Fatal myocardial infarction in term neonate

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Abstract
Neonatal myocardial infarction (MI) is a life-threatening condition rarely encountered in neonates. It has high mortality rate but early recognition and intensive care management can be successful. We describe the case of a full-term male neonate, born by caesarean section in general good condition. Soon after the delivery respiratory difficulties began and the neonate had a circulatory collapse due to myocardial infarction. His heart and coronary arteries were anatomically normal and a massive thrombotic occlusion of the left main coronary artery was believed to be the cause of MI. Myocarditides caused by enterovirus was ruled out. Although the aggressive treatment with anticoagulant agents, catecholamines and diuretics the patient did not survive. All the attending neonatologists and paediatricians should take into account the possibility of MI when evaluating a neonate with an acute onset of collapse.

Key words: neonatal myocardial infarction, coronary thrombosis, coronary arteries, enteroviruses myocarditis, troponin T, neonate

Introduction
Myocardial infarction (MI) in the neonatal period is a very rare phenomenon. The prognosis is rather poor with the risk of death up to 80-90% despite aggressive treatment in tertiary centers. The most commonly described causes in structurally normal heart include: tromboembolism, perinatal asphyxia, coagulopathy, entero viral myocarditis and maternal diabetes. Congenital heart anomalies predisposing to this condition are: anomalous left coronary artery from pulmonary artery (ALCAPA), hypoplastic left heart syndrome (HLHS), total anomalous pulmonary venous return (TAPVR), critical aortic stenosis and pulmonary atresia [1]. The highest mortality rate is noted in neonates with thromboembolism.

Obstetric history
A male Caucasian baby was born by caesarean section at 37 weeks of gestation to a 28-year-old gravida 1, para 1 mother. The birth weight was 3140 g. No evidence of congenital malformations was found on prenatal ultrasounds. No family history was known of any congenital diseases. All three trimesters of pregnancy were uneventful. Current GBS screening test was negative. The first stage of labor lasted for seven hours and during that time the oxytocin administration to mother was started. Because acute fetal life-threatening symptoms were present (decelerations in the cardiotocography (CTG) record), caesarean section was performed.

Case presentation
A term neonate was delivered by caesarean section due to a signs of fetal distress. Apgar score was 10 and 10 at 1st and 5th minute respectively. pH obtained from both scalp and cord blood was within the norms 7.30 (BE – 3.9 mmol/l) and 7.37 (BE – 4.8 mmol/l). Soon after birth, respiratory difficulties appeared with tachypnea, grunting and retractions. Heart rhythm was found to be normal and arrhythmia was noted during physical examination. The baby was treated with oxygen (FiO2 30%) and diagnostic approach to rule out infection was performed (CRP, complete blood count, blood smear and blood culture). Also electrolytes and glucose level were checked and were in a normal range. Chest X-ray did not show any significant abnormalities. Acid-base balance one hour after birth and thereafter revealed respiratory, and later – metabolic acidosis (pH 7.16; pCO2 65 mm Hg, BE – 6.0 mmol/l; pH 7.13; pCO2 49.9 mm Hg; BE – 12.5 mmol/l), lactate level was 90 mg/dl. Patient was transferred to Neonatal Intensive Care Unit and supported with non invasive ventilation with FiO2 30-40%. Because of tachycardia (190 bpm) which appeared few
hours later, echocardiographic study (ECHO) was performed by neonatologist. Hypoplastic aortic arch was suspected, and because of that, infusion of prostaglandin E1 was started. At about 11th hour of life, due to further deterioration, including increasing oxygen demand, low systemic pressure and tachycardia, the baby was intubated and ventilated using SIMV mode with 100% oxygen. Fluid resuscitation and catecholamines were started. Consulting cardiologist diagnosed the following items: anatomically normal heart, extremely low cardiac output with low left ventricle ejection fraction (LVEF) about 28%, severe mitral insufficiency, tricuspid insufficiency, patent ductus arteriosus and foramen ovale with bilateral flow, maximal flow velocity through aortic valve only at 0.3 m/s. In the aortic bulb, abnormal structure (1.1 cm × 0.3 cm) was found (Fig. 1, 2).

![Fig. 1. Echocardiography: parasternal view, short axis, arrow shows an abnormal structure in the aortic bulb](image)

It was suspected to be a massive thrombus or a vegetation, akinesis of lateral, posterior and anterior wall of LV was dominant. Mean systemic pressure was about 50 mm Hg with the supply of catecholamines. Strong suspicion of cardiac infarction appeared which was based on electrocardiogram performed immediately. Normal, sinus rhythm (150 bpm), right axis deviation, PR interval 100 ms, QRS interval 100 ms, QT interval 240 ms. Complete right bundle branch block (CRBB), QS complexes in I, V5, V6 leads. In addition to previous treatment (dopamine, dobutamine, fentanyl, antibiotics, prostaglandin E1, parental nutrition), infusion of heparine, furosemide and nitrate was started. Among many biochemical tests, troponin T level (TNT) was found to be several times above normal range (10ng/ml on day 1st; 15.0 ng/ml on 2nd day; 9.95 ng/dl on 3rd day, falling down thereafter, but still above normal range on day 21st. Also the aspartate aminotransferase (AST) was very high: 785 U/L – on 1st day; 357 U/L until 3rd day; normal range on day 9th). Blood culture was negative, as well as CRP (serial samples), cholesterol, triglicerides, coagulation and antithrombin III level (slightly below normal activity).

To ruled out myocarditis caused by enteroviruses – ELISA test was performed and was negative. The infant was still unstable, on moderate respiratory settings with FiO2 30-40%. On third day another cardiologist consultation was performed which showed similar picture findings to the previous one. The cloth near left coronary artery was still present. Three days later – pericardial effusion and left atrium enlargement were found in addiction to previous ECHO findings. At the end of the first week of life, the cloth was not observed during echocardiographic examination, but all previously detected heart „injury” was still present and the baby had severe heart insufficiency. At second week of life – cardiac catheterization was performed and did not reveal any left coronary artery anomaly. At that time, the baby was still on dopamine, dobutamie, milrinone, prostaglandin E1, furosemide, aldacton and fraxiparine infusion – with very poor cardiac output. Ascites was found during abdominal examination. Head ultrasound, performed three times, was normal. On 21st day after birth, the baby was transported to Polish Mother’s Memorial Hospital, Neonatal Intensive Care Unit of Department of Intensive Care and Congenital Malformations of Newborns and Infants in Łódź for further, invasive diagnosis and treatment including stem cells therapy. Further treatment course and the patient’s condition were as follows: antibiotic therapy was continued, milrinon and dobutamine infusions were continued for two more days. The patient condition was stable for 7 days after admission to Łódź. On 29th day of life, deterioration...
Discussion

There are very few reports concerning neonates with myocardial infarction and mortality rate in this condition is very high. Bernstein et al. [2] presented 27 cases of MI with only two survivals and Boulton et. al. reviewed 14 cases, two of whom survived [3]. Thrombus was identifying in one baby treated with inotropes and digoxine. Peeters [4] described a symptomatic neonate with antithrombin III deficiency. Fesslowa et al. [5] described a case of full term infant with birth asphyxia, severe anemia and MI. The baby died soon after birth. Umbilical vein catheterization was suggested to be a possible source of thromboembolism leading do myocardial infarction as suggested by Poonai et al. [6] but our patient did not undergo this procedure. Also coronary vasoconstriction secondary to oxytocin administration to the mother was suggested to be a possible mechanism leading to MI [7]. Oxytocin was administered to the mother in discussed case. Thromboembolism seems to be the most fatal condition and can also originate from paradoxical embolism, from ductus venosus [8] or umbilical cord hematoma also [9]. Until 2011, eighteen out of twenty published neonatal deaths with MI were caused by thrombotic event. Some cases still remain of unknown etiology. Hypercholesterolemia can also cause MI but even in cases with homozygotic familiar form, the known etiology. Hypercholesterolemia can also cause MI by thrombotic event. Some cases still remain of un-

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A typical ECG findings allows the diagnosis of infarction. According to Towbin and colleagues [12], these include: Q waves more than 35 mm with or without notching, ST elevation greater than 2 mm and prolongation of the QT interval corrected for heart rate beyond 440 ms with accompanying abnormalities of the Q wave.

As far as therapy is concerned, among the reports: inotropes, vasodilatators, diuretis, oxygen and parental nutrition are the main ways of therapy. Thrombolysis have been used with varying results in neonatal MI. Tissue plasminogen activator have been used successfully in 3 months old infant with Kawasaki disease for massive thrombus in left coronary artery [13]. Streptokinase was also used for the same reason in older infant as described by Burtt et al. [14]. We have considered the use of actylise, but do the risk of intracranial hemorrhage we decided to withdraw from this. On the other hand, this treatment appeared to be successful with emergency catheterization, as described by Cesna et al. [15]. They have injected tissue plasminogen activator directly into left coronary artery, despite a significant risk, in a hemodynamically unstable patient. The initial goal of thrombolytic therapy was restoration of myocardial perfusion. The same way of treatment has recently been performed by Deutsch et. al. [25]. Intracoronary lysis during catheterization was found to be very effective and should be considered in cases of MI due to thrombus event. Prompt and aggressive treatment is the only one chance for survival. It was also reported a few
months ago by Ramlogan et al. [26]. They performed thrombectomy during urgent heart catheterization. It’s worth mentioning, that in this case, there was no echocardiographic evidence of left coronary artery obstruction, but clinical suspicion was strong enough to perform invasive intervention. It is not possible to expect a patient to be stable, while MI appear, therefore aggressive treatment including angiography seems to be fully explained and reasonable. It is well known that neonatal myocardium has no well established coronary collateral flow [16, 17], therefore aggressive therapy is necessary. In case of discussed patient – cardiosurgeon refused to perform this procedure urgently because of high instability of the baby. ECMO therapy allows recovery of left ventricular function but unfortunately, is not available in most neonatal centers in Poland. Similar case was described by Sandhya [27]. This patient was a term baby, delivered vaginally, who developed acidosis and cardiogenic shock. ECHO revealed no structural abnormalities, but profound left ventricular dysfunction, moderate mitral valve regurgitation and a linear mass in the aortic root, which seems to be similar to reported case. Troponine level (TNT) was elevated to 36.3 ng/ml. At 37th hour of life, the patient had cardiac catheterization which revealed no flow through left main coronary artery (LMCA). Thrombectomy was performed and patient’s condition was stable. Postoperative ECHO showed no residual thrombus and laminar flow in left main coronary artery. Similarly to discussed case, milrinon, prostaglandin, nitropruside, epinephrine and heparin were administered. Within 6 days after operation, the baby’s state was unstable and worsening with persist left ventricular disfunction. Despite transferring to transplant centre, intracranial insult happened, due to multiorgan failure, he was deemed no longer a transplant candidate and died soon after that.

The specific predictors of functional recovery following MI in the newborn, has not been evaluated. However, it is suggested, that neonatal myocardium has a great ability to make complete recovery, therefore aggressive treatment seems to be explained and necessary. In some cases – ventricular assist device – often used as a bridge to transplantation – may be a bridge to recovery after MI [18-23]. The Berlin Heart EXCOR is currently the only one ventricular assist device approved by the FDA for use in neonates and pediatric patients as small as 3 kg. As far as diagnosis, it’s worth mentioning, that even in the absence of echocardiography or cardiologist at neonatology unit, simple tests can be performed in patients with cardiovascular collapse, besides troponin estimation when ductal-dependent congenital heart disease is suspected. These include troponin estimation. The major advantage of the evaluation of troponin results from being specific of myocardium. Its high sensitivity and wide diagnostic window with an initial fast rise within a few hours after cardiac lesion, makes it complimentary/alternative tool to ECHO in patients with cardiac collapse. Following myocardial damage, troponin appears in blood 2-4 hours later and persist up to 21 days. The detection, using immunoassay, is quick, available and not expensive. In presented case, troponin was extremely high, and persist elevated until 3rd week after birth.

**Summary**

We should remain aware that myocardial infarction can be a possible cause of early neonatal cardiogenic shock, difficult to differentiate from critical left heart defects. In many cases, this is a condition leading to death. It may result from embolic occlusion of the left coronary artery. We should try to perform prompt cardiac diagnosis, including cardiac catheterization if necessary and start full, even aggressive treatment, including cardiosurgeon intervention and/or ECMO therapy which seems to be life saving.

**References**

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