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THE OBSERVATION OF MEXILETINE TO TREAT A CHINESE TIMOTHY SYNDROME INFANT WITH MOSAIC INHERITANCE

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Objectives Timothy syndrome is a rare LQTS caused by CACNA1C- α mutations G406R (TS1) and G402S (TS2). Management of TS is of challenge and the prognosis is poor. This study aimed to further explore the inherited pattern and mechanism of sodium channel blocker, mexiletine, to improve clinical manifestation in TS.

Methods A 2.5-year-old Chinese girl showing a typical TS phenotype was undergone candidate gene screening. Mosaicism analysis was performed using specific primers to amplify the mutated allele for family members. Therapeutic effects of mexiletine and propranolol were evaluated using ECG and Holter monitoring.

Results This girl presented with severe bilateral syndactyly, cutaneously syndactyly, patent ovale foramen and delayed language learning. Her baseline ECG showed markedly prolonged QTc (640 ms), intermittent 2:1 AV block (AVB) and macro-T wave alternans (TWA). A few R-on-T extrasystoles occurred during 2:1 AVB caused bradycardia. Candidate gene search identified G406R mutation in CACNA1C- α . G406R was absent in her mother but partly present in her father's oral mucosa, sperm and white blood cells. Though completely asymptomatic he had mild-moderate QTc prolongation (470–490 ms) and syndactyly. Further analysis demonstrated that the proband's other paternal family members were also mosaic.

Conclusions Mexiletine but not propranolol is highly effective in a Chinese TS1 by shortening QTc, abolishing 2:1 AVB, and minimising TWA.