Usefulness of Genetic Screening for Long QT syndrome in the School-Based Electrocardiographic Screening Programs

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Introduction : In Japan, school-based electrocardiographic screening program at the admission to primary school (PS), middle school (MS), and high-school (HS) has been established. Inherited arrhythmia diseases have been often pointed out in this program, especially long QT syndrome (LQTS). We aimed to evaluate the usefulness of genetic analysis in the screening program.

Methods : The study cohort consists of 378 probands at age of 6-7 (PS, n=78), 12-13 (MS, n=177), and 15-16 (HS, n=123), who received genetic analysis in our institute during the last decade (2007-2017). Extracted LQTS probands were divided into 4 groups; 1) screening + asymptomatic, 2) screening + symptomatic, 3) non-screening + symptomatic, 4) non-screening + asymptomatic. About 4 groups, we investigated their clinical and genotype characteristics.

Result : The number of the probands with LQTS were 259; 59(76%) in PS, 132 (75%) in MS, 68 (55%) in HS, respectively. Among them, screening based LQTS probands were 167 including 9 symptomatic patients; 46 (78%) in PS, 84 (64%) in MS, and 37 (55%) in HS. In screening based probands, 96 (57%) probands carried mutations; 40 in PS, 38 in MS, 18 in HS, and the mutations in KCNQ1 gene (LQT1) were the most frequent in PS and MS group (n=22, and 17), and those in KCNH2 (LQT2) in HS group (n=7). Surprisingly, 9 of CACNA1C variants (LQT8) were identified which were as frequent as SCN5A variants (LQT3, n=10). Most of symptomatic children were in non-screening, and syncope was the most frequent. Notably, fatal arrhythmic attacks were shown in only non-screening group, and increased in HS group. 17 of 19 probands with fatal arrhythmic attacks carried mutations of LQTS causative gene (n=3 in PS, n=8 in MS, and n=6 in HS). Additionally, mean QTc intervals were longer in mutation carriers (> 480msec) in the all of generations, and most of probands were identified causative gene mutation of LQTS (> 90%) in the group with Schwartz score ≥ 3.5. Summarizing the above, the cases with a) QTc interval ≥ 480ms, b) Symptomatic, c) Schwartz score ≥ 3.5 are highly carrying causative mutations of LQTS.

Conclusion : More than half of the LQTS patients who were detected in the school-based electrocardiographic screening programs carried the causative mutations. The mutation detection rate was the highest in the PS. Therefore, genetic analysis should be performed in their younger age, and it would be useful for their treatment.