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Research article

Prediction of the functional consequences of a novel homozygous TBX5 variant in isolated AVSD patient

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Key words: Isolated cardiac septal defects; TBX5 gene; Novel homozygous variant.

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Abstract

Objectives: The T-box transcription factor TBX5 gene is an important factor in mammalian cardiac development for both cardiac septation and morphogenesis. Autosomal dominant variants in the human TBX5 gene cause the known Holt-Oram syndrome (HOS); a disorder characterized by heart and upper limb deformities. Because there are rare studies for detection of TBX5 variants in isolated congenital cardiac septal defects, the current study aimed to identify the putative function of novel detected TBX5 gene variant in non-HOS patient with congenital cardiac septal defects (CSD). **Methods:** This is a case study of a one year old female congenital heart disease (CHD) patient with atrioventricular septal defect (AVSD). Using Direct Sanger sequencing, screening of T-box DNA binding domain corresponding exons for the patient who had normal Nkx2-5 and GATA4 genotyping was performed, as well as, a group of twenty eight non-cardiac children were screened as controls. **Results:** A novel homozygous missense (p.L135R) variant in the N- terminal of the T- box domain was detected with a predictive disease causing effect. This variant was absent in the variants registration databases and in 28 healthy controls, indicating its possible role in causing (CHD). **Conclusions:** To our knowledge, we show for the first time homozygous TBX5 variant in non-HOS associated cardiac malformations in an Egyptian patient. Absence of definite congenital heart defects symptoms in the unaffected carrier parents for the p.L135R variant supporting dosage-sensitivity hypothesis and a probable new mode of Tbx5 variants inheritance.