CONGENITAL CARDITIS IN A NEWBORN (CASE REPORT)

Gonchar M.O., Senatorova A.V., Matsiyevskaya N.K., Zatoloka D.V.

Kharkiv National Medical University, Ukraine

Abstract
Diagnosis of carditis in newborns presents a number of difficulties, even with the results of high-technology research methods. Carditis is characterized by the absence of specific diagnostic criteria, similarity of clinical manifestations of cardiovascular and respiratory failure in young children, including secondary to generalized infectious diseases. The article presents a case of an atypical clinical presentation of carditis in a child with a confirmed intrauterine infection.
Key words: *newborns, carditis, intrauterine infection.*

Difficulties in diagnosing carditis in pediatric practice, especially in newborns, are due to the lack of specific diagnostic criteria, similarity of clinical manifestations of cardiovascular and respiratory failure in young children, especially secondary to generalized infectious diseases [1, 7].

The incidence of carditis is not exactly established. According to autopsy, it develops in 3–8% of children. Two thirds of newborns with carditis have a fulminant course, and the mortality rate is high, in 50% or more [3].

Mothers of newborns with carditis often have signs of infection during pregnancy, manifestations of heart failure can be registered in utero or in the maternity hospital. The risk of horizontal or vertical transmission from mother to newborn is high [7].

There is no generally accepted classification of carditis. It is a common practice to differentiate congenital (antenatal) and acquired (postnatal) carditis of newborns [2].

Carditis is considered reliably congenital in the presence of severe clinical symptoms of prenatal generalized infection, early manifestation of severe HF and cardiomegaly of varying severity in combination with damage to many organs and systems, and with appropriate reliable instrumental and laboratory (virological, bacteriological, immuno-biochemical) markers of myocardial damage. Congenital carditis is considered probable if HF and cardiomegaly are detected in the first 6 months of life (less frequently at the age of 2–3 years) without a prior intercurrent disease of the child, but with indications of the mother's disease during pregnancy in history. Congenital carditis is classified into early and late forms, depending on the expected timing of the intrauterine onset of the process and differences in the morphological substrate of pathology. The condition is characterized by endomyocardial fibroelastosis in the fetus with an infection up to 28 weeks of gestation and the usual phasic inflammatory process at later stages.

Acquired (postnatal) carditis in newborns and infants more often has viral etiology and acute course. The presence in the history of previous infections of the upper respiratory tract, febrile fever, diarrhea syndrome in the mother and the newborn is of great importance in the diagnosis. There can also be nosocomial infections.

The course of carditis can be acute (up to 3 months), subacute (up to 18 months), chronic (more than 18 months, relapsing and primary chronic). Subacute course is not typical for carditis manifesting in the neonatal period.

The most common cause of carditis in newborns are Coxsackie enterovirus (types B and less often A) and ECHO, a number of cardiotropic poliomyelitis viruses, some types of influenza virus, herpes simplex virus I and II, adenovirus, CMV

Corresponding Author:
Anastasiya Senatorova, MD, PhD,
Professor asssistant of Department of Pediatrics 1 and Neonatology of Kharkiv National Medical Univeristy, Ukraine.
E-mail: anastasya.senatorova@gmail.com

and toxoplasma infection. This is explained by the cardiotropic nature of these viruses and the imperfection of immunological protection of newborns and young children predisposed to this heart disease [7].

Myocarditis and pancarditis can be a complication of any infectious disease (of bacterial, fungal, rickettsial and parasitic etiology) or a consequence of toxic effects (medication, ionizing radiation, chemical). In recent years, there have been cases of congenital carditis in newborns as one of the symptoms of the visceral form of early congenital symptomatic syphilis. There are single descriptions of Kawasaki disease with myocarditis, coronaritis, acute HF in the 1st month of life.

According to the literature, the introduction of virus into the cell is most likely important in the pathogenesis of carditis only when associated with disorders of the immune system. This stage is accompanied by a violation of myocardial metabolism, dystrophic and necrotic changes, development of an immunological imbalance. Protection mechanisms become effective only after the peak of virus replication on the 3rd or 4th day and are due to the combined participation of the macrophage defense system, T-lymphocytes and B-lymphocytes and interferon in virus elimination. Lymphocyte-macrophage inflammatory infiltration is accompanied by lysis of myofibrils infected with cytotoxic T-lymphocytes with fibroblast production, increased production of pro-inflammatory cytokines. Thus, myocardial damage is the result of both direct and indirect cytotoxic effects. The developing HF is accompanied by hyperproduction of neurohormones and a further increase in the secretion of proinflammatory cytokines (TNF-2, IL-1, IL-6, IL-8), which initiate remodeling and progressive myocardial dysfunction. The mechanism of action of cytokines in inflammation and HF comprises negative inotropic action, cardiac remodeling, impaired endothelium-dependent arteriole dilatation (due to activation of endogenous nitric oxide synthase) and increased cardiomyocyte apoptosis. Clinically, this correlates with impaired left ventricular function, contractility, cardiomegaly, severity of clinical manifestations and prognosis of the disease [2, 3].

Clinically, in congenital carditis, symptoms of the disease develop in utero or in a maternity hospital. In acquired (postnatal) carditis, symptoms develop on the 5th–7th day of a viral infection, after contact with a sick mother, relatives, and sometimes in nosocomial contacts. The severity of the condition progressively increases and depends on the severity of infectious toxicosis, severity of myocardial damage, CH mainly of the left ventricular and/or right ventricular type, the presence of circulatory collapse.

In moderate forms only moderate cardiomegaly, electrophotographic and ECHO changes, and moderately elevated concentrations of biochemical markers serve as criteria for myocarditis.

In severe course, symptoms of acute left ventricular and then right ventricular insufficiency with dyspnea, cyanosis of the mucous membranes, tachycardia, palpitations, congestive moist rales in the lungs, enlarged liver, less often splenomegaly, and limb pastosity develop quickly. Edema of the limbs, polyserositis and ascites appear in the terminal stage. Extracardiac manifestations may include symptoms of enterocolitis, meningitis, encephalitis [3, 4].

Newborns are found to have manifestations of intrauterine growth retardation. Fever, acrocyanosis or general cyanosis, fatigue during feeding up to anorexia, shortness of breath are possible. On examination, there are no chest deformity in the form of a heart hump and visual abnormal pulsations. Percussion reveals varying degrees of heart enlargement, up to cardiomegaly. The apical impulse is not changed or moderately weakened, shifted to the left depending on the degree of heart enlargement.

Physical changes are characterized by varying degrees of tachycardia, muffled heart sounds, sometimes weakening of I tone, embryocardia, development of myocardial cantering rhythm (most often diastolic or presystolic as a symptom of pressure increase in the atria or valvulitis of the mitral valve) at the apex. Systolic murmur of muscular character is typical, somewhat later patient develop systolic murmur of relative insufficiency of atrioventricular valves, mainly mitral, with a maximum volume at the apex of the heart. Rhythm and conduction disturbances are observed quite frequently.

In some newborns, myocarditis is associated with pericarditis, which is clinically accompanied by a sharp deafness of heart tones up to aphonia [1, 6].

Routine laboratory tests in the diagnosis of carditis are not sufficiently informative, non-specific and have diagnostic value only in combination with clinical findings and functional research data.

The increase in the activity of cardiac isoenzymes CPK-MB, LDH1 and LDH2 is more specific (there is evidence of an increase in their activity in the acute phase to values comparable to those in myocardial infarction).

In recent years, troponin and its isoenzymes (troponin I and troponin T) are considered to be a rather informative biochemical marker of myocardial damage. In absence of clinical or ECG signs of ischemia, an increase in troponin I or troponin T in blood indicates non-coronary damage (necrosis), which is very important for pediatrics and neonatology.

Bacteriological and virological studies of blood and other biological fluids (in particular, pericardial effusion), serological and enzyme immunoassay methods establish the bacterial or viral etiology of the disease. Ig M antibodies (AT) have diagnostic value for acute carditis. AT titres usually increase four times in the recovery period compared with the acute period. Polymerase chain reaction is informative. In recent years, data have appeared on the correspondence of the increase in AT titres to various structures of the myocardium (to cardiomyocytes, the conduction system, endothelium, and other structures) to different clinical manifestations of carditis [2, 6].

An x-ray study determines an increase in the size of the heart (up to cardiomegaly), with an increase in the cardio-thoracic index of more than 0.6–0.7. Patients are typically found to have changed shape of heart (pathological remodeling) with smoothness of contours and development of sphericity, occasionally signs of venous congestion in the lungs or moderate pleural effusion.

ECG changes depend on the degree of myocarditis activity and are characterized by transient unstable non-specific changes in repolarization in the form of isoelectricity or depression (when combined with pericarditis in the form of elevation) in more than three leads of the ST segment, in the form of amplitude reduction, isoelectricity, T wave inversion. Patients are often found to have a decrease in QRS complex voltage. Pseudo-infarction changes and pronounced signs of subendocardial ischemia can be signs of coronaritis. Early changes may include different types of blockades of the bundle of the His branch, AV blockades. Extrasystole is observed in 60% of cases, less frequently paroxysmal tachycardia, atrial fibrillation. High scale extrasystole, ventricular arrhythmia and alorrhythmia are prognostically unfavorable. Rhythm disorders can be persistent and difficult to treat with metabolic and antiarrhythmic agents before the onset of the clinical effect of anti-inflammatory therapy. The severity of signs of overload (hypertrophy) of the left heart chambers is variable. Development of HF with congestion in the pulmonary and systemic blood circulation is characterized by signs of overload of both the atria and the right ventricle [4, 6].

ECHO shows myocardial edema, moderate dilation of the heart cavities, a decrease in pumping indices (left ventricular ejection fraction) and contractile function of the myocardium. Doppler examination determines relative mitral and tricuspid insufficiency, impaired left ventricular diastolic function. If there are signs of pericarditis, a pericardial effusion is quantified (1 mm of pericardial separation corresponds to approximately 10 ml of effusion) [7].

Radionuclide methods of examination and especially new radiological methods of simultaneous study of metabolism and myocardial function are sufficiently informative for the differential diagnosis of reversible (inflammatory and ischemic) and irreversible (destructive) myocardial changes, clarification or diagnosis. These studies are just beginning to be used in pediatric practice.

Case report

A boy was born in the perinatal center from the 2nd pregnancy, 1st labor at the gestation term of 39 weeks by caesarean section. The mother has a high degree of disturbance of fetal hemodynamics with the formation of ascites. At 11 weeks, she was found to have positive titres of Ig G antibodies to cytomegalovirus, herpetic, toxoplasmic infections. Prenatal examination of the fetal Doppler echocardiography revealed a marked predominance of the right heart chambers, ventricular myocardial hypertrophy and interventricular septum; moderate tricuspid regurgitation.

The function of fetal communications is not impaired, the Botallo's duct is narrowed to 1.4 mm, the aorta at the base is narrowed to 7 mm, the PA at the valve level is 11.8 mm, the left ventricle is reduced in size; ascitic strip of fluid up to 20 mm. Fetal-placental blood flow is normal, pulsation index in the umbilical artery is 1.05 (68‰); systolic-diastolic ratio is (S/D) is 2.57. Fetal blood flow is decompensated - reverse blood flow in the venous duct. The pulsation index PI in the middle cerebral artery (MCA) is 1.09. There is two-phase pulsation in the umbilical vein. The uterine-placental blood flow is impaired – highly resistant PI in the right uterine artery (UA) is

1.34, PI in the left UA is 0.69, average PI is 1.17 (98‰) (*Fig. 1.1*).

The child was born with a mass of 2380 g, height 47 cm, head circumference 33 cm, chest circumference 31 cm. Apgar score is 7–8 points. At birth, the general condition is satisfactory, flexor position, loud cry, muscular hyper tone, body temperature 37.1°C. The frequency of respiratory movements is 46/min, heart rate is 142/min. Heart sounds are rhythmic, systolic murmur. The abdomen is soft and palpable. Acid-base indices at birth: pH – 7.19, pCO_2 – 68.7 mmHg, pO2 – 41 mmHg, HCO_2 – 28.8, BE 3.6 mmol/l – compensated respiratory acidosis. Blood count and biochemical blood count (total cord blood bilirubin, direct bilirubin, glucose): without abnormalities. The child was transferred to the department of joint residence with the mother, where he stayed for 8–10 days.

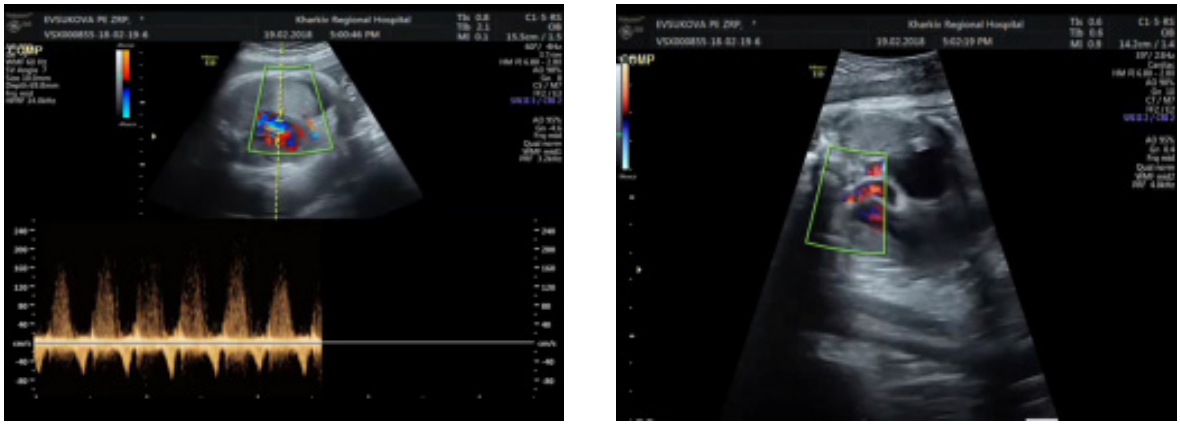

Fig. 1. Fetal Doppler echocardiography, gestation term of 39 weeks

During the first days of life the general condition of the child is without impairments. His cry is loud. Spontaneous motor activity is sufficient. The skin is pink, clean and dry. Elasticity and skin turgor aare reduced. Breathing is spontaneous, rhythmic, with intercostal retraction. On auscultation: breathing in the lungs is carried out in all departments on both sides. Breathing rate – 44/min. On auscultation heart sounds are rhythmic, muffled. Heart rate – 140/min. The abdomen is soft. Liver + 1.5 cm below the edge of the costal arch. Urination is sufficient. Clinical blood assay did not show any abnormalities.

Doppler echocardiography in the first day of life: diastolic diameter of the left ventricle (DdLV) – 14.3 mm (norm – 20.0mm), thickness of the posterior wall of the left ventricle (Tpwlv) – 6.0 mm (norm – 4.0mm), ejection fraction (EF) – 72% (norm – up to 65–75%), ΔD – 40% (norm – up to 45%), diameter of the left atrium (DLA) – 9.0 mm (norm – up to 12 mm), diastolic diameter of the right ventricle (DdRV) – 15.7 mm (norm – up to 8.0 mm), diameter of the right atrium (DRA) – 13.1 mm (norm – up to 9.0 mm), aortic diameter (Ao) – 9.0 mm (norm – to 10.0 mm), diameter of the pulmonary artery (PA) – 12.0 mm (norm – up to 10.0 mm), Δp of Ao valve – 6.3 mmHg (norm – up to 10.0 mmHg), Δp of PA valve – 7.4 mm Hg (norm – to 10.0 mmHg), average pressure in the PA trunk – 43 mmHg (norm – to 25 mmHg). Conclusion: LV hypoplasia, RV hypertophy, dilation of right chambers. Patent foramen ovale, diameter – 3.2 mm, left-right shunt. Open arterial duct, diameter is 1.0 mm. The blood flow in the abdominal aorta is pulsating.

Cardiac surgeon's conclusions: Congenital heart disease (persistent ductus arteriosus, patent foramen ovale). Pulmonary hypertension. Follow-up Doppler echocardiography is recommended.

In the follow-up observation the child's condition is stable. Biochemical blood assay: ALT – 307.9 U / l (norm – up to 45 U / l), ACT – 176.1 U/l (norm – up to 75 U/l), total bilirubin – 63.5 μmol / l (normal – up to 21 μmol / l), direct bilirubin – 10.5 μmol / l (norm – up to 6.8 μmol /l), indirect bilirubin – 53 μmol/l (norm – up to 14.2 μmol /l), CPK – 364 U/l (norm – up to 190 U/l), CPK-MB – 251.3 U/l (norm – up to 25 U/l), LDH – 1200,1 U/l (norm – up to 750 U/l), blood urea – 6.8 mmol/l (norm – 2.5–4.4 mmol/l), C-reactive protein – 10.49 mg/l.

Doppler echocardiography findings on the third day of life: DdLV – 14.0 mm (norm – 20.0 mm), EF 75% (norm – up to 75%), ΔD – 40% (norm – up to 45%), DLA – 9.0 mm (norm – to 10.0 mmHg), DdRV – 15.6 mm (norm – to 10.0 mmHg), DRA –13.0 mm (norm – to 10.0 mmHg), Ao diameter – 9.0 mm (norm – up to 10.0 mmHg), PA diameter – 4.0 mm (norm – up to 10.0 mmHg), Δp of Ao valve – 7.0 mmHg, Δp of PA valve – 7.1 mmHg (norm – up to 10.0 mmHg), Δp of asc. Ao – 7.7 mmHg (norm – to 10.0 mm Hg), the average pressure in PA trunk – 27 mmHg

(norm – up to 30 mmHg). Conclusion: severe hypertrophy of the RV. Dilatation of right chambers, 1st–2nd degree tricuspid regurgitation. Pulmonary hypertension. Open oval window, diameter – 3.0 mm, with left-right shunting. Open arterial duct, diameter – 1.2 mm. The blood flow in the abdominal aorta is pulsating (*Fig. 2, Fig. 3*).

An ECG study was performed: overloading of the right chambers, myocardial hypertrophy of the interventricular septum and right ventricle. Slowing down of AV conduction. Incomplete blockade of the right bundle of His. Violation of repolarization processes (*Fig. 4*).

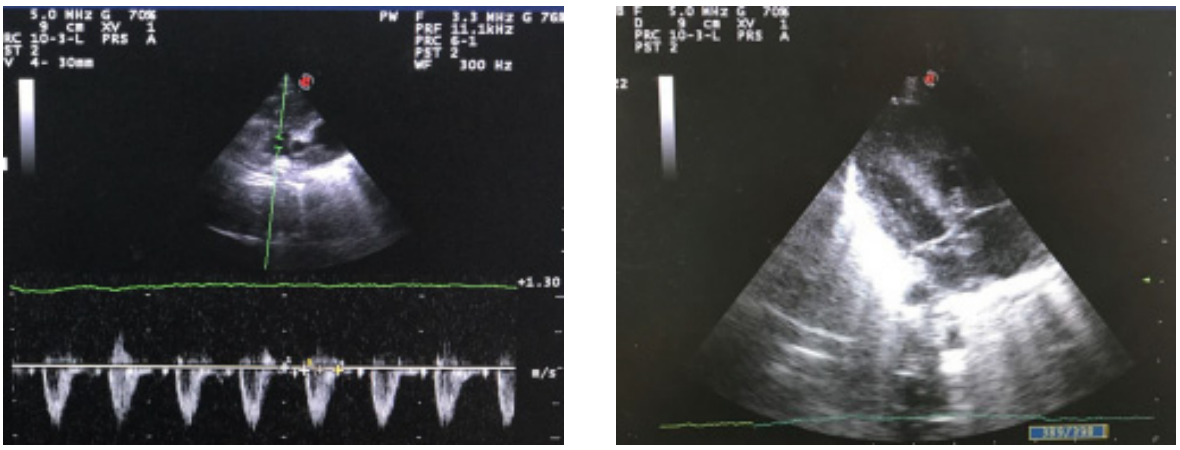

Fig. 2. Doppler echocardiography (M-mode) of a newborn (boy) on the 3rd day of life

Holter heart rate monitoring: during the day heart rate (HR) without abnormalities. Arrhythmias are not registered. Episodes of sinus "tachy-brady" arrhythmia. The patient was found to have 21 episodes of ST depression.

The child underwent immunoassay for antibodies to infectious agents:

Cytomegalovirus infection IgM 0.01 (norm – 0.384), IgG 1.75 (norm – 0.3) positive; herpes simplex IgM 0.046 (norm – 0.287), IgG 2.25 (norm – 0.215) positive; Toxoplasma IgM 0.012 (norm – 0.412), IgG 0.025 (norm – 1.21) negative. Hepatitis B and C markers are negative.

The mother refused to perform any PCR tests for the newborn. Diagnosis: intrauterine viral infection (carditis, hepatitis). 1st degree Pulmonary hypertension.

The newborn received antiviral treatment according to the protocol [4, 5, 7].

In the follow-up observation on the 10th day C-reactive protein normalized to 4.1 mg/l. Biochemical blood assay: total bilirubin 28.3 μmol/l, direct 9.8 μmol/l, ALT 42.4 U/l (normal), AsT 56.1 U/l (normal).

Repeated ECG studies: sinus rhythm. Overloading of the right chambers, myocardial hypertrophy of the interventricular septum and right ventricle. Slowing down of AV conduction. Incomplete blockade of the right bundle of His. Disruption of repolarization processes (*Fig. 5*).

Doppler echocardiography on the tenth day of life: DdLV – 15.3 mm (norm – 20.0mm), Tpwlv – 7.0 mm (norm – 2.0mm), EF – 70% (norm – up to 75%), DΔ – 40% (norm – up to 45%), DLA – 8.0 mm (norm – up to 12 mm), DdRV – 15.7 mm (norm – up to 8.0 mm), DRA – 13.4 mm (norm – up to 9.0 mm), Ao diameter – 9.0 mm

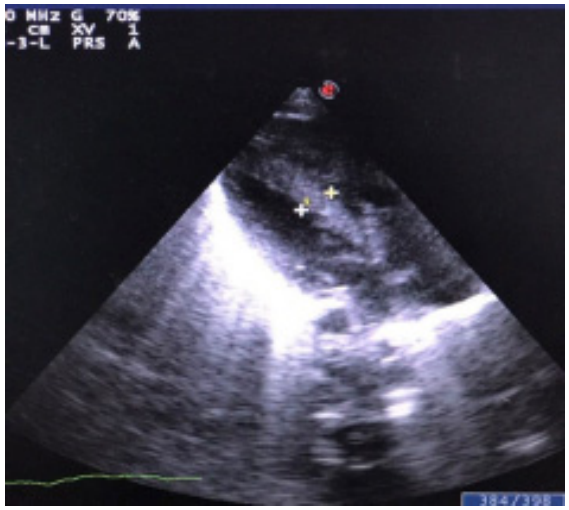

Fig. 3. Doppler echocardiography (M-mode) of a newborn (boy) on the 3rd day of life

(norm – up to 9.0 mm), PA diameter – 11.0 mm (norm – up to 9.0 mm), Δp of Ao valve – 5.2 mmHg (norm – to 10.0 mm Hg), Δp PA valve – 6.4 mmHg (norm – up to 10.0 mmHg), the average pressure in the PA trunk – 29 mmHg (norm – up to 30 mmHg). Conclusion: LV hypoplasia, RV hypertophy, dilation of right chambers. Open oval window, diameter – 3.2 mm, left-right shunt. The open arterial duct diameter is 1.0 mm. The blood flow in the abdominal aorta is pulsating.

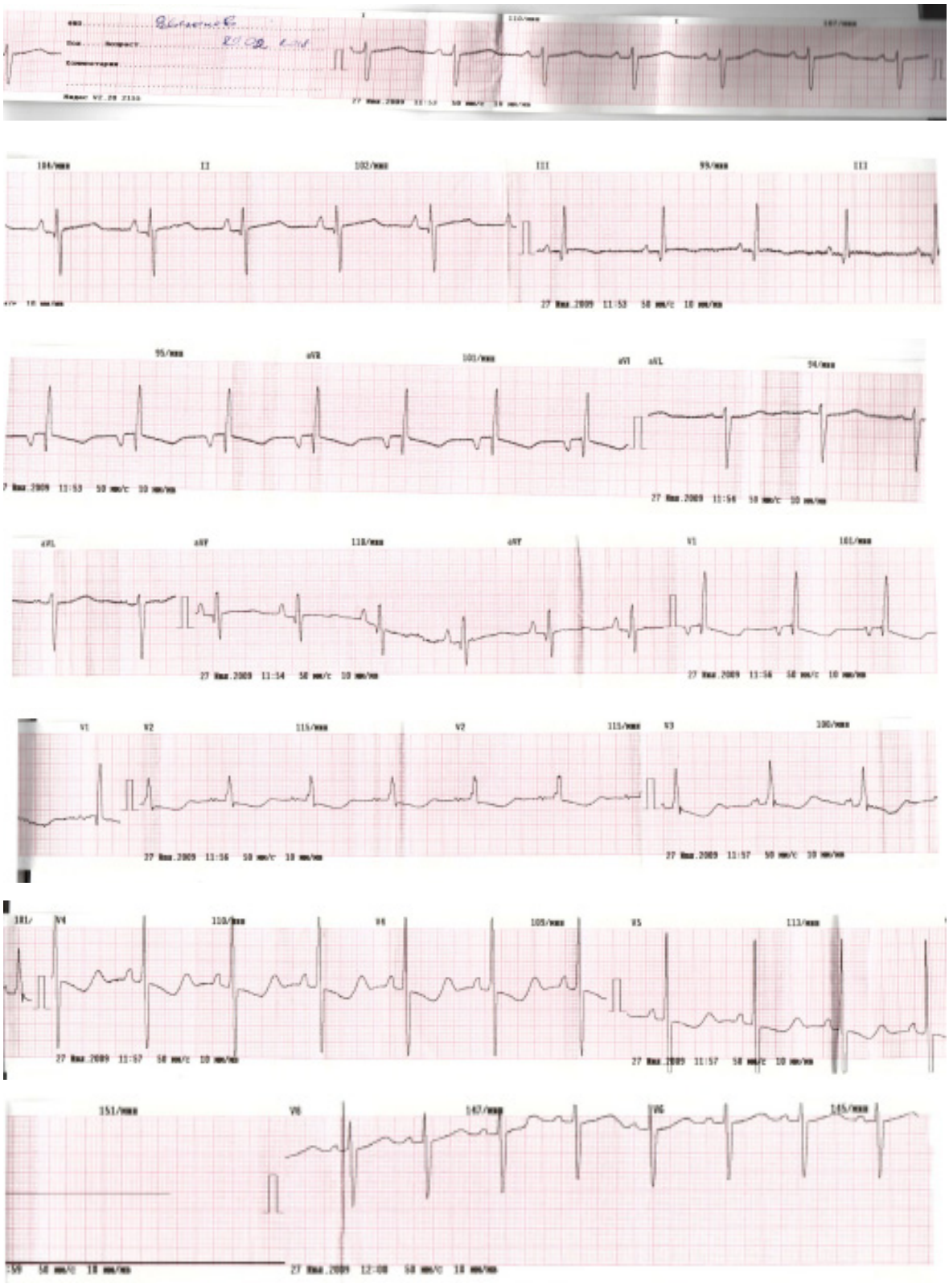

Fig. 4. ECG of a newborn (boy) on the 1st day of life

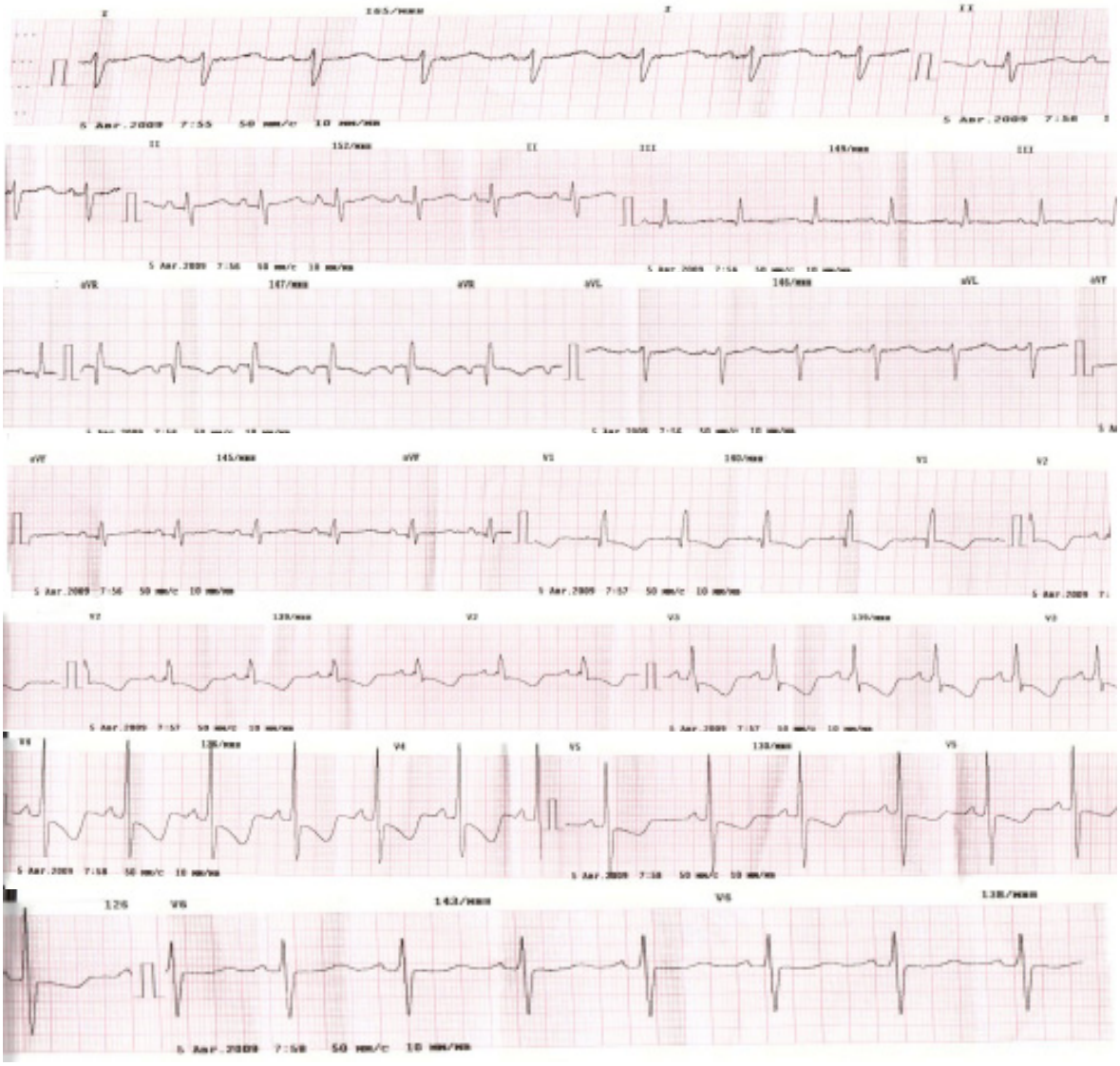

Fig. 5. ECG of a newborn E. (boy) on the 10th day of life

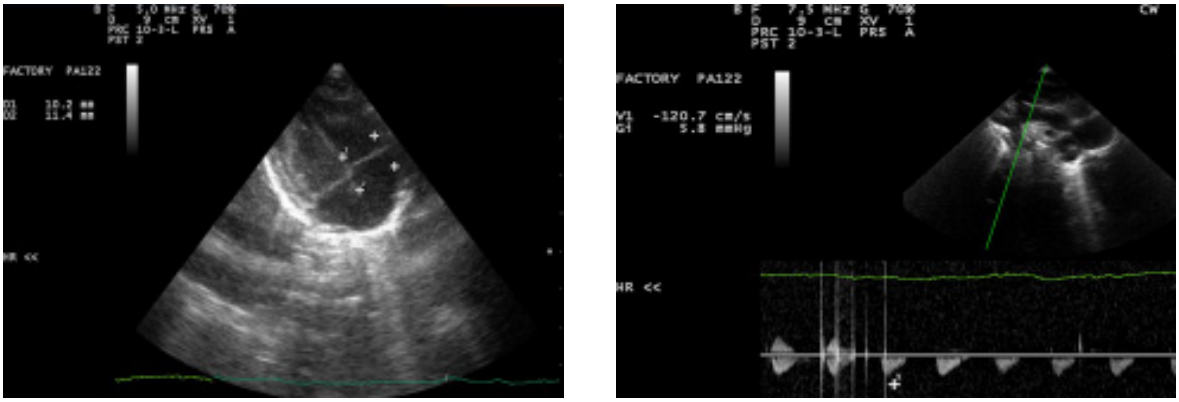

Fig. 6. Doppler echocardiography of a newborn E. (boy) on the 10th day of life

Conclusions:

Carditis in a newborn with an intrauterine viral infection may be manifested by significant hypertrophy of the right chambers. Diagnosis of carditis requires the exclusion of congenital heart disease, premature closure of the ductus arteriosus.

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