Heart: first published as 10.1136/heartjnl-2011-300867.103 on 12 October 2011. Downloaded from http://heart.bmj.com/ on April 10, 2024 by guest. Protected by copyright.

[gw22-e0604] **GENOTYPE PHENOTYPIC ANALYSIS IN THREE CHINESE JERVELL AND LANGE–NIELSEN SYNDROME FAMILIES**

Gao Yuanfeng, Li Cuilan, Liu Wenling, Qiu Xiaoliang, Li Lei, Liang Ruijuan, Hu Dayi *Peking University People's Hospital, Fuchengmen, China*

10.1136/heartjnl-2011-300867.103

Background and purpose Long QT syndrome (LQTS) is an inherited cardiac disorder characterised by QT interval prolongation on ECG, ventricular arrhythmias and sudden death. Two forms of LQTS have been identified: autosomal-dominant Romano-Ward syndrome (RWS) without deafness and rare autosomal recessive Jervell and Lange–Nielsen syndrome (JLNS) with deafness. So far, only three mutations were reported from Chinese JLNS individuals among 31 mutations worldwide. To further explore the causes and clinical manifestations of JLNS in Chinese, the gene screening was performed in three Chinese JLNS kindreds and genotype-phenotypic correlation was analysed.

Methods Three JLNS kindreds from 160 LQTS families recruited to the Chinese Channelopathy Register Study were selected. Blood samples and clinical data were obtained under written consents. Individuals are considered affected if they have a prolonged QTc interval and profound sensorineural deafness. A QTc greater than 450 ms in males and greater than 470 ms in females is considered to be abnormal on ECG. Mutational screening of KCNQ1 and KCNE1 was performed by polymerase chain reaction (PCR) and direct DNA sequence analysis.

Result The mutations found in family L155, 1117-1118ins86 (A372fs+9X) and 1319delT (T439fs+25X) were novel. The 16-year-old male proband had his first syncope at the age of 6 and a QTc of 620 ms. He was syncope-free after being treated with propranolol at a dosage of 2.0 mg/kg. His parents carried a single mutation and had normal QTc. A605-2A>G (D202sp) and G815A (G272D) were found in a 12-year-old girl and a 5-year-old boy in family L148. They both had profound deafness and markedly prolonged QTc intervals of 590 ms and 600 ms, respectively. Both experienced their first syncopal episode at the age of 2. During two-year follow-up after left cardiac sympathetic denervation and propranolol 2–2.5 mg/Kg, their syncope episodes were reduced (0.5 and 2.5 vs 5~10 times/year before). Their parents carried a single mutation and had normal QTc. G569A (R190Q) and G1032A (A344sp) were found from a 46-year-old male proband in family L151. There was also a novel missense mutation C574T (R192C) combined with A344sp, which contributes to the RWS phenotype of the proband's 16-year-old daughter. A rare single nucleotide polymorphism (SNP) D85N was also detected on KCNE1 in family L151. The proband had syncope when he was young, but no syncope after his 30's with QTc of 465 ms. His daughter had syncope after 2 and a QTc of 480 ms. She was syncope-free with metoprolol at the dosage of 0.91 mg/Kg (equivalent to 1.45 mg/Kg propranolol) in the last two years. Three of four JLNS patients showed broad, bifid or biphasic T waves, especially when they had symptoms. This abnormality became less severe after standard treatment.

Conclusion Our results provide further evidence that the mutation spectrum for JLNS consists predominately of compound and complex mutations such as splicing, deletion or insertion causing frameshifts on KCNQ1. We also found a rare SNP D85N on KCNE1 which may increase the susceptibility to LQTS. Genotype-phenotypic analysis showed that JLNS patients had early onset of cardiac events, marked QTc prolongation and more severely broad and bifid T waves on ECG, which was different from typical LQT1 ECG features reported by others and improved by various long-term treatment.

Heart: first published as 10.1136/heartjnl-2011-300867.103 on 12 October 2011. Downloaded from http://heart.bmj.com/ on April 10, 2024 by guest. Protected by copyright.