

# Smith-Lemli-Opitz Syndrome – a challenging prenatal diagnosis

## Zespół Smitha-Lemliego-Opitza – trudności w diagnostyce prenatalnej

Agata Szpera-Goździewicz, Ropacka-Lesiak Mariola, Paweł Rzymiski, Grzegorz H. Bręborowicz

Department of Perinatology and Gynecology; Poznan University of Medical Sciences, Poland

### Abstract

*The aim of the study was to present a case of Smith-Lemli-Opitz syndrome (SLOS) in a fetus of a 33-year-old patient. At 31 weeks of gestation, the following fetal malformations were detected on an ultrasound: atrioventricular septal defect (AVSD), aortic coarctation, shortening of the lower limbs, narrow forehead, hyperthelorum, micrognathia, anteverted nares, ambiguous genitalia, and signs of intrauterine growth restriction. The baby died 11 days after birth. Further genetic screening of the parents revealed the 7-DHCR enzyme mutation in both of them. Although the prenatal diagnosis of SLOS presents a challenge due to the fact that little is known about its prenatal phenotype but it may be vital while attempting to treat the fetus in utero.*

Key words: **Smith-Lemli-Opitz Syndrome / ultrasound / prenatal diagnosis /**

### Streszczenie

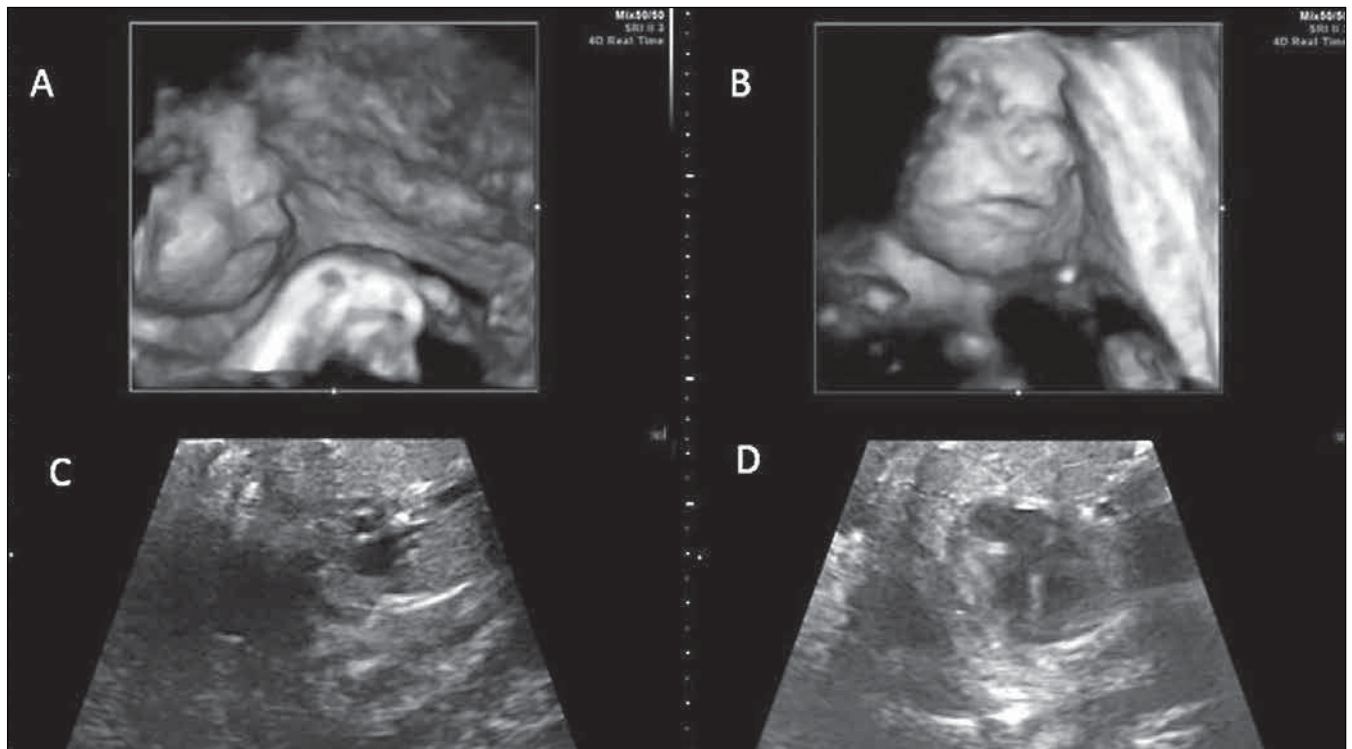
*Praca przedstawia przypadek zespołu Smitha-Lemliego-Opitza u płodu 33-letniej ciężarnej. W badaniu ultrasonograficznym przeprowadzonym w 31 tygodniu ciąży zdiagnozowano: wspólny kanał przedsionkowo-komorowy (AVSD), koarktację aorty, skrócenie kończyn dolnych, wąskie czoło, hyperteloryzm, mikrognatię, wysunięte do przodu nozdrza, obojnacze narządy płciowe oraz wewnątrzmaciczne ograniczenie wzrastania płodu. Noworodek zmarł w 11. dobie życia. Wykonane u rodziców badania genetyczne ujawniły mutację w genie DHCR7 u obojga z nich. Diagnostyka prenatalna SLOS jest trudna z uwagi na jego niezdefiniowany fenotyp u płodu, jednak może ona mieć kluczowe znaczenie w świetle skutecznych prób prowadzenia terapii wewnątrzmacicznej.*

Słowa kluczowe: **Zespół Smitha-Lemliego-Opitza / ultrasonografia /  
/ diagnostyka prenatalna /**

### Adres do korespondencji:

Mariola Ropacka-Lesiak  
Department of Perinatology and Gynecology  
Poland, 60-535 Poznań, Polna 33  
tel.: +48 61 841 92 83; fax: +48 61 841 92 04  
e-mail: mariolaropacka@poczta.onet.pl

Otrzymano: 20.02.2015  
Zaakceptowano do druku: 15.03.2015

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**Figure 1.** Ultrasonud images obtained at 31 week's gestation.

- A – fetal profile – notice a dysmorphic profile with micrognathia and anteverted nares;  
 B – frontal imaging shows a narrow forehead, micrognathia and anteverted nares;  
 C – three vessels view in the mediastinum – from the top – superior vena cava, aorta, pulmonary artery – the diameter of aorta is almost half of the diameter of pulmonary artery – aorta is narrow, hypoplastic what may suggest the coarctation of aorta;  
 D – the transverse view of the fetal chest on the level of 4 chamber view – notice an abnormal cardiac crux – the is an interatrial and interventricular defect, the atrioventricular valves are located on the same level what helps us to diagnose the atrioventricular septal defect.

Smith-Lemli-Opitz Syndrome (SLOS) is an autosomal recessive metabolic disorder expressed as distinctive facial, limb and genital anomalies, and mental retardation. It is caused by the mutation of the gene encoding 7-dehydrocholesterol reductase (7-DHCR) followed by a decreased level of cholesterol and an increased level of 7-dehydrocholesterol in body fluids and tissues [1]. The paper presents a case of Smith-Lemli-Opitz syndrome in a fetus of a 33-year-old patient. The woman (gravida III, para 1) was admitted to the hospital for suspected fetal malformations at 31 weeks of gestation. Her obstetric history revealed shortened fetal femur length (FL) in her first pregnancy, while the second pregnancy was terminated at 11 weeks of gestation because of acranial fetus. In the current pregnancy the several fetal malformations were detected: atrioventricular septal defect (AVSD), aortic coarctation and shortening of the lower limbs. The facial phenotype included a narrow forehead, hyperthelorism, micrognathia and anteverted nares. The fetus presented ambiguous genitalia. The phallus was small and bent ventrally, and the labioscrotal folds had an indentation in the midline. There were evident signs of intrauterine growth restriction. Fetal biometry was consistent with 25 weeks plus 5 days. The patient refused invasive prenatal diagnostic tests. At 38 weeks of gestation, cesarean section was performed due to an arrest of labor and signs of fetal distress. A newborn weighing 2240g was born. The baby was admitted into the NICU. Genetic consultation revealed flat facial profile, polydactyly of the

hands and feet and hyperthelorism. Necrotizing enterocolitis was diagnosed. Moreover, enlarged adrenal glands, lack of the uterus and ovaries, as well as the presence of a solid structure (most likely testicle) inside the pelvis were shown on ultrasound imaging. Transthoracic echocardiography revealed aortic coarctation, hypoplastic aortic arch, patent ductus arteriosus, AVSD and patent foramen ovale. An endocrinologist described adrenal hyperplasia, abnormal female genital organs structure without features of virilization, pale pink and swollen skin without features of dehydration and normal glycemia. Three days after the delivery increasing respiratory failure and infection exponents appeared. From day 8 of life, mechanical ventilation was used and chest radiograph showed fields of pulmonary atelectasis and attributes of pneumonia. Moreover, 3 units of platelet concentrate and 2 units of red blood cell concentrate were transfused due to thrombocytopenia and symptoms of bleeding diathesis. Despite antibiotic and prostaglandin E2 therapy the baby died on day 11 of life.

Karyotyping of a newborn revealed normal, male karyotype 46 XY. The suspicion of SLOS appeared after karyotyping and further genetic counseling was carried out. Both parents presented no significant signs of diseases but phenotypically they showed slightly shortened lower limbs. Further genetic screening revealed the 7-DHCR enzyme mutation in 11q12- q13 locus in both parents and SLOS was confirmed.

## Discussion

Prenatal diagnosis of SLOS may be crucial because some attempts to treat the fetus with fresh frozen plasma transfusion in utero are now available. Moreover, it allows to provide genetic counseling to the parents and enables early postnatal dietary management with the use of high cholesterol intake. It is also important with regard to subsequent pregnancy, because every child of such a parent is burdened with a 25% of the risk of disease recurrence. Postnatal symptoms of SLOS have been well-described, but little is known about prenatal phenotype. The presence of major structural anomalies, pseudo-hermaphroditism, and a high incidence of neonatal death usually referred to SLOS Type II, as presented in our case. Nowadays, prenatal testing can be performed to rule out SLOS in the fetus [2, 3]. Also, the literature offers reports about intrauterine therapy of SLOS, as mentioned above, and the possibility of pre-implantational diagnosis [4, 5]. In the case of our patient, even the refusal of prenatal karyotyping would not have changed the pregnancy course because the suspicion of SLOS was postnatal, in the third pregnancy.

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2. Mariola Ropacka-Lesiak – autor koncepcji i założeń pracy, współautor tekstu pracy, współautor protokołu, korekta i aktualizacja literatury, przygotowanie manuskryptu.
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### Źródło finansowania:

Praca nie była finansowana przez żadną instytucję naukowo-badawczą, stowarzyszenie ani inny podmiot, autorzy nie otrzymali żadnego grantu.

### Konflikt interesów:

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