A new inherited syndrome causing sudden cardiac death with specific ECG changes and idiopathic left ventricular hypertrophy

Swojanowsky P.[1]; Von Korn H.[1]; Basso C.[2]; Pilichou K.[2]; Stefan V.[1]; Muenzel T.[3]

[1]Hospital Hetzelstift Neustadt, Neustadt, Germany
[2]University Hospital of Padova, Department of Cardiac, Thoracic and Vascular Sciences and Public Health, Padua, Italy
[3]University Medical Center Mainz, Cardiology I, Mainz, Germany

Funding Acknowledgements: Type of funding sources: None.

Introduction

Sudden cardiac death (SCD) is a serious threat. In individuals under the age of 35 years sudden arrhythmic death is the most frequent cause. In younger persons, genetically determined cardiac diseases (e.g., cardiomyopathies, ion-channel diseases) account for an important proportion of these cases.

Purpose

We discovered a unusual combination of ECG changes and left ventricular hypertrophy that lead to a cumulation of sudden cardiac death in a single family. We therefore did a scientific work-up of this finding.

Methods: We investigated the case of a 23 year-old male with SCD, specific ECG changes and left ventricular hypertrophy (Figure 1). Family history was significant for SCD in the paternal line. A precise analysis was performed by an international multidisciplinary expert panel including autopsy of the index patient's heart, molecular autopsy, whole exome sequencing, analysis of the pedigree and examination of available family members (Figure 2).

Results

Three cases of SCD were reported in paternal relatives. The index patient exhibited specific ECG changes (ST-depression), which were also found in five paternal relatives and the brother of the index Patient (Figure 3). Post-mortem analysis of the heart yielded mild idiopathic concentric hypertrophy without myocardial disarray.

The genetic analysis of the index patient showed two nucleotide variations in two different genes (ANK2: c.11791G > A , MYO18B: c.3761G > A), which were also expressed in five relatives. Two family members had showed all indicators of the inherited syndrome including specific ECG changes, genetic changes and left ventricular hypertrophy.

Conclusions: We described a distinct inheritable syndrome causing SCD, characterized by specific ECG changes, idiopathic left ventricular hypertrophy and mutations of ANK2 and MYO18. As far as we know this is the first description of this syndrom. We hypothesize that if all features (ECG-changes, described genetic mutations, left ventricular hypertrophy) are positive, the risk for SCD may be considerably increased.

Abstract Figure. ECG of index patient and pedigree