Cardiology in the Young

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A new discovered gene mutation in a child with dilated cardiomyopathy

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Abstract

Dilated cardiomyopathy is characterised by dilatation and impaired contraction of the left ventricle or both ventricles, which is the most common childhood cardiomyopathy. In recent years, it has been recognised that many sorts of genetic mutations may contribute to dilated cardiomyopathy. We now report a rare association of dilated cardiomyopathy with site mutation of BMPR2 gene. We did not find such an association reported in the medical literature.

Brief Report

Cite this article: Chen X, Xie Y, Li X, Gong J, Shen L, and Zhang R (2021) A new discovered gene mutation in a child with dilated cardiomyopathy. *Cardiology in the Young* **31**: 1530–1531. doi: 10.1017/S1047951121001104

Received: 1 January 2021
Revised: 22 February 2021
Accepted: 26 February 2021
First published online: 5 April 2021

Keywords:
Dilated cardiomyopathy; child; BMPR2; gene mutation

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Characterised by dilatation and impaired contraction of the left ventricle or both ventricles, dilated cardiomyopathy is caused by various factors, which may be idiopathic, familial/genetic, viral and/or immune, alcoholic/toxic.[1] For progressive heart failure, arrhythmia, systemic embolism as the main clinical manifestations, patients have high rates of death and sudden death. At present, for lack of specific treatment at present, dilated cardiomyopathy is mainly treated with symptomatic and supportive therapy. As more and more cases with dilated cardiomyopathy are found to be associated with certain genetic mutation, gene therapy may possibly be the development direction in the future.

Case report

A male patient aged 8 years and 9 months was treated at our hospital for a progressive decline in the amount of activity. The patient presented with clear consciousness, average mental status, steady breathing, and no cyanosis of lips. Physical examination revealed precardiac prominence with a tremor, normal breathing sound in both lungs, without obvious dry or wet rales, high heart rate, normal heart rhythm, low heart sound, and a 3/6 grade continuous murmur in the apical region of the heart and between 4 and 5 ribs on the left edge of the sternum.

After stabilisation in the emergency room, the child was taken to the cardiac intensive care unit. Echocardiographic showed left ventricular globoid dilation especially, left ventricular systolic dysfunction (ejection fraction = 27.8%), severe mitral regurgitation (none mitral leaflet malformation), and moderate tricuspid regurgitation (see Fig 1).

Corresponding supportive treatments were provided, such as use of dopamine as a cardiac stimulant, injection of frusemide for its diuretic property, and infusion of anti-shock agents. The patient suffered from frequent cardiac arrhythmia, in a form of borderline tachycardia, complete left bundle branch block or ventricular tachycardia, with a heart rate of about 160–180/minute, lasting about 1–5 minutes each time. During the examination of inherited metabolism, there were no abnormal signs seen in terms of glucose, lipid or amino acid metabolise. However, the gene test manifested a heterozygous mutation of BMPR2 gene (c.2795C > A) (See Table 1). According to clinical manifestation and auxiliary examination, the patient was diagnosed as dilated cardiomyopathy.

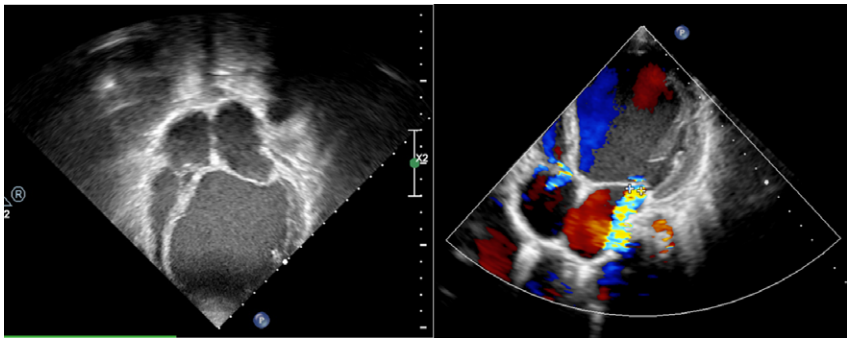

Figure 1. Left ventricular globoid dilation and mitral regurgitation, the width of regurgitant flow is 0.65 cm.

Table 1. Gene test result.

Gene	Transcript	Genetic model	Nucleotide / Amino acid	Zygote state
BMPR2	NM-001204.6	AD	c.2795C > A (p. Pro932His)	Heterozygosity

AD: Autosomal dominance

Past surgery history

On account of ventricular septal defect, atrial septal defect and severe pulmonary arterial hypertension, when the patient was 2 months old, both repair of ventricular septal defect and repair of atrial septal defect were performed. The infant's heart was functioning ordinarily at the time, although with mild tricuspid regurgitation, the mitral valve was in good condition with no occurrence of regurgitation. The outpatient follow-up lasted for 1 year after the surgery, showing no abnormality. And then subsequent visits were missed.

Discussion

Gene mutation is highly related to the pathogenesis, clinical phenotype and prognosis of dilated cardiomyopathy. An increasing number of gene mutations, including sarcomere-related genes, cytoskeleton-related genes, nuclear membrane protein-related genes, ion channel related-genes and other dilated cardiomyopathy-related genes has been found to be high associated with dilated cardiomyopathy. According to the current literature, dilated cardiomyopathy is associated with 110 nuclear protein coding genes and 24 mitochondrial DNA coding genes.[2–5] However, BMPR2 gene mutation has not been reported to be associated with dilated cardiomyopathy.

BMPR2 gene is located on chromosome 2q31-33,[6] it encodes bone morphogenetic protein type II receptor, which mainly regulates cell proliferation, differentiation and apoptosis. In pulmonary vascular circulation, BMPR2 related signalling pathway may inhibit the proliferation of small pulmonary artery vascular cells.[7] About 55–70% of familial pulmonary arterial hypertension and 11–40% of idiopathic pulmonary hypertension are associated with BMPR2 gene mutation,[8] and the inheritance mode is autosomal dominant inheritance.

A heterozygous mutation of BMPR2 gene (c.2795c > A, p.pro932his) was found in this patient. The above mutation was missense mutation. Referring to the database of gnomAD and PubMed, the above mutation has not been reported in the past. However, in order to determine whether these mutations can lead to dilated cardiomyopathy, it is necessary to further study the BMPR2 gene mutation on animal model.

Acknowledgements. None.

Financial support. None.

Conflict of interest. None.

Ethical standards. This article does not contain any studies with human participants or animals performed by any of the authors.

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https://doi.org/10.1017/S1047951121001104 Published online by Cambridge University Press