Case **report**

PREMATURE CLOSURE OF THE DUCTUS ARTERIOSUS - CASE PRESENTATION

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Abstract

Spontaneous premature closure of the human fetal ductus arteriosus is an uncommon event that often results in significant morbidity and mortality. We present a case of a fetus with prenatal previously not detected bone defect that presented with idiopathic intrauterine closure of the ductus arteriosus. A 23-year-old mother at 39 weeks of gestation was admitted to the hospital because of an abnormal findings in four chamber screening view of the fetal heart on routine ultrasonography. The fetal echocardiography showed no detectable flow through the ductus arteriosus. Cesarean section was performed 1 hour later. A female newborn weighing 2640g with Apgar scores of 0, 2, 4 and 6 at 1, 3, 5, and 10 minutes, respectively, was delivered.

Key words: *premature closure of the ductus arteriosus, prenatal diagnosis, ventricular hypertrophy, echocardiography*

CASE PRESENTATION

A primipara aged 23 was admitted to the Holy Trinity Hospital in Płock in the 39th week of pregnancy because of her irregular systolic function. In the 34th week of pregnancy, she was hospitalised due to threatening premature delivery and urinary tract infection. She underwent intravenous tocolysis and then oral tocolysis (Fenoterol and Isoptin), steroid treatment (Dexaven) and antibiotic treatment (Biocefal).

The woman suffered from epilepsy, which was treated with Depakine Chrono before the pregnancy. During the pregnancy, she did not go into convulsions and her epilepsy was not treated. Her family history was one of autism, amblyacousia and epilepsy. The baby's father underwent brain surgery in childhood (no medical documentation available).

The woman got pregnant naturally. The results of the ultrasound examinations which she underwent in the 13th and 20th weeks of pregnancy were positive. In the 31st/32nd week of pregnancy, she had a gynaecologist appointment during which the foetus was examined in terms of its structure and development, both of which turned out to be normal. Also, umbilical artery Doppler velocimetry and cerebral artery Doppler velocimetry were performed, which confirmed the good health of the foetus.

Having experienced a slight intermittent pain in the lower stomach and the lumbar and sacral regions, the woman was admitted to the gynaecologist ward of the hospital in the 39th week of pregnancy. The CTG was normal, demonstrating reactivity and no decelerations; the baseline foetal heart rate variability was 6.4 msec. She underwent an ultrasound examination with biometry and umbilical artery Doppler velocimetry and middle cerebral artery Doppler velocimetry; no abnormalities were diagnosed. The amount of amniotic fluid was also normal.

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On the second day of her hospitalisation, her systolic function increased. In an obstetric test, the cervical dilation reached 3 centimetres. The CTG was abnormal – fluctuations in the baseline foetal heart rate were absent (52.5%) and minimal (32.8%), the baseline foetal heart rate variability was 2.7 msec., 2 accelerations. After 2 hours, a monitoring CTG was performed – fluctuations in the baseline foetal heart rate were absent (30%) and minimal (40%), the baseline foetal heart rate variability was 4.1 msec., 3 accelerations. A monitoring ultrasound examination indicated the

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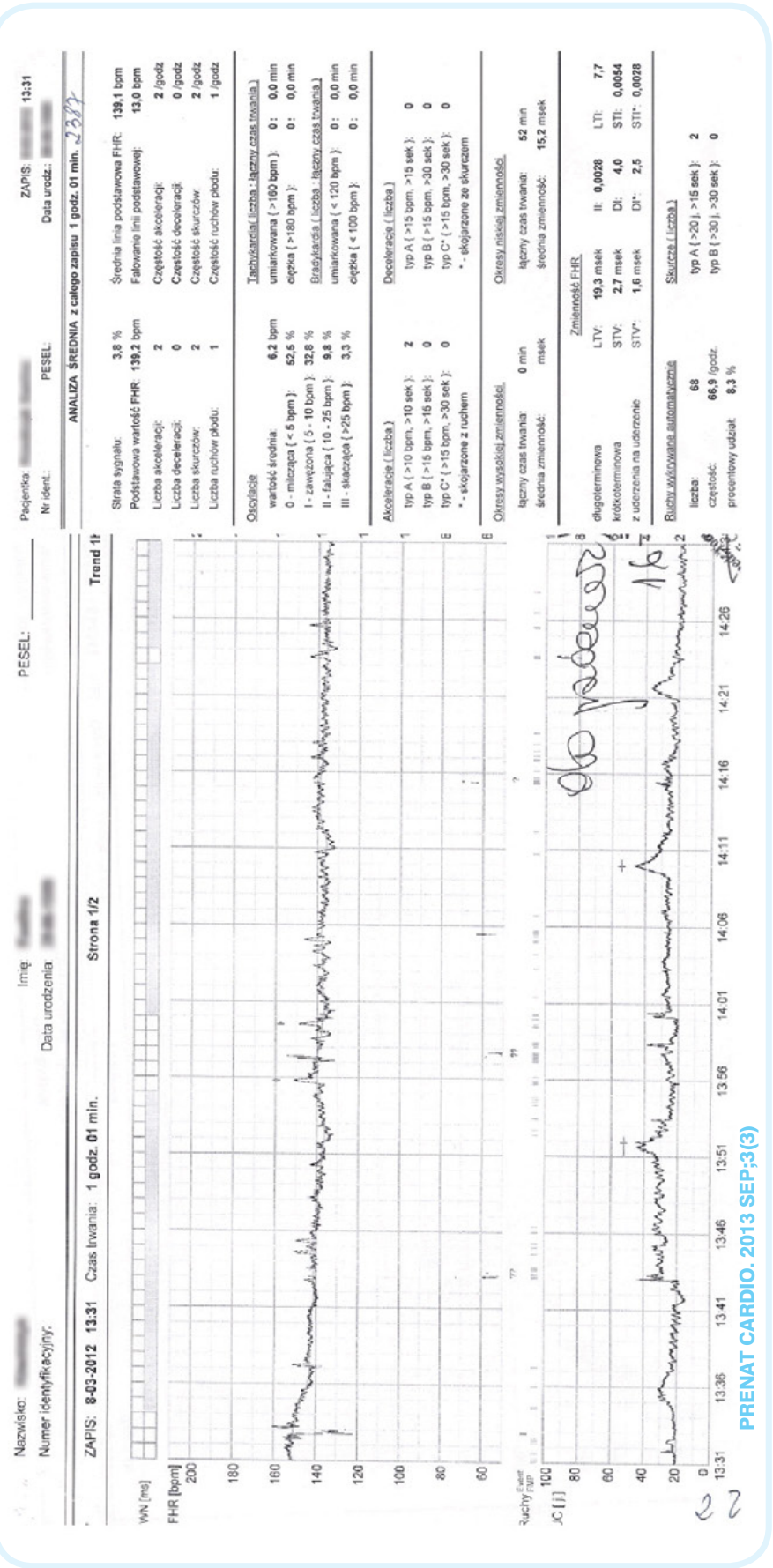
abnormal image of the four heart cavities. An echocardiogram examination revealed cardiomegaly, right ventricular systolic function failure, holosystolic tricuspid insufficiency, increased blood flow through the aortic valve (at the maximum speed of 180 centimetres per second), and wide pulmonary trunk. No detectable flow through the ductus arteriosus was shown. Because of the suspected premature ductus arteriosus closure and a risk of intrauterine foetal asphyxia, the pregnant woman was scheduled for an urgent Caesarean section.

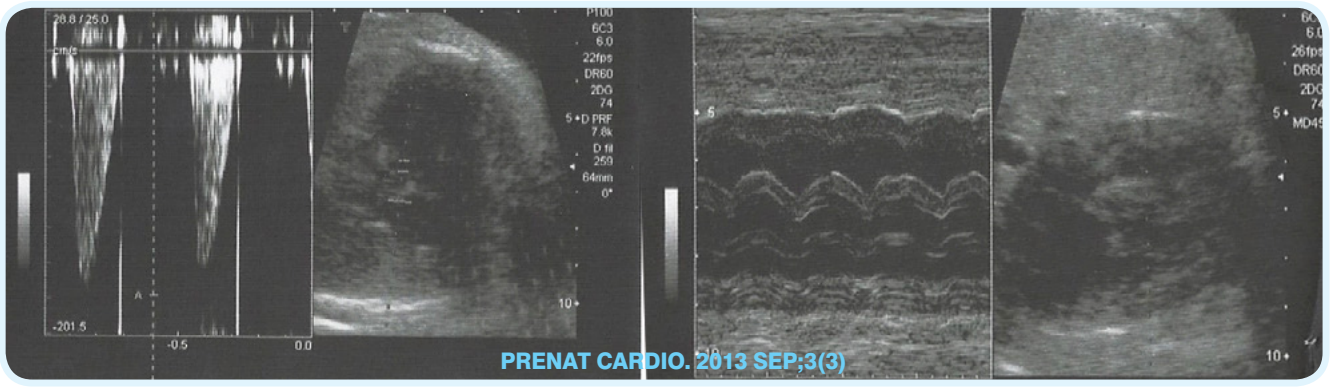
The female infant was 49 centimetres long and weighed 2640 grams. Immediately after the birth, her Apgar score was 0; she was blue and frail, with no respiration or cardiac output. In the subsequent minutes of her life, her Apgar score was 2, 4 and 6 respectively.

The infant was stimulated and her nose and mouth were cleaned. She was also provided with AMBU ventilation, indirect cardiac massage and oxygenation. The infant was orally intubated and mechanically ventilated. Adrenaline was injected into the umbilical vein and the infant's heart started beating; the initial heart rate was 100 beats per minute and later it was > 120-140 beats per minute. With assisted ventilation, the infant turned pinkish and started responding to stimuli. Her stomach was probed in and her life parameters were assessed – the oxygen saturation was 70%->86%->93-95%, AS 140-129', RR 76/55 and the temperature in the anus 37.4°C. The markers of inflammation were normal (CRP – 0.01mg/l). As the baby's condition was serious, she was transported to the Children's Health Institute in Warsaw.

In the beginning, the infant was hospitalised in the Intensive Care Unit, where the mechanical ventilation was continued; its intensity was gradually being decreased. The baby suffered from peripheral oedema. While listening to the lungs, the doctors identified such breath sounds as wheezes and crackles. The heart rate was 100-130 beats per minute, while the respiratory rate was 70 breaths per 45 seconds (the values were comparable on all four limbs). The saturation was between 92% and 95%. An

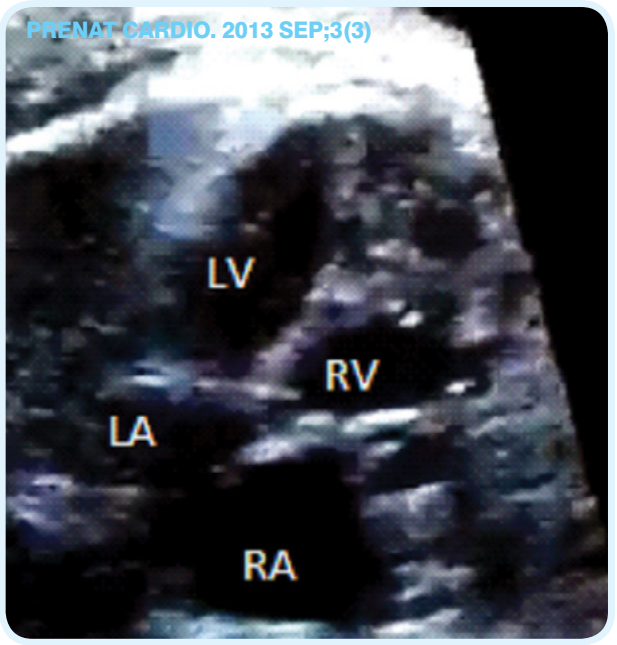


Fot.1 Fetal cardiotocogram with spontaneous closure of the ductus arteriosus.



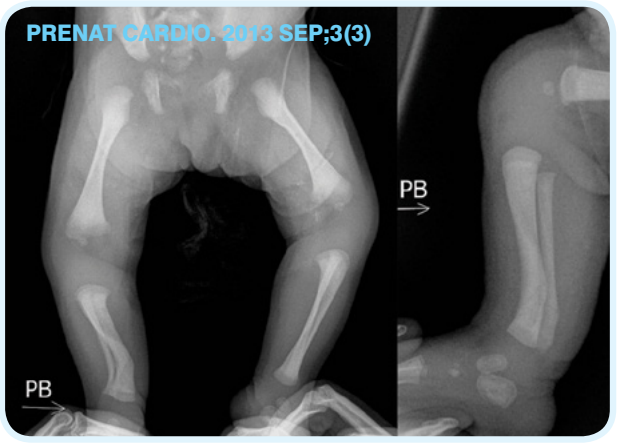
Fot. 2 Doppler tracing of left ventricular outflow. Impaired right ventricular systolic function.

echocardiogram test performed on short notice showed



Fot. 3 Foetal four-chamber view with prenatal ductus arteriosus closure. Cardiomegaly. Right ventricular hypertrophy.
LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle

patent foramen ovale with ballotable valvula foraminis



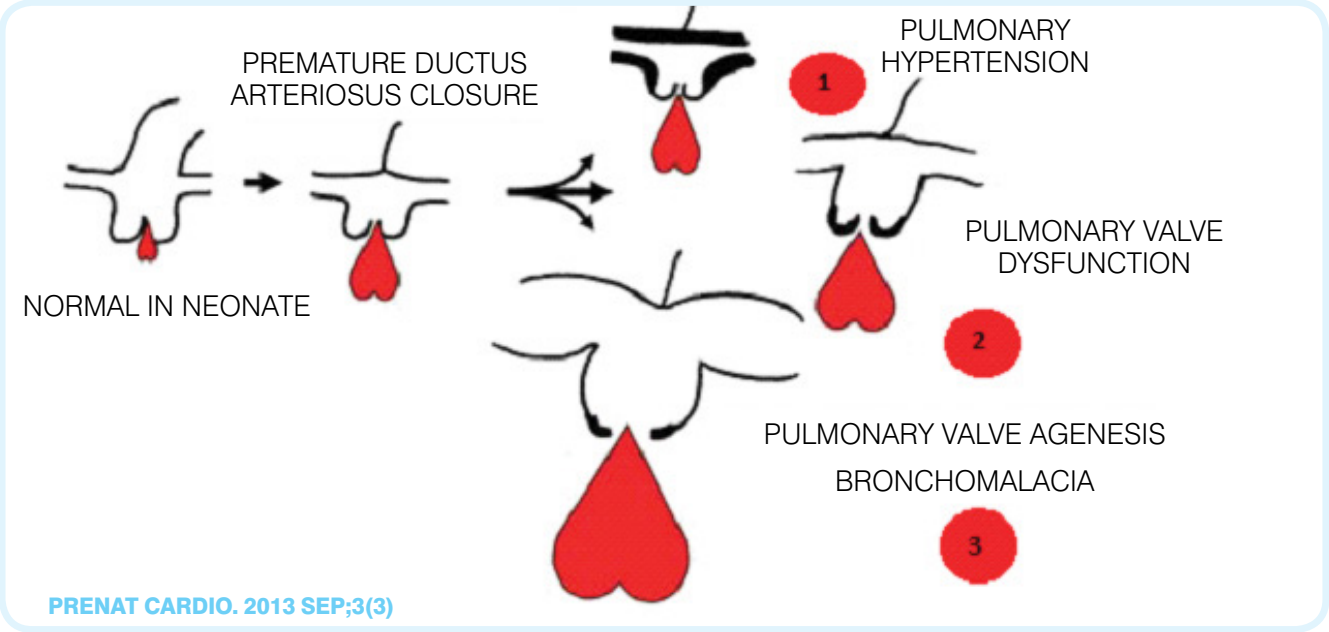
Fot. 4 Congenital tibial bending

ovalis and two-way blood flow, the right ventricle with abnormal, hypertrophic muscularis without acceleration of blood flow. No detectable flow was shown at the ductus arteriosus. Her chest X-ray showed no densities in the lung parenchyma (index 0.61), and some fluid in the right pleural cavity. The baby needed no catecholamines and was treated with Furosemide. On the second day of her life, the baby went into clonic convulsions once, which was counteracted with Rivotril; later on, she was treated with Luminal.

When her general condition improved and the intubation was stopped on the third day of her life, she was taken to the Neonatal and Infant Intensive Care Clinic. The moment she was admitted to the clinic, her general condition was fairly good, her respiratory effort being slightly increased. While listening to the lungs, the doctors identified some crackles in both of them and a prolonged expiratory phase. A quite murmur was heard in the systole; it was best auscultated in the apex of the heart. The first and second heart tones were quiet. What drew the doctors' attention were the infant's minor dysmorphic features: her nose was quite big, the creases were transverse and the lower jaw was receiding. Also, the right lower limb was found to be c. 1,5 cm shorter than the left one. Indolent on palpitation, right tibial retroversion – with no loosening within the tibial and fibular bones – was identified, too. A radiological test confirmed tibia retrocurvata cong.

In the beginning, the baby needed little passive oxygenation. Her respiratory effort was gradually abating. An ultrasound examination did not show the abovementioned fluid in the pleura. A postnatal echocardiogram test indicated a considerable improvement in comparison to the test performed on the second day of the infant's life. ASD/PFO with left-to-right shunt had no features of pulmonary hypertension. Persistent right ventricular hypertrophy was identified – the right ventricle wall was 4,5mm (n=1,4-3,6mm). Dyskinetic movements of the Interventricular septum were also identified. An ECG test revealed regular sinus rhythm, right axis deviation and some features of right ventricular hypertrophy. The concentration of the cardiac enzymes was normal throughout the hospitalisation.

Since the doctors suspected cardiomyopathy, they



Fot.5 Schematic diagram of possibilities after prenatal ductal closure.

performed a number of metabolic test. The results of Gas Chromatography Mass Spectrometry and Tandem Mass Spectrometry were normal, carnitine level was also normal, and glycosylation disorders were ruled out. Initially, the result of a chromatographic assessment of oligosaccharide excretion in the urine was abnormal; later on, the result of a postnatal test was normal.

Because of the identified dysmorphic features, a karyotype test was done; the result was normal (46XX). Her general condition being good, the baby was discharged and taken home; she weighed 2755 grams. The doctors' instructions were that she should be under observation and looked after by several clinical specialists. The final diagnosis was of cardiovascular disorders begun in the perinatal period – premature ductus arteriosus closure.

It follows from the observations of the outpatient that currently she is developing normally, being active and cheerful. No features of cardiac insufficiency are being observed; the results of a postnatal ECG test are: regular sinus rhythm, normogram, right ventricular enlargement within normal range. A postnatal echocardiogram has shown persistent foramen ovale, dyskinetic movements of the interventricular septum and right ventricular hypertrophy. A chest X-ray has shown 0.6 cardiac index. The baby is being treated with Verospiron and is eligible for an isotope heart scan.

DISCUSSION

Intrauterine ductus arteriosus closure is a rare occurrence which has not been fully explored. It is usually hard to diagnose[1] and both its incidence and prognosis are unknown[2].

The ductus arteriosus is normally found only in the foetal circulation; it connects the pulmonary trunk to the aorta at the place where the aortic isthmus turns into the descending aorta. The function of the ductus arteriosus is to incorporate the output of the right ventricle into the systemic circulation instead of the lungs, which are inactive in this period of life. In the foetal period, the patency of the ductus arteriosus is maintained mainly due to the high concentration of PGE2 prostaglandin and less oxygenated (60%-65%) blood. As a pregnancy progresses, the ductus arteriosus is becoming less and less sensitive to the expanding effect which prostaglandins have, and more and more sensitive to the effect which is produced by cyclooxygenase inhibitors. Constriction should normally take place within 24 hours after delivery, while permanent closure within the first weeks of an infant's life[2,3,4].

Ductus arteriosus closure may be idiopathic[2,5] or caused by drugs administered to a pregnant woman. It has been proved that oxygenase inhibitors – non-steroidal anti-inflammatory drugs and some herbal medications – may cause ductus arteriosus closure[6]. Some food products with a high polyphenolic compound content may change the metabolism of foetal prostaglandins, resulting in ductus arteriosus closure. The role performed by corticosteroids is open to question. The authors of some publications direct their readers' attention to the commonly used corticosteroids as factors causing ductus arteriosus closure[5,9], while in other publications this is ruled out[10,11]. In the presented case, the pregnant woman was given Dexamethasone in order to prevent breathing disorders connected with the threatening premature delivery. Conducted several days after corticosteroids were administered, a postnatal ultrasound examination indicated no abnormalities in the image of the four heart cavities. Cardiomegaly was first observed five weeks later. The pregnant woman was given no anti-inflammatory drugs.

Before the age of ultrasonography, intrauterine ductus arteriosus closure was diagnosed after the infant's death only [12]. It is very difficult for doctors to suspect premature ductus arteriosus closure; it is even impossible to detect it by means of routine ultrasound examinations. This is why it seems to be essential to perform echocardiogram tests during the third trimester (if the results of the earlier ultrasound heart imaging were normal) in the case of abnormal images of the infant's four heart cavities, which Prof. Maria Respondek-Liberska emphasises in her numerous publications[13]. Ultrasound-echocardiogram imaging is dominated by cardiomegaly, dilated pulmonary artery[14], tricuspid regurgitation and pulmonary valve regurgitation, lack of detectable flow through the ductus arteriosus and sometimes hydrops fetalis[11,12]. The analysis of the publications shows that right ventricular hypertrophy is the commonest symptom detected in echocardiogram tests[5]. Oligohydramniosis may be – more often than anhydramniosis[2] – another symptom of premature ductus arteriosus closure (a few publications also mention polihydramniosis)[5,6]. In the presented case, no abnormalities connected with the amount of amniotic fluid were detected. What dominated here was cardiomegaly accompanied by right ventricular hypertrophy with defective systolic function, tricuspid regurgitation and lack of detectable flow through the ductus arteriosus.

While diagnosing premature ductus arteriosus closure, it is worth paying attention to CTG records, which often indicate abnormalities[5]. In the presented case, our attention was drawn by the abnormal baseline foetal heart rate variability and the high percentage of fluctuations in the baseline foetal heart rate. Hofstadler describes cases of pregnant women with suspected ductus arteriosus closure whose CTG was abnormal (right chamber cardiectasia, tricuspid regurgitation, no hydrops fetalis). On account of the established diagnosis, all the labours were induced. However, one of the pregnant women had to have a Caesarean section after 18 hours of fruitless attempts to give birth; another pregnant woman gave spontaneous birth. Postnatal echocardiogram tests confirmed ductus arteriosus closure.

None of the authors of the publications on prenatal ductus arteriosus closure determined the moment of occlusion or its duration before establishing the diagnosis[5]. This is why we cannot precisely determine the time when the cardiac muscle is seriously damaged after the ductus arteriosus is closed. A diagnosis of premature ductus arteriosus closure is usually established in the 32nd-34th weeks of pregnancy[15].

Foetal premature ductus arteriosus closure may cause symptoms of circulatory failure and result in intrauterine death. In the case of infants, premature ductus arteriosus closure may cause right ventricular failure and their death[11,16]. Intrauterine ductus arteriosus closure leads to an increase in the afterload of the right ventricle, which results in right ventricular systolic dysfunction, right ventricular hypertrophy or cardiectasia, tricuspid regurgitation, papillary muscles ischemia[5,17] and some fluid being present in the pericardial sac[11]. At an advanced stage, this leads to hydrops fetalis[5]and umbilical venous pulsations[5].

Three out of eight hundred still-born infants who underwent post-mortem examinations died of complete ductus arteriosus closure. The post-mortem examinations revealed cardiomegaly, right ventricular cardiectasia and pulmonary congestion[16,18].

Ductus arteriosus closure births may be spontaneous or Caesarean. Taking into account progression of the lesion in the right ventricle and tricuspid regurgitation, one should make a decision about when to complete the pregnancy[11]. If there is hydrops fetalis and the right ventricle is seriously damaged, pregnancies should usually be completed through a surgery[5]. In the case of five out of the eight foetuses described by Gewillig, the pregnancies had to be completed urgently in order to avoid cardiac insufficiency, pulmonary hypertension and cardiac arrhythmia[2,5]. Delayed labour considerably increases the risk of intrauterine death. The majority of pregnancies with suspected ductus arteriosus closure are completed through Caesarean sections. The cases in which pregnancies are not urgently completed despite changes in the heart suggesting ductus arteriosus closure are rare[1,5,15]. Gewillig describes the case of a foetus in the 20th week of pregnancy with right ventricular hypertrophy, slightly narrowed pulmonary artery, severe pulmonary valve regurgitation and lack of the ductus arteriosus; the pregnancy was completed as late as the 37th week.

In the presented case, the newborn infant was asphyxiated although the pregnancy was completed within the subsequent hour; the Apgar score was 0, 2, 4 and 6 respectively.

The life parameters of the majority of newborn infants who suffered from perinatal asphyxia normalise within the several subsequent days, or even hours. Dr Janiak observed right ventricular dysfunctions on the very first day of life of 27% of foetuses with closed ductus arteriosus; the dysfunctions cleared up within 6 months after delivery[15]. However, right ventricular dysfunctions are sometimes permanent[5].

SUMMARY

The article presents the case of a foetal ductus arteriosus closure detected prenatally in the perinatal period. The pregnancy was burdened with threatening premature delivery, urinary tract infection (which the woman suffered from during the pregnancy; it was treated pharmacologically) and positive family history (epilepsy and deafness). Apart from the single-course corticosteroid therapy, no premature ductus arteriosus closure risk factors were identified. The disorders were diagnosed by means of an echocardiogram test performed on short

notice after cardiomegaly had been shown by a monitoring ultrasound test. On account of the unknown incidence of this disease, hardly recognised risk factors and tragic consequences, the importance of the performance of foetal echocardiogram tests in the case of any abnormal ultrasound imaging of the four heart cavities must be emphasised. In the presented case, our attention was also drawn by some CTG abnormalities, which are often described while discussing prenatal ductus arteriosus closure. The presented pregnancy was urgently completed through a Caesarean section. Decisions on when and how to complete pregnancies need to be made on the basis of the assessment of foetal maturity and pathologic changes in the heart. Urgent pregnancy completion may prevent the progression of cardiac muscle damage and improve the prognosis.

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