Very rare case of Noonan syndrome, type 2

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Background. Noonan syndrome, type 2 (NS2) is rare autosomal recessive disorder of RASopathies group, caused by mutations in the *LZTR1* gene. NS2 characterized by a typical face, short stature, broad, short neck, congenital heart disease, developmental delay. The most common heart disease in children with NS2 is hypertrophic cardiomyopathy.

Methods. Patient is a boy, 15 years old with short stature, developmental delay at 1 first year of life and heart disease. He had distinctive facial features of NS: downslanting palpebral fissures, epicanthic folds, hypertelorism, low-set ears short neck, wing-like folds on the neck, pectus deformity. Hypertrophic cardiomyopathy was identified at 1 month old. Now patient have obstructive, hypertrophic cardiomyopathy, cardiac arrhythmia: ventricular extrasystoles, 4A Lown, intraventricular block combined with bundle branch block, transient WPW. Syncopal episodes.

Surgical correction of obstructive hypertrophic cardiomyopathy: septal myomectomy was performed on the child due to the high risk of developing sudden death syndrome. Target areas of the exome were investigated by next generation sequencing (NGS). Bioinformatic analysis was carried out using ACMG recommendation. Validation of the identified variants was carried out by the Sanger method.

Results. We revealed nucleotide missens VUS: c.1259A>G, p.Q420R and c.2051T>C, p.I684T in the heterozygous state in *LZTR1* gene. All variants were absent in HGMD professional and genome aggregational database.

Conclusion. Child with severe hypertrophic cardiomyopathy and typical phenotype of Noonan syndrome was detected NS 2, caused by compound heterozygous missense variants c.2051T>C, p.I684T and c.1259A>G, p.Q420R in *LZTR1* gene.