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Meeting abstract

2062 Use of cardiac magnetic resonance imaging to identify variable phenotypic expression of an identical sarcomeric protein mutation

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Introduction

Hypertrophic cardiomyopathy (HCM) resulting from mutations in genes encoding sarcomeric proteins is the most common genetic cardiovascular disease.

Purpose

The aim of this study was to investigate whether cardiac magnetic resonance (CMR) can identify the phenotypic variability in family members sharing an identical single genetic mutation.

Methods

A large kindred who exhibit a mixed phenotype of HCM, dilated cardiomypopathy (DCM) and sudden cardiac death segregating in an autosomal dominant inheritance were evaluated. Six individuals from 2 generations the proband, her husband, and their 4 offspring, one son and three daughters, ages 20, 25, 23 and 18 years of age, respectively were followed. The proband had a known history of DCM; offspring had normal cardiac morphology by baseline CMR examination with delayed post-gadolinium enhancement (DME). This cohort was followed with yearly cardiac imaging to detect initial phenotypic expression. Direct DNA sequencing of the coding regions and splice sites of the *MYH7*, *MYBPC3*, *TNNT2*, *TNNI3*, and *TPM1* genes was performed on all 6 members of this nuclear family.

Results

Genotyping in this selected family revealed a novel heterozygous 2105T>A (I702N) missense mutation in exon 19 of the *MYH7* gene in the proband, the son and one daughter. Three unaffected family members tested negative for the mutation. The phenotype in the proband and her 18 year-old daughter progressed to exhibit DCM with evidence of early fibrotic changes by DME. The son progressed to asymmetrical septal hypertrophy, not initially apparent by echocardiography, consistent with early stage HCM. The 3 other members of the family had normal CMR examinations. Figure 1.

Conclusion

CMR has sufficient sensitivity to identify early myocardial changes and variable phenotypic expression, including both dilated and hypertrophic cardiomyopathies, due to a novel mutation in exon 19 of the *MYH7* gene. Earlier detection affords timely institution of therapies proven to improve outcomes in patients with heritable cardiomyopathies. CMR may also facilitate further investigations of post-translational mechanisms that result in variable disease expression.

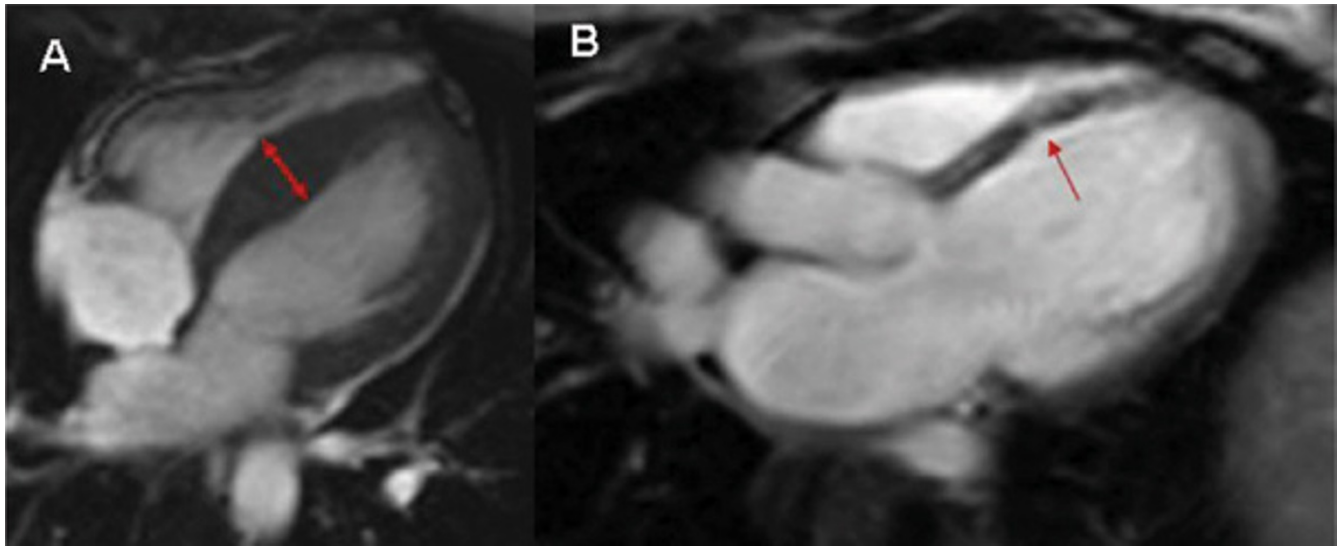

Figure 1
Initial phenotypic expression for indentical novel genetic mutation in two siblings as diagnosed early by CMR. **(A)** represents the son with asymmetrical septal hypertrophy. **(B)** represents the daughter with DCM and evidence of early fibrotic changes by DME.