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New Genetic finding in a Combination of Long QT Syndrome and Hypertrophic Cardiomyopathy in a Single Patient

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Case Report

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In 2000 the description of a family (a mother and three sons) with a typical long QT ECG and echocardiographic diagnosis of classical hypertrophic non-obstructive cardiomyopathy was published [1]. The ECG of three family members was characterised by typical long QT syndrome (QTc intervals between 460 up to nearly 500 msec), but without signs of left ventricular hypertrophy, pathologic Q-wave and T-wave abnormalities as shown in ECG figures [1]. The mother of the family developed atypical angina; coronary angiography revealed slight coronary abnormalities. One of her sons had pre-syncope. In the later follow-up the mother developed severe ventricular arrhythmias; the implantation of an ICD has been discussed.

In the following years the laboratory of Prof. Dr. med. Eric Schulze-Bahr, genetic cardiovascular institute of the University Hospital of Munster, Germany, investigated single genes with overall negative results.

Not until 2019 we decided to make a Next Generation sequencing analysis for all long QT and hypertrophic cardiomyopathy genes which resulted in the positive missense mutation in the MYBPC3+ gene.

Conclusion:

Hypertrophic cardiomyopathy is electrocardiographically characterised by left ventricular hypertrophy measured by SOKOLOW-LYON-index above 3.5 mV [2] or LEWIS-index above 1.6 mV [3], Cornell criteria above 2,0 mV for females and above 2,8 mV for males [4], Peguero-LoPresti ECG criteria above 2.3 mV for females and 2,8 mV for males [5], right ventricular SOKOLOW-LYON-index [6], signs of biventricular hypertrophy criteria [7] and pathologic Q-waves and T-wave inversions [8]

Echocardiographically, HCM is characterised by asymmetrical left and right ventricular hypertrophy and usually with abnormalities of mitral valve with leaflet elongation, chordae and papillary muscle abnormalities enhancing left ventricular outflow tract obstruction as demonstrated in the three patients of this family.

Slight QTc prolongation associated with signs of left, right, or biventricular ventricular hypertrophy is a quite normal finding in hypertrophic cardiomyopathy. An association between hypertrophic cardiomyopathy and long QT syndrome has been described in alpha-Actinin 2 mutation, however with ECG signs of left ventricular hypertrophy and T-wave abnormalities [9].

Another association between hypertrophic cardiomyopathy and long QT syndrome was reported in the TNNI3 gene, co-inherited with a damaging variant in KCNQ1, again with signs of ECG ventricular hypertrophy [10].

Hypertrophic cardiomyopathy with pure long QT syndrome without any signs of electrocardiographic left ventricular hypertrophy, biventricular hypertrophy, Q-wave and T-wave abnormalities can be up to now only demonstrated in the MYBPC3+ gene, which can be found in the mother of the family and characterises a unique, not yet described phenomenon.

After thorough analysis of the medline services only one patient with long QT 1 syndrome revealed a missense mutation in the MYBPC3+ gene published in 2014 [11] without hints of any form of cardiomyopathy. After years these findings are not well understood.

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