Problems of early diagnosis and perinatology care in osteogenesis imperfecta – experience of clinic team

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Abstract
We present difficulties in prenatal diagnosis and treatment in newborns with brittle bone diseases type II and III. It has been noted that skeletal dysplasia can be recognised with fetal ultrasound examination. The methods of osteogenesis imperfecta infant care in the first day of life have been proposed.

Key words: brittle bone disease, neonate, fetal ultrasound diagnosis

Introduction
A multidirectional development in the care of mother and her child is a measure of medical advancement, both in obstetrics and neonatology. Fetal ultrasound examination allows e.g. for an early detection of bone dysplasia, which includes brittle bone disease [1]. Osteogenesis imperfecta (OI) – a genetic disorder, mainly connected with Type 1 collagen synthesis (COL1A1, COL1A2), in the neonatal stage it can be classified as Types II or III according to Sillence [2, 3]. Both these types are characterized with skeletal calcification abnormalities and frequent, in most cases, spontaneous bone fractures which lead to deformities and unproportional body. They can appear in intrauterine life or just after birth. They might result in the deterioration of the general state of the neonate, strong pain as well as circulatory and respiratory disorders [4].

The aim of the study is to present difficulties in early diagnosis of bone dysplasia in a fetus and then in the medical treatment in the perinatal period. The parents of presented neonates orally expressed their consent for publication of this clinical data.

Case report
A male neonate born at 40 hbd by caesarean section (breech presentation), with birth weight of 2900 g and with Apgar score of 8/9. The obstetric physical examination confirmed a regular course of pregnancy but at 23 hbd after performing an ultrasound examination the doctor diagnosed osteogenesis imperfecta and agenesis of the venous duct. A physical examination after birth allowed to diagnose soft, parchment-like cranial bones, wide cranial sutures, blue sclera, narrow thorax, short arch-shaped lower and upper limbs. Spontaneous locomotor activity was considerably limited. A baby-gram examination (Fig. 1) confirmed numerous fractures of long bones, both scapulas, clavicles, ribs 3-10 on the right side and 2-10 on the left side as well as cranial bones. Paresis of the radial and fibular nerves.

A male neonate born at 39 hbd by caesarean section (breech presentation), with birth weight of 2780 g and with Apgar score of 10. On the basis of an ultrasound examination performed in the prenatal stage the doctor diagnosed bone dysplasia with short limbs. After the baby was born he was diagnosed with soft cranial bones, the anterior fontanel 5 × 7 cm with bone lamellae, poste-

Fig. 1. The baby-gram of newborn with osteogenesis imperfecta

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rior fontanel 3 × 3 cm, flattened occiput, blue sclerae and short upper and lower limbs. A baby-gram examination confirmed widened metaphyses of femoral and tibial bones, anteflexion of the tibia. On the third day of life there was a fracture of the left femoral bone and on the tenth day the neonate suffered from a fracture of the right femoral bone.

A female neonate born at 38 hbd, by caesarean section, (due to potential chondrodysplasia and a fracture of the femoral bone), with birth weight of 4270 g and with Apgar score of 5/8/8. After the birth the baby girl required a respiratory resuscitation and the NCPAP respiratory support method. In the physical examination the doctor observed thin cranial integument, deformities of lower limbs. A radiological examination (baby-gram examination) confirmed past intrauterine fractures of femoral bones and metaphyses of left forearm distal bones. The doctor suspected osteogenesis imperfecta.

An X-ray photograph allowed to observe recent fractures of both humeral bones and forearm bones, which was probably connected with transport. A female neonate born at 38 hbd, by caesarean section, with birth weight of 2560 g, with Apgar score of 9/9. A prenatal ultrasound examination allowed to suspect Type I tana-tophoric dysplasia. After birth the baby demonstrated short long bones of the limbs, the left foot in the equinovarus position, the right foot in the valgus position, a contracture in the left wrist, bending cranial bones, gothic palate and micrognathia. A radiological examination confirmed past intrauterine fractures of femoral bones and curved crural bones; long bones of the upper limbs had widened metaphyses and they were distorted and arch-shaped. After birth the baby got her right humeral bone fractured. On the basis of clinical symptoms and an ultrasound examination the doctor diagnosed osteogenesis imperfecta. The baby girl was discharged from the Neonatology Ward and became a patient of a home hospice.

Discussion

The most common classification of osteogenesis imperfecta gives four clinical types of this disease. It was introduced in 1979 by Sillence [2] and is still in use despite many modifications connected with the development of genetic diagnostics [5]. Type I is the mildest, Type II is called a lethal type due to frequent fractures observed as early as in the fetal life. In Type III bone fractures can occur in the prenatal stage and lead to many skeletal deformations; in Type IV fractures can occur more or less frequently [3, 6]. The incidence of OI is 6-7 per 100 000 neonates, in 90% of cases the disease results from mutations in the gene for type I collagen, the remaining cases of OI might be a consequence of abnormalities of other genes involved in bone metabolism [5, 7]. The diagnosis of brittle bone disease in the neonatal period is based on the medical history, physical examination and an X-ray of the whole body [2, 7, 8]. The presented children met these requirements; moreover, their mothers underwent an ultrasound examination in pregnancy. The examination showed fetal abnormalities which confirmed bone dysplasia. Despite the disease all the babies were born at term (all by caesarean section), with birth weight above 2500 g. Their general condition was good (the Apgar score was 8/9, 10 and 9/9). Only one baby received 5/8 Apgar score in the first minutes of life. Diagnosing bone dysplasia in the fetal stage is difficult but possible as early as in the second trimester of pregnancy [1, 7, 8]. The suspicion of Type II OI on the basis of an ultrasound examination in the early period of fetal life should be confirmed with a genetic and/or biochemical examination because the disease, potentially lethal, might lead to serious implications, including abortion [9-12]. Type II OI can be detected between 14 and 16 pregnancy weeks due to the following ultrasound observations: fetal hypotrophia with a short stature and much reduced bone mineralization, bone fractures, long bones curved or bent at an angle, wide, short “crushed” limbs, thin beaded ribs with numerous fractures, narrow thorax, flattened vertebrae, distorted skull [8, 11]. Type III, slightly milder than Type II, is observed later, between 18 and 20 weeks of fetal life. An ultrasonographer confirms bone fractures, reduced mineralization of the skeleton, including cranial bones, short long bones, short limbs and thin ribs [8, 11]. Telling the difference between Type II and Type III, both in an examination conducted in the prenatal and postnatal stage, is highly difficult because Type II-B, which can survive longer and Type III which is characterized with early death, have similar clinical and radiological symptoms [13, 14]. Moreover, thanks to the development of medicine, that is an improved neonatal care and new therapeutic possibilities, the prognosis in these two types of the disease is much better than before. It is thus difficult to prognosticate a further progression in every individual patient. A prenatal ultrasound examination conducted in L of the patients made the doctors suspect OI of Type II and in the remaining three babies – other bone dysplasia. All the tree pregnancies finished with cesarean sections, which was a positive solution. However, for many years we have been observing that such methods are not
always used although it is known that a physiological labour might worsen the condition of the newborn. Due to suspicion of brittle bone disease three newborns were directly admitted to the Neonate Pathology of the Department of Paediatric Propedeutics and Metabolic Bone Diseases so as to be properly diagnosed and then treated. One baby girl was discharged home and referred to the department in the sixth week of life. In the first days following the delivery two neonate were diagnosed with recent low-energy fractures of long bones. They were a result of care and transport. In utero transport might prevent further fractures, which would improve prognoses. Further fractures worsen the health of the neonate, are painful, cause deformities and require further medical procedures, including immobilization [4].

It should be pointed out that all the babies during their stay in the clinic, after their parents had given consent for the treatment, were administered bisphosphonates [15, 16]. However, the neonates were at different age while being admitted to the clinic. They were between three days and six weeks old so only half of the children could start a therapy in the neonatal period. It should be mentioned that initiating a therapy in a later period of life might reduce chances for a successful prognosis, especially with regards to a further development of locomotor abilities of the patient. Making a diagnosis and then initiating a treatment of brittle bone disease is a complex process and requires a cooperation of many specialist centres, already in the perinatal period. A chronic and long-term therapy, which should be planned in the neonatal stage, currently involves pharmacotherapy, orthopaedic procedures and physiotherapy [15-17].

Conclusion

A detection of bone dysplasia in the fetal stage, including a serious type of brittle bone disease, should allow for selecting the best possible kind of labour and place for delivery of the baby (providing high-reference neonatal care) and initiating a medical treatment as early as in the neonatal period.

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References


