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Genetic background of long QT syndrome in infants, children, and adolescents in Japan

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Introduction: Genetic studies for long QT syndrome (LQTS) have reported that prevalence of LQT1, LQT2, and LQT3 among these three mutations in adults is approximately 50%, 40%, and 10%, respectively. However, little data are available for pediatric population. In 1994, a school-based ECG screening program was started for all 1st, 7th, and 10th graders in Japan. The program screened children with definite LQTS without symptoms. We aimed to determine the characteristics of genetic background in childhood LQTS in Japan.
Methods: The study population included 170 family members from 81 probands (0-18 years; median, 9.5 years; M:F = 45:36) who were referred to our center from 1993-2010. Probands had a QTc value of $0.45^{0.5}$. Genomic DNA was isolated from blood and screening for LQT1-LQT8, except for LQT4, was re-performed by PCR and direct DNA sequencing. When multiple mutations were present, each mutation was counted in the number of each genotype.
Results: Genotypes were identified in 49 of 81 probands (60%) and in 84 of 170 family members. LQT1 was found in 43 family members (from 24 probands), LQT2 in 21 (15), LQT3 in 17 (9), LQT5 in seven (3), LQT7 in four (2), and LQT8 in one (1). Double mutations or gene variants were found in eight subjects and triple mutations or gene variants were found in one subject. The prevalence of LQT3 among the three main genotypes in probands (9/44, 20%) and in family members (17/77, 22%) in the present study was significantly higher (both p=0.004) than the data for the adult population (11/192 in probands and 82/812 in family members by Sauer AJ, et al. in 2007). Of 81 probands, the screened subjects showed a higher rate of genotypic determination (27/33) than symptomatic subjects (17/37, p=0.003) or a miscellaneous group including family examinations (5/11, p=0.045). The QTc values were not different between the screened and symptomatic groups.
Conclusions: A high prevalence of the LQT3 genotype in the pediatric population suggests progress in the medical management of these patients during infancy and childhood. School-based ECG screening and genetic testing may help prevention of LQTS-related symptoms in Japan.

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