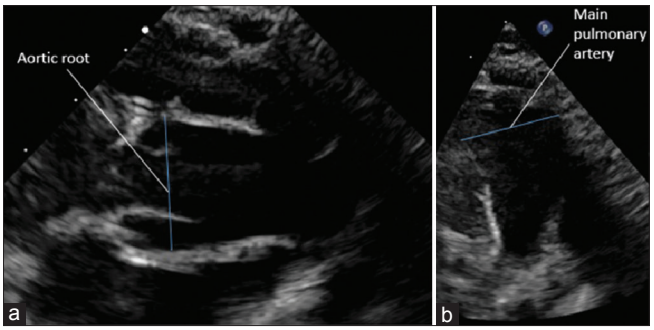

Figure 2: Repeat echocardiogram at 9 months of age demonstrating persistent dilatation of the (a) aortic root and (b) main pulmonary artery

Loeys–Dietz, our patient lacks the genotypic association characteristic of the disease.[8-10]

Experience with dilatation of the aortic root in patients with Marfan syndrome prompted the decision to initiate atenolol in our patient. It is unclear whether progressive dilatation or aneurysmal changes would be of concern in patients with isolated fibrillin-2 mutation or Beals syndrome though the findings by Gupta *et al.* suggest that trending this dilatation would be prudent.[7] While there is some evidence of the role of fibrillin genes in aortic root dilatation, there are no data to suggest the mechanism of dilatation of the main pulmonary artery demonstrated in our case. The persistent and progressive dilatation of the aortic root, ascending aorta, and main pulmonary artery seen beyond the neonatal period suggests that long-term follow-up is warranted. While atenolol had been prescribed to one of the patients with dilated aortic root in the case series by Gupta *et al.*, the patient was reportedly noncompliant.[7] The use of atenolol or losartan to address dilatation of the great vessels in Beals syndrome has not been explored. Further studies are needed to elucidate the role of fibrillin-2 in the pathophysiology of the great vessels and whether medical management with losartan or atenolol would be effective in slowing progression of great artery dilatation.

The role of fibrillin-2 gene mutations in arterial development is poorly understood. Our case suggests that patients with Beals syndrome require close echocardiographic assessment for dilatation of the great arteries, and medical management should be considered to prevent the progression of this dilatation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's parents have given their consent for her images and other clinical information to be reported in the journal. The parents understand that her name and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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