

## Isolated Cleft of the Posterior Mitral Valve Leaflet in a Patient with Marfan Phenotype

Abraham Benatar\*, Wendy Dewals and Tine Decraene

Department of Pediatric Cardiology, University Hospital Brussel (VUB), Free university of Brussels, Brussels, Belgium

### Abstract

Isolated cleft of the mitral valve is a very uncommon congenital cause of mitral regurgitation. Most of the clefts involve the anterior leaflet while isolated clefts of the posterior leaflet have been anecdotally reported. We present a child with a Marfan phenotype with mitral incompetence due to a midline (P2) cleft in the posterior mitral leaflet. Marfan syndrome frequently involves the mitral valve causing mitral valve prolapse. Occurrence of a posterior cleft may be an extension of its mitral valve involvement.

### Introduction

Cleft mitral valve leaflet is an uncommon congenital cause of mitral regurgitation. Clefts are slit-like holes or defects of the leaflet, hypothesized to be a result of incomplete expression of an endocardial cushion defect which most commonly involves the anterior mitral valve leaflet. The pediatric incidence is estimated at 1:1340 [1,2]. Clefts affecting only the posterior mitral valve leaflet are extremely rare with only few cases reported in the medical literature. The important co-existing anomalies with either anterior or posterior cleft mitral valve leaflet include counterclockwise rotation of the papillary muscles, the presence of an accessory papillary muscle or mitral valve leaflet, and mitral valve prolapse. We report a girl with Marfan phenotype associated with an isolated midline cleft of the posterior mitral leaflet, a combination only once previously reported [3].

### Case Report

A 10 year old girl was referred for evaluation of a cardiac murmur. She had seen an ophthalmologist who diagnosed bilateral ectopia lentis.

She was asymptomatic from a cardiac standpoint. There was no family history of Marfan syndrome or tall stature.

Clinical examination revealed a girl with a length of 160 cm, arm span of 162 cm, weight 40 kg. She had evident arachnodactyli, bilateral supero-temporal ectopia lentis, and shorter trunk than lower limbs.

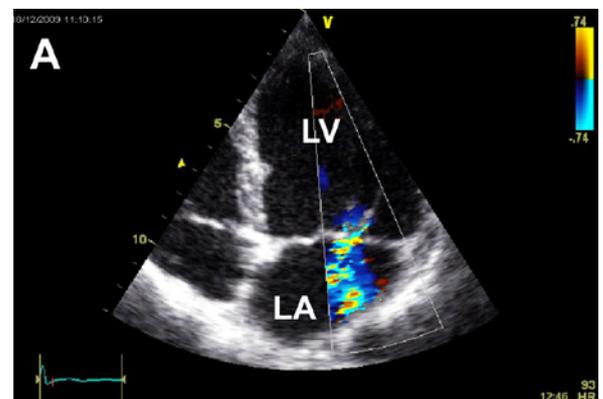
Cardiovascular examination revealed normal pulses, blood pressure and jugular venous pressure. The apex was not displaced. Auscultation revealed an apical grade 3 over 6 high frequency holosystolic systolic murmur irradiating to the axilla. Heart sounds were normal, no third heart sound. Rest of the examination was normal.

The electrocardiogram showed sinus rhythm, normal PR interval and normal frontal QRS axis of 72°. No left ventricular hypertrophy or ST segment T wave changes.

Transthoracic echocardiographic examination revealed a situs solitus, laevocardia and concordant atrio-ventricular and ventriculo-arterial connections. There was mild to moderate mitral regurgitation (grade 2 over 4) with normal left ventricular dimensions and systolic function as evidenced by normal shortening fraction, ejection fraction and mitral incompetence jet DP/dt of 864.2 mm Hg/second (Figure 1E). There was billowing of both the anterior and posterior mitral leaflets in the parasternal long axis image (Figure 1A and D). From the parasternal short axis images a cleft in the middle of the posterior leaflet (P2) was identified (Figure 1B and C). The posterior leaflet was

bisected by the midline cleft in two equal parts giving the mitral valve appearance of a trileaflet structure. The cleft masqueraded as a third commissure between the bisected posterior leaflets (Figure 1F and G). Color Doppler examination revealed a single jet of mitral regurgitation arising from the midline cleft extending postero-superiorly (Figure 1D). Three dimensional reconstruction of the image confirmed the posterior cleft leaflet at P2 segment (Carpentier classification). The number and location of the papillary muscles and chordal structures were normal. There was no dilatation of the aortic root or the ascending aorta (Z score for aortic annulus and sinus of Valsalva was respectively 0.1 and 0.3). There were no other cardiac anomalies known to accompany a mitral cleft such as an atrioventricular septal defect.

Genetic analysis was performed in particular for the FBN1 gene (Marfan syndrome) and the genes encoding transforming growth



**Figure 1a:** Apical four chamber view showing a mild eccentric mitral regurgitant jet through the posterior mitral leaflet.

\*Corresponding author: A. Benatar, Pediatric cardiology, UZ Brussel, 101 Laarbeeklaan, 1090 Brussels, Belgium, Tel: 00322-4775763; Fax: 00322-4775773; E-mail: [Abraham.benatar@uzbrussel.be](mailto:Abraham.benatar@uzbrussel.be)

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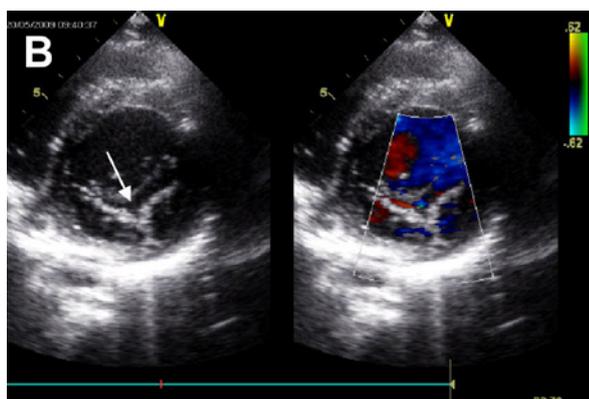
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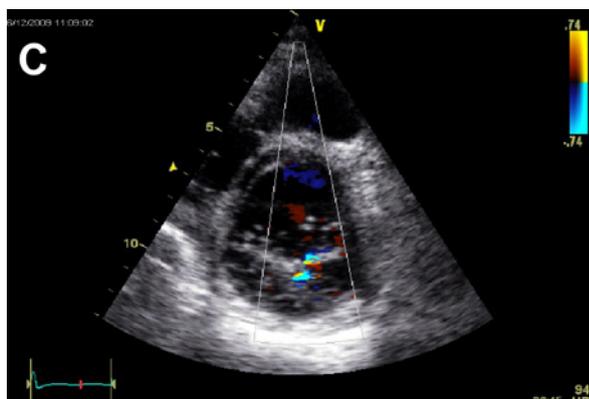
factor beta receptor 1 (TGFBFR1) and beta receptor 2 (TGFBFR2) for Loey's - Dietz syndrome. No mutations of these genes were identified.

## Discussion

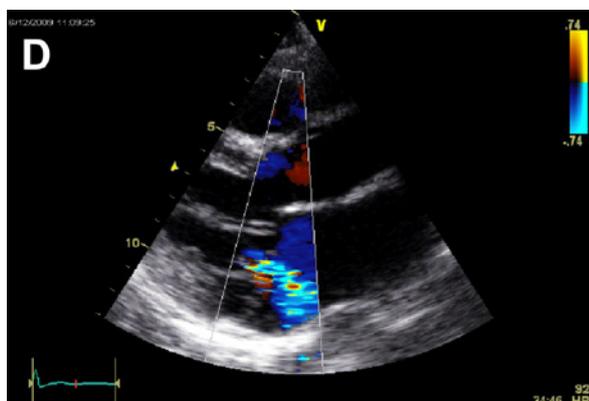
Cleft of the posterior mitral valve leaflet is an extremely rare congenital cardiovascular malformation. Only thirty one cases have



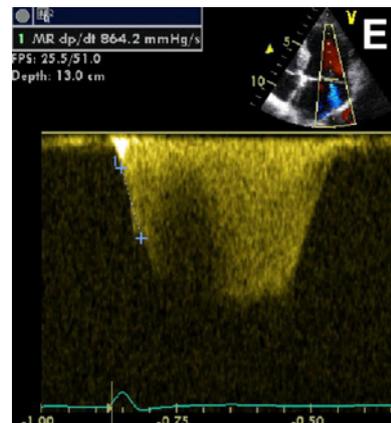
**Figure 1b:** Parasternal short axis view at mitral level showing a trileaflet mitral valve with a 'V' shaped posterior cleft, white arrow. Color Doppler shows onset of regurgitation.



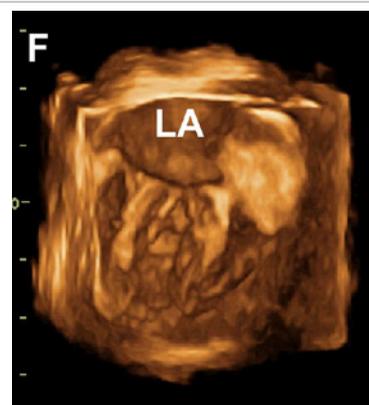
**Figure 1c:** Parasternal short axis view at mitral level showing regurgitant jet arising from posterior midline cleft as well as at commissure junction with anterior leaflet.



**Figure 1d:** Parasternal long axis view showing regurgitant jet directed postero-superiorly.



**Figure 1e:** Measurement of mitral regurgitant DP/dt in mm Hg per second.



**Figure 1f:** Three dimensional reconstructions from four chamber frames at posterior leaflet level showing open 'V' shaped cleft and open bisected leaflets. LA = left atrium.



**Figure 1g:** Three dimensional reconstructions shows the 'V' shape of the cleft as viewed from the left ventricle, white arrow.

been reported in the literature [1-11]. Associated anomalies include counterclockwise papillary muscles [6] or an accessory mitral valve tissue [7]. Only one of these reported patients had an associated Marfan syndrome [3]. A recent retrospective echocardiographic adult patient study identified twenty two subjects from 19,320 adults with cleft of the posterior mitral leaflet. Of these, 4 patients had associated heart disease.

In 13 of the 22 patients, the cleft was in segment P2.

To our knowledge, our report is the second patient with a Marfan phenotype and an isolated posterior mitral cleft. No mutations were found on the FBN1, TGFBR1 or TGFBR2 genes.

Isolated mitral clefts which occur in the absence of an atrioventricular septal defect are rare and mostly affect the anterior leaflet. In an echocardiographic study involving more than 13000 children, only 10 isolated mitral clefts were identified with all involving the anterior leaflet [12]. This entity is distinct from atrioventricular septal defect clefts [13]. Most reports of clefts of the posterior mitral leaflet have been anecdotal.

The cleft is a slit-like defect which can be clearly imaged by the two-dimensional echocardiography. Three dimensional echocardiographic reconstructions can be very useful in anatomical localization of the papillary muscles and chordal attachments. Mitral valve cleft can cause mitral regurgitation and left ventricular outflow tract obstruction in the presence of abnormal chordal attachments [6], which was not the case in our patient.

Marfan syndrome is a systemic connective tissue disorder commonly involving the cardiovascular system [14, 15]. Mitral valve prolapse is the most frequent cardiovascular complication, occurring in 70–80% of cases, well beyond the prevalence in the general population. Aortic root dilatation and dissection remain the most feared in Marfan syndrome [14,15]. Marfan syndrome is linked to defects in the gene of fibrillin-1 protein and to abnormalities of TGF- $\beta$  signaling [14]. Signaling through several members of the TGF- $\beta$  family is involved in valvulogenesis and development of endocardial cushion in mouse [14,15]. Both Marfan syndrome and Loeys-Dietz syndrome are associated with increased TGF-beta signaling in the vessel wall.

It may be speculated that defects in these signaling pathways may have caused abnormal development of the endocardial cushion leading to formation of a cleft in the mitral valve of our patient. Further studies may supply clues supporting such a hypothesis.

In summary, we think that this case is notable since isolated posterior mitral valve cleft is extremely rare and its occurrence with Marfan phenotype has been reported only once previously.

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