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INTERDISCIPLINARY ASPECTS OF RARE FORMS OF CARDIOMYOPATHY IN CHILDREN

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Abstract

The clinical cases of rare forms of cardiomyopathy are presented in this article. We observed 8 children: two 4 and 8 months old children from the same family with long chain fatty acids metabolism disorders and cardiomyopathy, one 8 years old patient with the MELAS syndrome (mitochondrial myopathy - encephalopathy - lactic acidosis, stroke-episodes), and 5 children with the takotsubo cardiomyopathy.

The two children had congenital metabolic disorder - a disorder of long-chain fatty acids β-oxidation (fatty acids acyl coenzyme-A CoA dehydrogenase deficiency), hypertrophic cardiomyopathy, IIA grade heart failure. The Reye-like syndrome was diagnosed due to progressive lethargy, drowsiness, muscular hypotonia, cardiac disorders (symmetric hypertrophic cardiomyopathy), liver failure (Reye's syndrome), early clinical onset, regression of psychomotor skills, hyperlactatemia, increased transaminase levels, reduction of free carnitine with increasing acylcarnitines, high excretion of fumaric, adipic, 3-metilglutanolic and oxoglutaric acids. Both children died.

The MELAS syndrome was diagnosed in one child in conjunction with impaired physical and psychomotor development. Clinical manifestations included vomiting, diencephalic crises, weakness, lethargy, progressive multiple organ failure (heart failure due to hypertrophic cardiomyopathy, respiratory failure, myopathic syndrome, encephalopathy, endocrine disorders, gastrointestinal disorders, increased levels of lactic and pyruvic acids). A molecular genetic study revealed mutation 14470 T/C 14766 C/T 15326 A/G. The child died at the age of 8.

The takotsubo cardiomyopathy was diagnosed in 5 adolescents. The children were admitted to hospital with symptoms of acute coronary syndrome: retrosternal pain, palpitations, and shortness of breath suddenly appeared after physical and emotional stress. The electrocardiogram recorded ST segment elevation, T wave inversion in II, III, V5, V6 leads. Echocardiography revealed a dysfunction, left ventricular dyskinesia affecting the top and the interventricular septum. Vascular abnormalities and occlusions weren't identified during aorto-coronarography. Heart function became normal within 3-4 weeks.

The article shows that metabolic abnormalities are important pathogenetic aspects of cardiomyopathies. Early diagnosis allows for timely administration of specific treatment. Rare forms of cardiomyopathies require a multidisciplinary approach to diagnosis and monitoring of such patients.

Keywords: *children, metabolic cardiomyopathies, energy failure of mitochondria, MELAS syndrome, tacotsubo cardiomyopathy.*

Introduction

In 2006, the American Heart Association suggested to define cardiomyopathies (CM), as "a heterogeneous group of diseases of the myocardium associated with mechanical and/or electrical dysfunction, which usually (but not invariably) exhibits inappropriate ventricular hypertrophy or dilatation, due to a variety of etiologies that are frequently genetic. Cardiomyopathies are either confined to the heart or a part of generalized systemic disorders, and often lead to cardiovascular death or progressive heart failure-related disability." [*Maron BJ et al., 2006*]. The frequency of cardiomyopathies in children is approximately 1.3 cases per 100,000 children. Cardiomyopathies are grouped according to morphological or functional phenotype: hyper-

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trophic, dilated, arrhythmogenic, right ventricular, and restrictive [*Elliott P et al., 2008*].

Unclassified: non-compact myocardium, takotsubo CM. All phenotypes of the CM are divided into:

- Familial (genetic): unidentified gene defect and subtype of the disease.
- Non-familial (non-genetic): idiopathic and subtype of the disease.

Division of CM to familial and non-familial is designed to raise awareness of doctors about genetic determinants of the CM, and to guide them to run specific diagnostic tests, including the search for specific mutations in the respective cases.

An important aspect of the pathogenesis of metabolic cardiomyopathy is a disorder of cellular metabolism due to mitochondrial dysfunction. According to the register of pediatric hypertrophic CM, carnitine transport or fatty acid oxidation defects and disorders of oxidative phosphorylation are present in 20% of cases [*Colan SD et al., 2007*]. In the case of dilated CM such metabolic disturbances are in 40% of patients [*Towbin JA et al., 2006*]. Hereditary defects in fatty acid metabolism are the cause of at least 5% of cases of sudden infant death [*Bonnet D et al., 1999*].

One of the causes of CM in children and especially in adolescents may be dysautonomia in hypersympathetic state due to both primary increased functioning of the sympathoadrenal system and its increased reactivity as a result of load [*Belokon NA, Kuberger MB, 1987; Senatorova AS et al., 2012; Senatorova AS et al., 2013*]. The definition of load should be understood as any stress phenomenon: psychological, one resulting from physical disorders, etc. The levels of adrenaline and noradrenaline in the blood of such children, both at rest and during exercise increase twice compared to standard values. At the same time, heightened sensitivity of the myocardium to catecholamines may play a role in the mechanism of CM development [*Limankina IN, 2009*]. The effect of these hormones on the heart is realized via β-adrenergic receptors cardiomyocytes, which largely determines the final result of their impact on the myocardium. It lies in the activation of the enzyme adenylate cyclase and increased synthesis of cyclic adenosine monophosphate which increases the metabolism level. Such effect on pacemaker tissue causes a positive chronotropic effect, and positive inotropic effect - on the cells of the functioning myocardium. Excessive or prolonged exposure to catecholamines leads to impaired Na^{+}-Ca^{2+} balance, thus repolarization ends later than usual, and the positive inotropic effect becomes weaker. In these conditions cardiomyocytes' contractility may be reduced, i.e. hyperadrenergic metabolic myocardial injury starts to develop (takotsubo cardiomyopathy) [*Kuszakowski MS, 2000; Leontieva IV, 2005; Senatorova AS et al., 2011*].

It is extremely important to promptly detect congenital hereditary metabolic pathology (disease of energy metabolism), because it depends on patient management, treatment strategy and prognosis [*Senatorova AS et al., 2013*]. The clinical and genetic polymorphism of mitochondrial disease may complicate diagnosis. Cardiomyopathy can be isolated or associated with other symptoms. Terms of manifestations are different, mainly – in early childhood. The algorithm for the diagnosis of metabolic CM is based on a combination of specific clinical cardiac and noncardiac symptoms and laboratory data [*Leontieva IV, Belozerov YM, 2012*].

Extracardiac diagnostic criteria of metabolic CM:

- early onset of the disease
- lesion of many organs
- episodic course of the disease
- repeated vomiting, often in the background of hypoglycemia
- hypotonia
- the central nervous system abnormalities (microcephaly, seizures, mental retardation and motor development, lethargy, drowsiness, lethargy)
- retardation of physical development
- gastrointestinal tract disorders (vomiting, abdominal pain, hepatomegaly, hepatic steatosis, disorder of bowel movements)
- kidney disorders (tubulopathy, polycystic, kidney failure)
- facial dysmorphism

Cardiac diagnostic criteria of metabolic CM:

- dilatation of the heart chambers, decreased myocardial contractility
- symmetrical myocardial hypertrophy
- combination of myocardial hypertrophy and dilatation
- refractory to standard therapy of heart failure
- cardiac arrhythmias (ventricular tachycardia), violations of the conduction (sick sinus syndrome, atrioventricular block)
- giant T-waves on the electrocardiogram
- cases of sudden cardiac death in the family (arrhythmogenic)

Laboratory criteria of CM on the background of primary mitochondrial energy failure:

- hypoglycemia without ketosis
- metabolic acidosis
- hyperlactatemia and hyperpyruvataemia
- increase of creatine kinase
- increase in the activity of liver transaminases

To clarify the causes of metabolic disorders of carnitine and organic fatty acids, the most important starting point is to determine the levels of total, free carnitine and acylcarnitines in combination with the assessment of the presence or absence of dicarboxylic aciduria [*Cox GF, 2007*]. The diagnosis verification requires molecular genetic diagnostics. Identification of mutations requires creation of a well-equipped specialized laboratory that is available only in few diagnostic centers.

Objective: to improve the diagnosis of rare CM forms in children.

We observed 8 children: 2 from one and the same family - with the long-chain fatty acids metabolism disorder and cardiomyopathy, 1 patient with MELAS-syndrome, 5 children with takotsubo cardiomyopathy.

Clinical observation No 1.

Patient K., 6.5 months old, was admitted to hospital with complaints of shortness of breath, increased body temperature to 38°C, lethargy, weakness, refusal to eat, showing the symptoms of severe myopathic syndrome. According to the medical history, the child was from the 1st pregnancy, complicated with anemia, placental insufficiency and mild preeclampsia. The child experienced drowsiness, poor weight gain, frequent noisy breathing in the first months of life. The child began holding head at the age of 4 months, did not turn around and did not sit. At the age of 6 months the child was examined by a family physician, and because of dyspnea and child malnutrition was sent to the Regional Children's Clinical Hospital (RCCH) for examination that resulted in the diagnosis of symmetric hypertrophic cardiomyopathy, 0 grade heart failure. The child was discharged from hospital under the supervision of a pediatrician with the recommendations in line with the guidelines. After 2 weeks, the baby's condition deteriorated rapidly, therefore the child was re-hospitalized.

At the time of admission to hospital the child was in severe condition due to cardiorespiratory failure, pathological neurological symptoms, and metabolic disorders.

On the second day in the hospital hemorrhagic syndrome developed: there were "coffee grounds" vomiting, black stools, platelet count – 52,000 in *μl*, prothrombin index - 63%, fibrinogen 1.8 *g/l*, coagulation test - 13 *min* (normal range 16-18).

- *Clinical and instrumental examinations results*: Complete blood count: 1st degree deficiency anemia
- *Electrocardiogram*: sinus rhythm, delayed intraventricular conduction, overload of the left ventricle and left atrium.
- *Doppler Echocardiography*: symmetrical left ventricular hypertrophy, decreased myocardial contractility (ejection fraction EF 51%), grade II left ventricular diastolic dysfunction ("pseudonormal filling dynamics").
- *Neurosonography*: expressed swelling of membranes. Perfusion of nuclei and hemispheres diffusely reduced, small perivascular areas of gliosis in the nucleus, blood flow is reduced in the periphery.
- *Abdominal ultrasound*: the liver is enlarged to 8 *cm*, parenchyma with severe congestive-proliferative responses, high echogenicity, coarse-grained, perivascular edema, spleen +2 *cm*, increased echogenicity, kidneys - parenchymal edema and ischemia.
- *Fibrogastroduodenoscopy*: hemorrhagic gastroduodenopathy, duodenogastric reflux.

According to laboratory tests: persistent hypoglycemia 2.5-3.3 *mmol/l*, hypoproteinemia to 35.6 *g/l*, increase in the levels of liver enzymes alanine transaminase 6 ULN and aspartate aminotransferase 4 ULN, high blood urea nitrogen level (2 ULN), decompensated metabolic acidosis (pH 7.28, base excess 8.8 *mmol/l*).

Ophthalmologist's diagnosis: no pathology in eye fundus.

Neurologist's diagnosis: diffuse muscular hypotonia, delayed motor development pace.

Laboratory test results made in a specialized medical and genetic center: increased lactate dehydrogenase – 1320.0 U/l (normal up to 1100), triglycerides – 4.76 *mmol/l* (normal range 0.34-1.13), ammonia – 74.83 *mmol/l* (normal range 18-72), increased level of lactic acid in the blood to 3.15 *mmol/l* (normal 1.2), pyruvic – 0.13 *mmol/l* (normal 0.1), lactate / pyruvate ratio - 24.2 (normal <15), decreased level of carnitine in serum at 18.8 *mmol/l* (normal 53±4,5).

Activity of mitochondrial enzymes of energy metabolism in peripheral blood lymphocytes was determined through a quantitative cytochemical method, suggested by Nartsissov R.P. (1969), which is expressed in granules per cell (g/cl). There was decrease in the activity of and the activity of mitochondrial enzymes of energy metabolism in peripheral blood lymphocytes - succinate dehydrogenase 12.4 *g/cl* (normal 15.76±0.4), glutamate dehydrogenase 5.5 *g/cl* (normal 6.3±0.33), alpha-glycerophosphate dehydrogenase 5 *g/cl* (normal 8.4±0.42), increase in extramitochondrial lactate dehydrogenase activity of anaerobic to 18.2 *g/cl* (normal 12.2±0.44), total cholesterol lowered to 2.89 *mmol/l*. There was high excretion of fumaric, adipic, 3-metilglutaric and oxoglutaric acids in the urine.

Combination of the medical history (pathological course of pregnancy, intrauterine growth retardation syndrome, I degree postnatal malnutrition, regression of psychomotor skills), multiorgan pathology (myopathy, heart, liver and gastrointestinal tract abnormalities), biochemical and cytochemical markers of mitochondrial dysfunction in a child with symmetrical hypertrophic CM, delayed psychomotor development, and intermittent course of the disease allowed for diagnosing the child with congenital metabolic disorder - a disorder of β-oxidation of long-chain fatty acids (fatty acids acyl-CoA dehydrogenase deficiency).

Therapy: low-fat diet, partial parenteral nutrition, 25% $MgSO_4$ 100 *mg/kg/day*, maxipime 100 *mg/kg/day*, prednisone 5 *mg/kg/day*, thiotriazoline 5 *mg/kg/day*, qudesan 50 *mg/day*, L-carnitine 75 *mg/kg/day*, riboflavin 10 *mg/day*, biotin ¼ tab daily, captopril 1.5 *mg/day*, spironolactone 6 *mg/day*, furosemide 3 *mg/kg/day*.

The child's condition improved on the 17th day of the therapy. The baby became active, began to smile, appetite improved, the cardiorespiratory failure symptoms reduced, myocardial contractility increased (EF increased to 58%), the liver shrank to 5 cm, but hypotonia and cardiac enlargement remained.

Due to the patient's improvement the child was discharged from hospital with the following recommendations: fat limitation; frequent small portions feedings without long periods of hunger; food rich in carbohydrates; glycine, corneplus, prednisone, asparkam, pantocaltsin, captopril, spironolactone, metabolic therapy.

At the age of 8.5 months, the child was re-hospitalized in critical condition due to a metabolic crisis (despite the diet restriction, the child was given goat milk with over 4.5% fat). The child died on 24th day after hospitalization due to multiple organ failure.

Pathology report: Congenital metabolic fatty acids disorder. Deposition of lipids in the nervous system (in meninges, in neurons of the basal ganglia and the anterior horn of the spinal cord - degenerative changes and deposition of lipids, in peripheral nerves - expansion of the perineurium and endoneurium, deposition of amorphous PAS-positive substance, the number of axons is reduced, they are surrounded by connective tissue that forms onion-like structures in cross sections), heart (hypertrophic cardiomyopathy, interstitial fibrosis (Fig. 1), liver (Fig. 2) and kidney (Fig. 3) (fatty infiltration of the epithelium).

Clinical observation No 2.

The second child of this family, E., 2 months old, was admitted to the cardiology department of the RCCH for a routine examination, because of the family medical history: 1st child in the family died at the age of 8.5 months (clinical observation has been presented above).

Medical history: a child from 2nd pregnancy, complicated with moderate preeclampsia in the first trimester. Condition at birth was satisfactory. The baby was breast-fed. Starting from the age of 1 month the child was able to hold head, smiled. The child's muscle tone was satisfactory. Weight gain was normal.

Laboratory and instrumental tests:

Doppler echocardiography: symmetric hypertrophic cardiomyopathy. Decrease in myocardial contractility. Left ventricle grade I diastolic dysfunction.

Electrocardiographic examination: voltage in standard leads is reduced. Electrical axis shifted to the right. QRS of type rS_{V1-6}. Severe disturbances of repolarization.

Gas chromatography mass-spectrometry of organic urine acids: increased level of suberic acid (fatty acid metabolites) 115.65 units (normal 0-48.62), 3-hydroxysebacic acid 329.62 units (normal 0-37.66), 3-methyladipic, 2-hydroxyadipic, 3-hydroxyadipic, 3-ketosebacic acids and metabolites of the Krebs cycle (fumaric acid).

Tandem mass spectrometry of blood amino acids and acylcarnitines: reduced levels of free carnitine

8.387 *mmol/l* (normal 15-50), increased level of 3-OH-hexadecanoilcarnitine 0.251 (normal 0.06), tetradecanoilcarntine 0.288 (normal 0.24) 3-OH-tetradecanoilcarntine 0.097 (normal 0.08), 3-OH-hexadecenoilcarnitine 0.091 (normal 0.06).

Cytochemical activity of aerobic mitochondrial enzymes in peripheral blood lymphocytes was reduced: succinate dehydrogenase 10.4 *g/cl*, glutamate dehydrogenase 4.8 *c/c*, increased activity of anaerobic alpha-glycerophosphate dehydrogenase to 8.2 *g/cl*, lactate dehydrogenase to 16.6 *g/cl*.

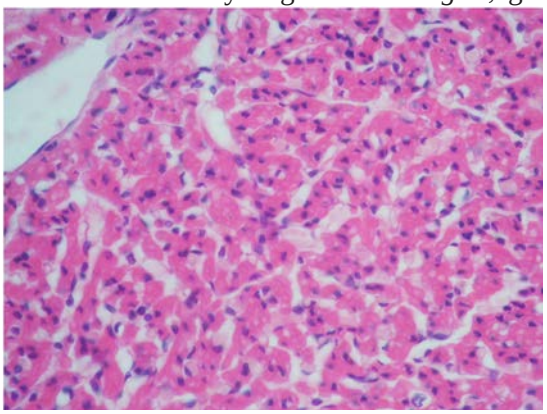

***Figure 1**. The myocardium. Discomplexity, swelling of the interstitium, irregular hypertrophy of cardiomyocytes.*

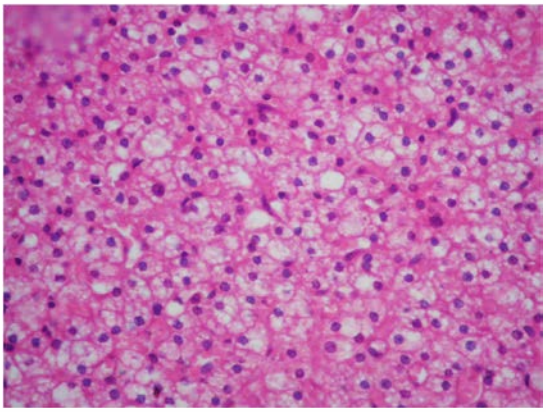

***Figure 2.** Liver. Total fatty degeneration of hepatocytes with necrosis in some of them.*

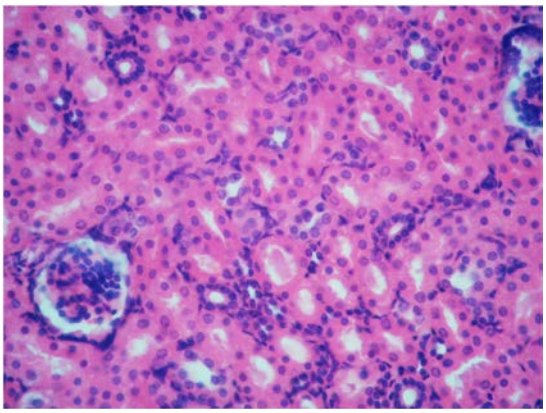

***Figure 3.** Kidneys. Expressed granular and fatty degeneration of the tubular epithelium drip, isolated hyaline casts in the tubules.*

Hereditary metabolic disturbance - a disorder of β-oxidation of long chain fatty acids and symmetrical hypertrophic cardiomyopathy, I grade heart failure was diagnosed.

Child was discharged from hospital with recommendations: on-demand breastfeeding, low-fat diet for the mother, L-carnitine.

A child was hospitalized again at the age of 4 months in critical condition due to cardiac decompensation, and the development of Reye-like syndrome.

The child died 18 hours later after hospitalization.

Pathologist's report: congenital disorder of fatty acid metabolism, hypertrophic cardiomyopathy (Fig. 4), Reye-like syndrome, and secondary right-sided desquamative-purulent pneumonia.

Clinical observation No 3.

We observed one patient with the MELAS-syndrome (mitochondrial myopathy - encephalopathy - lactic acidosis, stroke-episodes).

Girl G., aged 7 years, was hospitalized with complaints of shortness of breath, weakness, lethargy, drowsiness, vomiting, headache, abdominal and cardiac pain, palpitations, polydipsia, and polyuria. According to the information received from the mother, the girl started to walk at the age of 2, her weight gain was poor, and she had retardation in speech development. At the age of 2 she was diagnosed with cerebral palsy, right hemiparesis, cysts of the brain (left hemisphere, subcortical nuclei area on the right), and diencephalic crisis with respiratory distress syndrome. One month after leaving hospital her condition deteriorated again, and the child was placed in the intensive care unit.

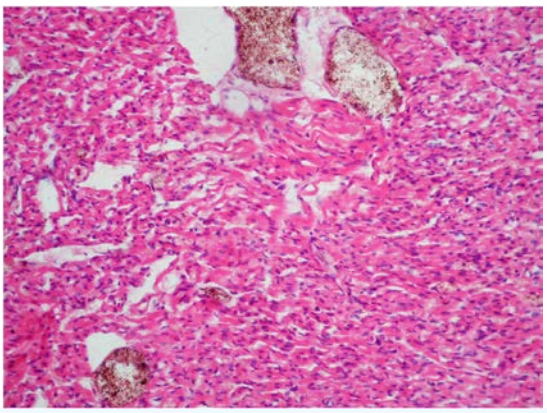

***Figure 4.** Heart. Dyscomplexity, irregular hypertrophy, congestion of blood vessels.*

Observation of the patient revealed progressive heart failure: weakness, tachycardia, face and legs edematous appeared, umbilical flattening, increased neck vessels pulsation, expanding of the relative cardiac dullness to the left, rough systolic murmur over the heart, enlarged liver, decreased urination, and lip cyanosis. Changes in neurological status were characterized by muscle weakness, dysarthria, divergent strabismus, and ptosis of the left eyelid.

Doppler echocardiogram revealed sharp apical hypertrophy of the left ventricular wall and interventricular septum. Moderate dilatation of the right chambers, right ventricular free wall hypertrophy. Decrease in myocardial contractility, and grade II left ventricular diastolic dysfunction.

Electrocardiogram - Wolff - Parkinson - White phenomenon.

Electroencephalogram: focus of seizure activity in brain stem, reduced brain bioelectrical activity.

Magnetic resonance imaging revealed brain cysts and hypoxic-ischemic injury in the left temporal region, and confirmed the presence of intracranial hypertension.

The child was examined by neurosurgeon and no neurosurgical pathology was detected.

Chest X-ray - community-acquired bilateral pneumonia, complicated course.

During the stay in the hospital progressive diffuse muscular hypotonia, weakness of the respiratory muscles, low efficiency of the diaphragm contraction were observed. During extubation oxygen saturation decreased, mixed acidosis and acetonuria progressed. On the 25th day tracheostomy was performed due to required prolonged mechanical ventilation. Spontaneous breathing through tracheostomy was superficial, arrhythmic, diaphragm muscle did not take part in the act of breathing, and there was a complete absence of the swallowing reflex.

Congenital metabolism disorder was diagnosed on the basis of the medical history (delayed physical and psychomotor development), complaints (vomiting, diencephalic crises, weakness, lethargy, and ventilation disorders), progressive multiorgan injury (myopathic syndrome, nerve damage, heart disease, endocrine disorders, gastrointestinal disorders) and biochemical markers.

The study of the metabolic status:

Thin-layer chromatography of amino acids in urine - increase of glycine, proline, serine, alanine, valine levels;

High-performance liquid chromatography of blood amino acids – increased levels of aspartic and glutamic acid, asparagine, arginine, decreased level of creatinine, hydroxyproline, and cystine.

Biochemical analysis showed increased lactic acid up to 3.37 *mmol/l* (normal 1.2) and pyruvic acid up to 0.21 *mmol/l* (normal up to 0.1) in the blood, the ratio of lactate / pyruvate - 22.1 (normal <15).

The results of molecular genetic testing: a complete sequencing of mitochondrial deoxyribonucleic acid was conducted. The mutations found were 14470 T/C, 14766 C/T 15326 A/G.

Mitochondrial encephalomyopathy – the MELAS syndrome – was diagnosed.

Besides the syndrome and symptomatic treatment, a therapy was prescribed to stimulate the processes of tissue respiration. Some improvement in patient's condition was observed.

However, the child died at the age of 9. Multiple organ failure was the cause of death.

We observed 5 teenagers at the age of 14-17 who were hospitalized at the Cardiology Center, Regional Children's Hospital in Kharkiv, with complaints of retrosternal pain, palpitation, and shortness of breath.

Disease began after psycho-emotional stress (conflict with peers, entrance exams, and work at the farm). All the children were admitted to clinic after 1 to 3 days with a diagnosis of acute coronary syndrome.

Clinical observation No 4.

A 15-year-old boy was placed in the intensive care unit because of severe chest pain that had spread to the left arm, being accompanied by numbness of the fingers tips and an increase of blood pressure to 140/85 *mm Hg*. The medical history reveals that the symptoms started after a serious quarrel between him and a girlfriend. The ambulance was called and the child was taken to the City Hospital. In order to alleviate the child`s pain ambulance doctors administered magnesium sulfate 25% - 5.0 ml intramuscularly and 30 drops of korvalol per os. ECG (Fig. 5) showed ST-segment elevation in precordial leads up to 4-5 *mm*.

According to the child's medical history, he was born after the 2nd normal pregnancy of 39-40 weeks' gestation, and with no complications. Weight at birth was 3300 *g*, he cried at once. Breastfeeding lasted up to 3 months. The child's growth and development was consistent with age. The boy often suf-

fered from acute bronchitis, pneumonia, and rubella. His mother suffered from hypertension.

Upon arrival at the cardiology department, the patient had no complaints. He had clear consciousness reacted to examination adequately. Physical development was average and balanced. He had pale skin, the rash was not present. Percussion and auscultation over the lung was clear. Borders of the cardiac dullness were normal. The heart sound was rhythmic, slightly muffled, with a tendency to tachycardia, systolic murmur was short, with a maximum in the IV intercostal space, heart rate was 96 beats per minute, blood pressure - 125/65 *mm Hg*. Abdomen was soft, painless in all areas. The liver and the spleen were not palpable. Physiological functions were in the normal range. Thyroid gland was enlarged, of elastic consistency, and painless on palpation. Sexual development was consistent with his age.

Laboratory data: common analyses of blood and urine, the levels of the C-reactive protein (CRP) and haptoglobine were normal. Markers of myocardial damage - Troponin I and creatine phosphokinase MB 18 were normal too (normal 25). The value of β-adrenoreactivity was 69.96 units that indicated activation of the sympathetic nervous system. The level of adrenaline in the daily urine decreased (24 *mmol/L*, normal range 28-55 *mmol/L*), which can be explained as exhaustion of the sympathetic-adrenal system after significant release of catecholamines because of the stress.

ECG on the 2-d day showed ST-segment (Fig. 6) elevation in the chest leads to 4-5 *mm* in the form of an arc concave upwards, as well as T-wave inversion.

Holter ECG without any chest pain in patient showed ST-segment elevation up to 438 *mkV*. Echocardiography, performed in the hospital, revealed enlarged left ventricle that normalized during supervision. Ultrasound data: end-diastolic dimension – 50.5 *mm* (normal range 39.2-48.0 *mm*), end-systolic dimension – 31.9 *mm* (normal range 23.6-28.8 *mm*), left ventricular posterior wall thickness – 9.3 (normal range 5.0-9.0 *mm*), end-diastolic volume 120.8 *ml* (normal range 60.4-81.7 *ml*), end-systolic volume 40.8 *ml* (normal range 21.9-29.6 *ml*), stroke volume 80 *ml* (50.0-67.7 *ml*), ejection fraction 66% (65-75%). The diastolic function was normal.

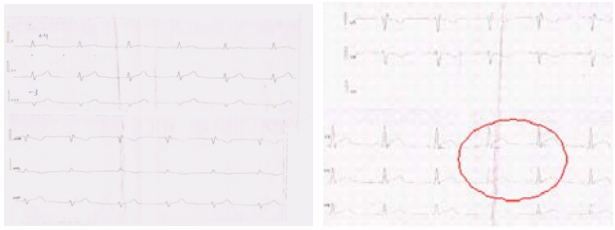

Figure 5. *ECG of 15 years old boy M., Low voltage in standard leads. Right bundle branch block. Disturbance of repolarization: ST-segment elevation up to 4-5 mm in precordial leads.*

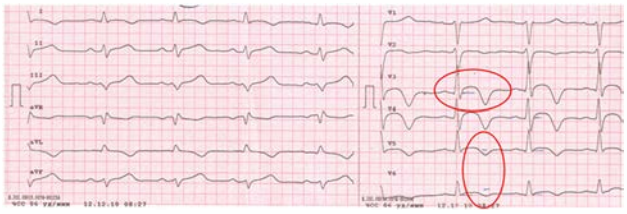

Figure 6. *Low voltage in standard leads. Disturbance of repolarization: ST-segment elevation up to 4-5 mm in precordial leads, T-wave inversion.*

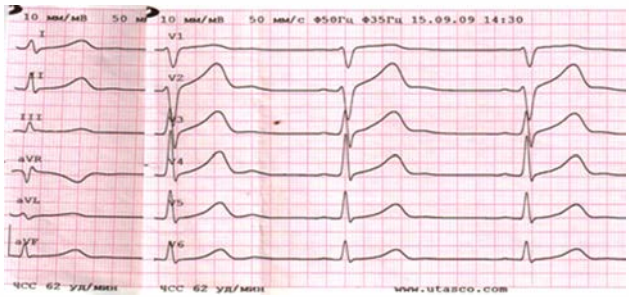

Figure 7. *Sinus rhythm. Repolarization disorder regressed.*

Bicycle ergometry test 5 days later resulted in ST-depression on the chest leads and decreasing tolerance of physical activity.

There were no occlusions and anomalies of vessels detected by aorto-coronarography.

The administered treatment included beta blockers (carvedilol), cardiometabolites and sedatives.

In 1.5 months after the onset, the child was examined again. ECG was within normal limits (Fig. 7), new episodes did not recur.

Presented clinical observations of rare forms of cardiomyopathy show polymorphism of clinical symptoms, early onset of the disease, its hereditary nature and require a multidisciplinary approach to the diagnosis and monitoring of patients.

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