

Cardiac involvement in children with TMEM70 deficiency

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Introduction: TMEM70 deficiency is the most common nuclear-encoded defect affecting the mitochondrial ATP synthase. Cardiac findings typically reveal hypertrophic cardiomyopathy. Congenital heart defects, WPW syndrome and pulmonary hypertension of the newborn with cardiac failure were also reported. Objective of the study was to determine the significance and course of cardiac involvement.

Methods: Retrospective analysis of cardiac findings and clinical outcome in Slovak children with confirmed TMEM70 deficiency.

Results: Sixteen Roma children who all were homozygous for the common mutation c.317-2A>G were evaluated. Median gestational age at birth was 37th week (range 31-40) and median birth weight was 2.0 kg (range 1.5-2.8). Neonatal onset of metabolic deterioration was documented in 75% of patients. Eleven (92%) neonates required intubation and 5 (42%) had severe pulmonary hypertension with haemodynamic compromise. Echocardiography revealed two patients with mild valvular aortic stenosis and one neonate with coarctation of aorta. Eleven (69%) children were diagnosed with non-obstructive hypertrophic cardiomyopathy, and in 4 (25%) left ventricular outflow tract obstruction (LVOTO) was documented. Neonatal mortality was 25% with two early deaths and two deaths after initial stabilization. Two children died at age of 3 and 20 months, respectively. Symptomatic neonatal pulmonary hypertension was positively associated with mortality ($p=0.017$).

Cardiologic follow-up was performed during median of 14.5 months (range 0.1-153).

Echocardiography at birth, 3, 6, 12, 24 and 36 months of age revealed median Z-scores of interventricular septal thickness of +10.4, +6.9, +8.3, +5.5, +8.3 and +8.6, respectively and median Z-scores of left ventricular posterior wall of +5.0, +5.2, +7.9, +4.4, +5.2 and +2.6, respectively. Of 4 patients with LVOTO, one neonate died and in 3 children gradient subsided during follow-up. Mild dilation of left ventricle and mild mitral regurgitation developed in 3 and 3 patients, respectively. One patient had WPW syndrome and in all but 2 infants ECG findings of left ventricular hypertrophy were documented.

Conclusions: Cardiac involvement of patients with TMEM70 deficiency is characterized by infantile non-progressive non-obstructive or regressive obstructive hypertrophic cardiomyopathy. Persistent pulmonary hypertension of the newborn with cardiac failure is common and it is associated with increased mortality.