

The yield of genetic testing in paediatric hypertrophic cardiomyopathy

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Introduction:

Genetic testing of patients with hypertrophic cardiomyopathy (HCM) is increasingly used to enable cascade screening of relatives and to shed light on underlying mechanisms of disease development and progression. We reviewed results of genetic panel testing in paediatric patients at our centre over a three-year period to establish the yield of testing and its diagnostic value.

Methods:

Results of all panel tests undertaken in HCM patients between 2015 and 2017 were recorded in a database. Fifteen patients underwent basic panel tests (16-21 genes) and eighteen underwent extended panels (90-104 genes). Relevant clinical details were sourced from patient records.

Results:

Thirty-three paediatric patients with HCM (aged 3 months to 17 years) underwent testing. Maximal left ventricular wall thickness in the group ranged from 8mm to 30mm. Three patients had a history of VF arrest, thirteen had an ICD in situ, one had undergone surgical myectomy and one underwent cardiac transplantation during the data collection period. Twenty-one of these patients were the family proband.

In twenty-four patients a pathogenic mutation was detected (a positive yield of 72.7%). In five patients, only variants of uncertain significance were detected, and in four cases no relevant mutations or variants were identified. Eleven patients with a pathogenic mutation had an additional variant of unknown significance in other panel genes.

Eleven patients had a pathogenic mutation in MYH7, six had a single mutation in MYBPC3 and three had two mutations in MYBPC3. Two patients had a TPM1 mutation and one had a TNNI3 mutation. One patient was found to have a mutation in FHL1, in keeping with his clinical phenotype. One patient with a severe cardiac phenotype and a previously identified DMD mutation was found to carry an additional MYH7 mutation.

Conclusions:

Genetic panel testing in paediatric HCM has a high positive yield and is of use in establishing underlying mechanisms of disease. It may be helpful in elucidating diagnoses when more than one disease process is contributing towards the HCM phenotype. All pathogenic mutations were found in the genes of the basic panel, however the additional variants detected may play a role as genetic modifiers, which warrants further investigation.