Genetical and clinical features in inherited pediatric LQT syndrome: single center data

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Introduction
Long QT syndrome is an inherited disorder characterized by Qt interval prolongation. Often first manifestation of the disease is sudden cardiac death. More than 1000 pathogenic genetic variations have been identified in 17 genes, encoding ion channel proteins or functional subunits associated with ion channels, most frequent genes involved are KCNQ1 (LQTS1), KCNH2 (LQTS2) and SCN5A (LQTS3). We present clinical data and genetic mutations in our pediatric LQTS.

Methods
Retrospectively, we revised clinical and genetic features of 52 pediatric patients with diagnosis of LQTS: epidemiological data, clinical features, age at diagnosis, QTc interval, modified Schwartz score, Holter/exercise stress test, genetic counseling and pharmacological and non-pharmacological therapy.

Results: 52 pediatric patients with diagnosis of LQTS (1 m-18 years, mean 7 years). In 6 cases (11.5%), pediatric patient was the index case and relatives were diagnosed later. Most frequent symptoms at onset were palpitations and syncope. In 4 cases (7.6%) the first manifestation was sudden cardiac death (2 not recovered), one of the recovered patients during exercise (swimming) with KCNQ1 mutation and the other one during a minor non-cardiac surgery with SCN5A mutation. Genetic testing was performed for any index case in which LQTS was suspected. All patients with modified Schwartz score ≥3 (48%) and those patients included in the cascade screening had a genetic testing, in order to identify all affected family members.

Genetic features: 42% of our patients had genetical mutation identified (59% KCNQ1, 22% KCNH2, 18% SCN5A, 9% CACNA1C). Propranolol and Bisoprolol was preferred in LQTS1 and LQTS2. In two patients with LQTS3, Flecainide treatment was started. Despite pharmacological treatment, a left cardiac sympathetic denervation was performed in two cases due to cardiogenic syncopes, with clear clinical improvement.

In our cascade familial screening, we detected 9.6% silent mutation carriers and 3.8% of patients were negative for the known parent’s mutation. At data, no ICD was needed in our pediatric patients.

Conclusions
Sudden cardiac death related to LQTS can be the first manifestation, in our data 7.6% of all patients. More than 80% of genetic mutations were KCNQ1, KCNH2 and SCN5A, and accordingly to published literature.

It’s important to determine genetic mutations detecting both the non-carriers and silent carriers who must be followed to detect ECG changes or clinical symptoms and avoid malignant arrhythmias and sudden death.