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A novel de novo mutation in the Cardiac Ryanodine Receptor Gene (RyR2) in a patient with concealed Long QT Syndrome

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Introduction: The congenital long QT syndrome (LQTS) is a potentially life threatening hereditary channelopathy and fifteen genetic forms have been defined. Here a concealed LQTS patient with a de novo mutation in the cardiac ryanodine receptor (*RyR2*) gene and a known germ line pathogenic mutation in desmoplakin (*DSP*) gene simultaneously is presented.

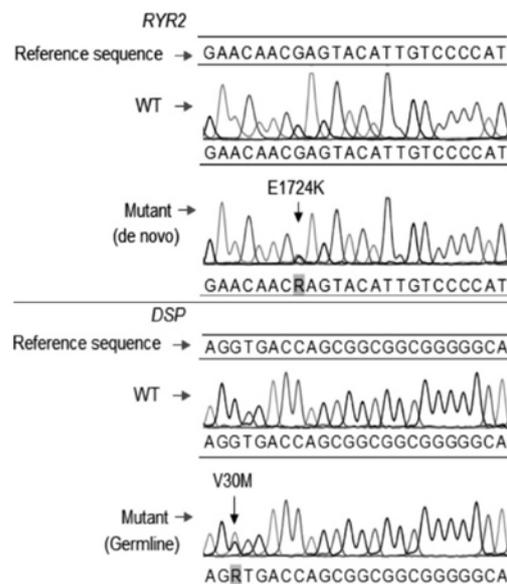
Case: A nine-year-old male patient, who had syncope episodes with spontaneous resolution in few minutes, admitted with cardiac arrest. After resuscitation electrocardiogram revealed a QT interval of 600 msec, corrected QT (QTc) interval of 620 msec and no T-wave abnormality or dysrhythmia.

Echocardiography showed no structural heart disease.

At 45th day of hospitalization the ECG showed a QTc of 430 msec. Epinephrine stress test confirmed the diagnosis of concealed LQTS and a de novo

heterozygote missense mutation at nucleotide 5170 in exon 37 of *RyR2* gene (GenBank: [NM_001035](#)) which

replaces glutamic acid with lysine at residue 1724 (c.5170G>A- p. Glu1724Lys) and a germ line heterozygote missense mutation at nucleotide 88 in exon 1 of *DSP* gene (GenBank: [NM_004415](#)) (c.88G>A (p.Val30Met), were identified on the genetic screening of the patient. (Figure)



Discussion: On genetic screening of our patient, a heterozygote missense mutation, (c.5170G>A- p.Glu1724Lys), on 37th exon in *RyR2* gene was identified. This mutation was first reported in a Dutch female patient with diagnosis of CPVT (1) and it affects the cytoplasmic loop and protein interaction (1,2). To the best of our knowledge this is the first concealed LQTS patient to have this de novo missense mutation. CPVT patients may be misdiagnosed as concealed LQTS. In both diseases the resting ECG is normal, but induction of bidirectional ventricular tachycardia and/or polymorphic ventricular premature beats during exercise or stress test is typical for CPVT. In our case epinephrine stress test was performed and a positive paradoxical QT response was observed, however any dysrhythmias or ventricular premature beats were not observed.

Conclusions: This is the first concealed LQTS patient to have this de novo missense mutation. In patients with concealed LQTS, provocative tests and genetic screening should be performed and identification of new gene mutations will be helpful for the definitive diagnosis.

References

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