# A SUDDEN DEATH FOLLOWING CARDIOMYOPATHY IN A CHILD

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## ABSTRACT

### Introduction

Paediatric cardiomyopathies are clinically heterogeneous heart muscle disorders responsible for a significant morbidity and mortality. Phenotypes include hypertrophic, dilated, restrictive and arrhythmogenic right ventricular cardiomyopathy. The aetiology is diverse and includes genetic and non-genetic causes. Restrictive cardiomyopathy (RCM) is uncommon in children, accounts for 5% of all cardiomyopathies and has the worst prognosis.

### Case Report

An eight-year-old girl with a history of syncopal attacks over one year, developed acute dyspnoea. She had a cardiac arrest on admission and died despite resuscitation. Her past clinical records showed an echocardiogram report revealing biventricular diastolic dysfunction, good ventricular systolic function, biatrial dilatation and biventricular hypertrophy. Myocardial biopsy showed mild interstitial fibrosis. She had been diagnosed as having RCM. At autopsy the heart weighted 210g with biatrial dilatation, symmetrical biventricular wall thickening (both right and left ventricular wall thickness 18mm) and subendocardial fibrosis. The histology of the myocardium revealed hypertrophy and mild disarray of myocytes and interstitial fibrosis. There was no amyloid or iron deposits, granulomas or tissue eosinophilia. Cause of death was ascertained as acute cardiac failure following cardiomyopathy.

### Discussion and Conclusion

RCM is a disease characterized by a primary decrease in ventricular compliance resulting in diastolic failure. This patient had classic functional and structural features of RCM which include biventricular diastolic dysfunction, good ventricular systolic function and biatrial dilatation. An increased biventricular wall thickness which is a classic feature of hypertrophic cardiomyopathy (HCM) suggests clinical overlap with HCM. Mixed phenotype of RCM/HCM has shown significant transplant free survival compared to pure RCM. Relatively less symptoms and longer survival in this child could be explained by mixed RCM/HCM phenotype.

***Key words:*** Cardiomyopathy, Paediatric, Restrictive

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## INTRODUCTION

Paediatric cardiomyopathies are clinically heterogeneous heart muscle disorders[1] associated with cardiac dysfunction and responsible for a significant morbidity and mortality[2]. Phenotypes include hypertrophic, dilated, restrictive and arrhythmogenic right ventricular cardiomyopathy[3]. The aetiology is diverse and include both genetic and non-genetic causes[4]. Restrictive cardiomyopathy (RCM) is uncommon in children, which accounts for approximately 5% of all cardiomyopathies and has the worst prognosis[2]. Rarity of this condition in childhood limits the knowledge on disease process and its outcome.

## CASE REPORT

An 8-year-old girl who had a history of syncopal attacks over one year period, developed sudden onset dyspnoea and cardiac arrest. In spite of resuscitation she died and the cause of death was ascertained as complications of cardiomyopathy.

There was no history of congenital disease or sudden deaths in her family.

She had been investigated for recurrent syncopal attacks over the past one year. Perusal of the initial clinical records revealed cardio-thoracic ratio (CTR) of 55%, normal cardiac valves, biventricular hypertrophy, trivial mitral and tricuspid regurgitation with no right or left ventricular outflow obstruction. At this point the patient had been diagnosed as having hypertrophic cardiomyopathy (HCM).

She had been investigated further as the syncopal attacks were continuing. The investigations has revealed elevated proBNP (pro-brain natriuretic peptide) of 5861pg/ml, normal renal function and normal eosinophilic count. The CTR had increased to 65%. Echocardiogram showed biventricular diastolic dysfunction, good ventricular systolic function, pulmonary plethora and systemic venous congestion. Myocardial biopsy had shown mild interstitial fibrosis and the diagnosis had been revised as RCM. She had been managed conservatively.

At autopsy the enlarged heart weighed 210g, showed biatrial dilatation and symmetrical biventricular wall thickening with no dilatation of the ventricles. Both right and left ventricles measure 18mm in thickness. The myocardium was firm with marked sub endocardial fibrosis (Figure 1). The valve cusps were irregular and firm with fibrotic and shortened chordae tendinae. The coronary arteries were normal.

The histology showed myofibre hypertrophy and disarray (Figure 2).There was diffuse interstitial fibrosis with prominent subendocardial fibrosis (Figures 3 and 4).

There was no amyloid or iron deposition, granulomas or tissue eosinophilia.

The lungs and the liver showed vascular congestion. Other organs were unremarkable. The cause of death was ascertained as acute cardiac failure following cardiomyopathy.

## DISCUSSION

Cardiomyopathy is a clinically heterogeneous disease in which myocardium itself is structurally and functionally abnormal[6]. In paediatric population, 40% of children with cardiomyopathy needs transplantation within 5 years of diagnosis otherwise they progress to death[2]. Paediatric cardiomyopathies have a genetic and non-genetic aetiology[6]. Majority of the cases are still considered idiopathic as aetiopathology of this disease is not completely elucidated[5]. RCM is characterized by impaired ventricular filling and reduced diastolic volume of ventricles with near normal systolic function[7]. Main structural changes are atrial dilatation, normal ventricular wall thickness and normal atrioventricular valves[8].

Hypertrophy of ventricular wall is a characteristic feature of HCM. In HCM the ventricular wall thickening could be asymmetrical or diffuse and symmetrical. Similar to RCM, HCM is also characterized by diastolic dysfunction[9].

In this case, presence of diastolic dysfunction, cardiomegaly, biatrial dilatation and symmetrical biventricular hypertrophy suggest clinical overlap between the two phenotypes RCM and HCM. In some families, distinct HCM and RCM phenotypes segregate with the same disease causing sarcometric mutation[10].

Interestingly, children with mixed phenotype frequently (25%) have a family history of pure or mixed phenotype[11]. However, in our case the family history was negative. Mixed phenotype of RCM/HCM has shown significant transplant free survival compared

to pure RCM[11]. However, the survival is independent of the phenotype and further genetic and clinical exploration is needed to recognize genotype-phenotype correlations[12].

Complications such as pulmonary hypertension, embolic events, heart failure, arrhythmias or sudden death develops if cardiac transplantation is not performed. Increase proBNP level and systemic venous congestion suggest heart failure in this case. The mechanism of sudden death in RCM is unclear and is hypothesized that patients with ongoing myocardial ischemia are at a higher risk[7].

Though most of the cases of paediatric cardiomyopathies are idiopathic (60-70%)[13,] familial, syndromic, metabolic and neuromuscular aetiologies are identified[7] with many complex processes[14]. In this case, history and investigations are not suggestive of haemochromatosis, glycogen storage disorder, Fabry disease or irradiation. The histology revealed no amyloid, iron or metastatic tumour deposition or sarcoid granulomas.

There was no peripheral eosinophilia or eosinophilic infiltrate in other organs to suggest Loeffler endocarditis. Before concluding that this is a case of idiopathic cardiomyopathy we need to exclude the possibility of genetic mutations which we are unable due to lack of facilities. Future research is needed to understand how mutations in the same gene can cause distinct phenotypes which is important in medical management and screening the family members.

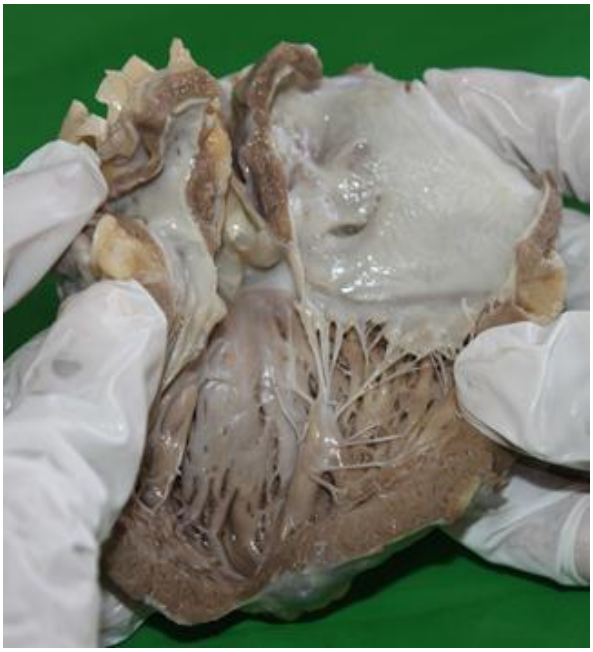

***Figure 1: The cut opened heart displaying dilated atria, thickened ventricular wall, subendocardial fibrosis and shortened chordae***

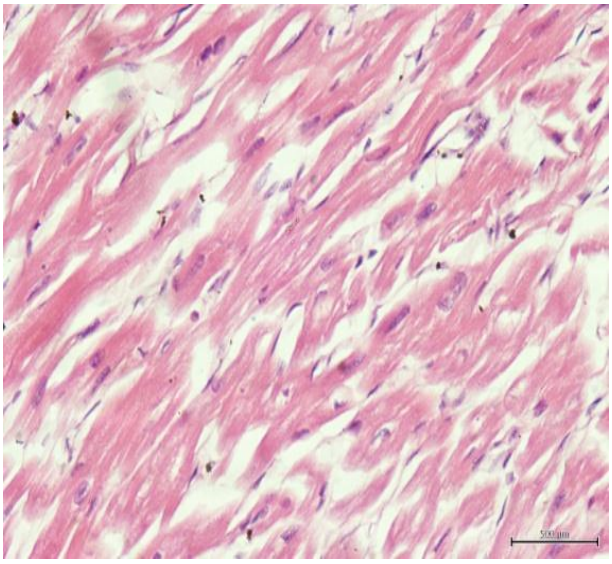

***Figure 2 :Myofiber hypertrophy and disarray (H & E 40x10)***

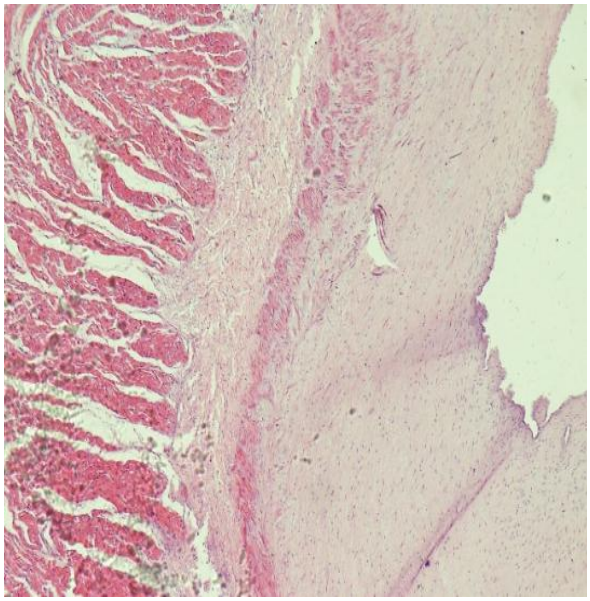

***Figure 3: The left ventricle displaying marked subendocardial fibrosis and hypertrophy of myocytes. (H & E 4x10)***

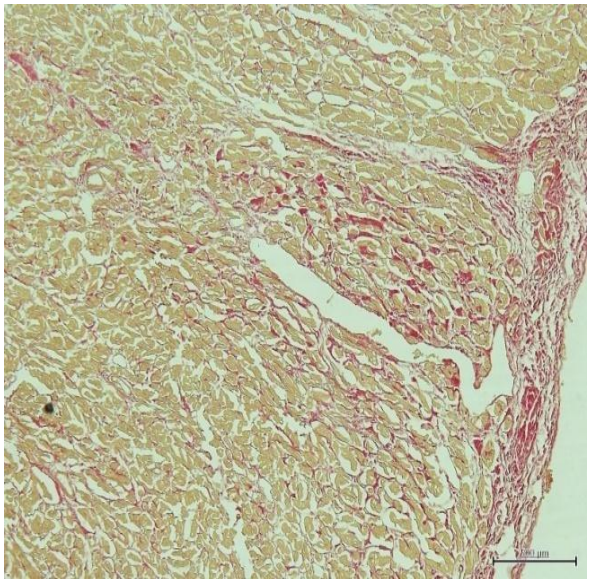

***Figure 4: Subendocardial and interstitial fibrosis (Van Gieson stain 4x10)***

## CONCLUSION

1. RCM is a rare form of cardiac disease with an extremely poor outlook in children. This patient had classic functional and structural features of RCM together with increased biventricular wall thickness, which is an overlapping feature with HCM. Relatively less symptoms and longer survival in this child may be explained by mixed RCM/HCM phenotype.

## REFERENCES


1. Petros Nihoyannopoulos, David Dawson. Restrictive cardiomyopathies, European Heart Journal - Cardiovascular Imaging, November 2009,Volume 10, Issue 8, DOI: http://dx.doi.org/10.1093/ejechocard/jep156iii23-iii33.

2. Steven E Lipshultz, Thomas R Cochran, Pediatric cardiomyopathies: causes, epidemiology, clinical course, preventive strategies and therapies Future Cardiology. Nov 2013; 9(6): 817–848. doi: 10.2217/fca.13.66.

3. McKennaWJ, Report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the Definition and Classification of Cardiomyopathies, Circulation. *1996; 93: 841-842* doi: 10.1161/01.CIR.93.5.841.

4. Denfield SW, Rosenthal G, Gajarski RJ, Bricker JT, Schowengerdt KO, Price JK, Towbin JA. Restrictive cardiomyopathies in childhood. Etiologies and natural history. Tex Heart Inst J 1997; 24: 38-44 [PMID: 9068138].

5. Susan W Denfield, Steven A. Webber,Restrictive Cardiomyopathy in Childhood, October 2010Volume 6, Issue 4, Pages 445452, DOI: http://dx.doi.org/10.1016/j.hfc.2010.05.005.

6. Towbin JA, Bowles NE. The failing heart, Nature 2002; 415: 227-233 [PMID: 11805847 DOI: 10.1038/415227a].

10. Lipshultz SE, Sleeper LA, Towbin JA, Lowe AM, Orav EJ, Cox GF, Lurie PR, McCoy KL, McDonald MA, Messere JE, Colan SD. The incidence of pediatric cardiomyopathy in two regions of the United States. N Engl J Med 2003; 348: 1647-1655 [PMID: 12711739 DOI: 10.1056/NEJMoa021715].

11. GewilligM,. MertensL, MoermanP., Dumoul inM.Idiopathic restrictive cardiomyopathy in childhood, European Heart Journal, Vol. 17, issue 9,pp 1413-1429.

12. T, NaritaT, SuminoS, Hypertrophic cardiomyopathy without asymmetric hypertrophy, British Heart Journal. May 1982; 47(5): 507–510.

13. Mogensen J, Kubo T, Duque M, Uribe W, Shaw A, Murphy R, Gimeno JR, Elliott P, McKenna WJ. Idiopathic restrictive cardiomyopathy is part of the clinical expression of cardiac troponin I mutations. Journal of Clinical Investigation 2003; 111: 209-216 [PMID: 12531876 DOI: 10.1172/JCI16336].

14. WebberA., Steven E. Lipshultzetal, Outcomes of Restrictive Cardiomyopathy in Childhood and the Influence of Phenotype A Report From the Pediatric Cardiomyopathy Registry, Circulation, September 4, 2012 ;126:1237-1244.

15. Muhammad Tariq, Stephanie M, Importance of genetic evaluation and testing in pediatric cardiomyopathy, World Journal of Cardiology, 2014 November 26; 6(11): 1156-1165.

16. Pierre-Yves Jean-Charles, Yue-Jin Li, Chang-Long Nan, and Xu-Pei Huang.

17. Monitoring Editor: Prof Yong-Fu Xiao Insights into restrictive cardiomyopathy from clinical and animal studies J Geriatric Cardiology. 2011 Sep; 8(3): 168–183.

18. Franz WM, Müller OJ, Katus HA. Cardiomyopathies: from genetics to the prospect of treatment. Lancet.2001;358:1627–1637.